advancing the art & science of medicine in the midwest

WMJ

2024 • volume 123 • issue 6

Maternal & Child Health

Special thanks to the Maternal & Child Health Issue Advisory Board

Fahad Aziz, MD
WMJ Editor-in-Chief
Associate Professor of Medicine (CHS)
Director – Nephrology Fellowship Program
Division of Nephrology – Section of Transplant Medicine
Department of Medicine
University of Wisconsin School of Medicine and Public Health

Jessica Dalby, MD
Associate Professor
Department of Family Medicine and Community Health
University of Wisconsin School of Medicine and Public Health

Emily R.W. Davidson, MD, FACOG
Assistant Professor
Department of Obstetrics and Gynecology, Urogynecology (Division Chief)
WISH (Women's Incontinence and Sexual Health) Clinic
Medical College of Wisconsin

Jill Denson, PhD, MSW, APSW
Assistant Professor
Director/Principal Investigator
UW–Madison Prevention Research Center

Lee T. Dresang, MD, Professor
UW Department of Family Medicine and Community Health Rural FMOB Fellowship Co-Director
Medical Advisor and Advisory Group Chair
Associate Editor
FCPC Chair
Department of Family Medicine and Community Health
University of Wisconsin School of Medicine and Public Health

Veronica Fitzpatrick, DrPH, MPH
Research Scientist
Advocate Aurora Research Institute

Mary Ingle, PhD, MPH
Research Scientist Associate
Advocate Aurora Research Institute

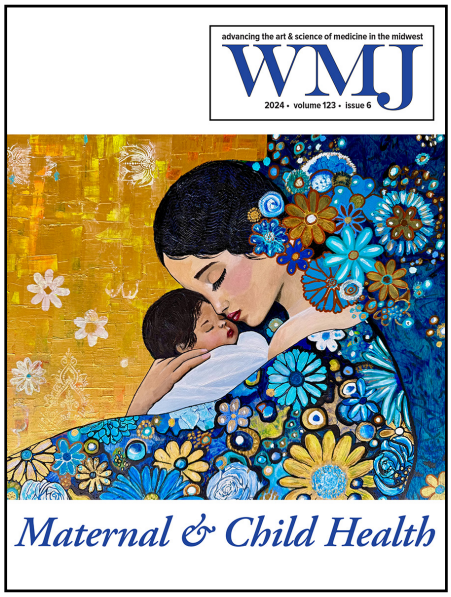
Timothy E. Klatt, MD
Associate Chief Medical Officer, Patient Safety
Froedtert Hospital
Co-Founder and Co-Director, Supporting our Staff
Co-Founder and Director, Radiology Safety Net
South Region, Froedtert ThedaCare Health, Inc.
Professor, Obstetrics and Gynecology
Medical College of Wisconsin

David Mallinson, PhD
Assistant Professor
Department of Family and Preventive Medicine
Rush Medical College
Rush University

Tara L. Petersen, MD, MSEd
Vice Chair for Education, Department of Pediatrics
Medical Director, The Pediatric Simulation Program at Children's Wisconsin 'Dairy Cares' Simulation Lab
Associate Professor of Pediatrics (Critical Care)
Medical College of Wisconsin

Ayanna Vasquez, MD, MS
Chief Resident (PGY-3)
UW Health Preventive Medicine Residency
Honorary Fellow
University of Wisconsin School of Medicine and Public Health

Jeremy Waldhart, DO
Associate Program Director
Froedtert & MCW South Side Family Medicine Residency and Ascension Columbia St. Mary's Family Medicine Residency
Department of Family and Community Medicine
Medical College of Wisconsin



Volume 123 • Issue 6 • 2024

WMJ

advancing the art & science of medicine in the midwest

COVER ART

The One Who Made It

Ryan McAdams, MD

Acrylic on Wood

Artist Statement:

This original 20" x 16" acrylic painting on wood honors the tender bond between mothers and neonates, celebrating their resilience, survival, and the sacred connection forged through adversity. Inspired by the journey of a NICU baby coming home, the piece invites reflection on love, loss, and perseverance.

• • •

The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues. *WMJ* is published through a partnership between the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health.

SOCIAL DETERMINANTS OF HEALTH SURROUNDING PREGNANCY

The *WMJ* (ISSN 1098-1861) is published by the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health and is devoted to the interests of the medical profession and health care in the Midwest. The managing editor is responsible for overseeing the production, business operation and contents of the *WMJ.* The editorial board, chaired by the medical editor, solicits and peer reviews all scientific articles; it does not screen public health, socioeconomic, or organizational articles. All articles and artwork published herein, including commentaries, letters to the editor, and editorials represent the views of the authors, for which neither *WMJ* nor the publisher take responsibility, unless clearly stated. Advertising content is the responsibility of the advertiser and does not imply an endorsement or sponsorship by *WMJ* or the publsiher and its affiliates unless specified. *WMJ* is indexed in Index Medicus, Hospital Literature Index, and Cambridge Scientific Abstracts.

Submit manuscripts at www.wmjonline.org.

Address all correspondence to: University of Wisconsin School of Medicine and Public Health, Attn: *WMJ* Editor, Health Sciences Learning Center, 750 Highland Ave, Madison, WI 537055; e-mail: wmj@med.wisc.edu

ISSN 1098-1861 • Established 1903

Published 4 times a year, beginning in March

OBSTETRIC HEALTH CARE DELIVERY

HEALTH BEHAVIORS, PRACTICES, AND BELIEFS

PEDIATRIC HEALTH

Thank you!

to the following artists who contributed their work to this special issue

Kristen Mahaffey
"Vital Moments"
Page 542

Ryan McAdams, MD
"The One Who Made It"
Acrylic on Wood
Front Cover

Ava Rowe
"Common Ground"
Digital Art
Inside Back Cover

Ronna Trapanese
Night Magic
Acrylic
Page 421

Mubashira Waseem
"Two Sides of the Same Coin: Mental Health"
Acrylic on Watercolor Paper
Page 502

Dian Yao
"The Complementarity of Motherhood"
Digitized Ink Drawing
Page 473

Shaping Tomorrow by Advancing Maternal and Child Health

Fahad Aziz, MD; David Mallinson, PhD; Tara L. Petersen, MD; Jill Denson, PhD; Timothy Klatt, MD

This special edition of the *Wisconsin Medical Journal* highlights the essential field of maternal and child health. The well-being of mothers and children is a critical indicator of societal progress, clearly reflecting the effectiveness of our health care systems. However, despite its importance, maternal and child health continues to face a host of challenges, including disparities in access to care and the growing recognition of the impact of social determinants on health outcomes. This issue strives to shed light on these complex challenges through in-depth studies, expert insights, and case reports that aim to improve care for mothers and children.

The reports in this issue come together to highlight several key themes: social determinants of health, obstetric health care delivery, health behaviors and practices, and pediatric health.

Social Determinants of Health

The issue opens with a focus on the social determinants of health surrounding pregnancy. This section explores topics such as the impact of childhood adversity on perinatal mental health, innovative ways to identify intimate partner violence in obstetric clinics, and the influence of geographic factors on birth weight.[1-3] These studies emphasize the critical role social factors play in shaping pregnancy-related health outcomes. For example, several studies use large-scale population data, including birth records, insurance claims, and social service records to understand how social context influences prenatal, perinatal, and postpartum health. One promising finding is the success of state-funded home visiting programs in reaching marginalized populations and improving health outcomes.[4] However, concerns remain, such as younger Medicaid beneficiaries being more likely to lose postpartum health care coverage, highlighting the need for continuous coverage for mothers after childbirth.[5]

This section also highlights the impact of Wisconsin's post-*Roe v Wade*[6] health care landscape. Following the Supreme Court's 2022 *Dobbs v Jackson Women's Health Organization* decision,[7] a pre-Civil War law in Wisconsin banned abortion for 15 months until overruled in 2023. During this period, legal uncertainty affected care for early pregnancy complications.[8] One study found an increase in sterilization procedures among younger individuals following the decision overturning of *Roe v Wade,* indicating that abortion restrictions influence individuals' reproductive and childbearing preferences.[9] Experts warn that restricting access to abortion harms reproductive autonomy and overall health, underscoring the urgent need to protect reproductive rights in this changing legal environment.[10,11]

> Despite its importance, maternal and child health continues to face a host of challenges, including disparities in access to care and the growing recognition of the impact of social determinants on health outcomes. This issue aims to shed light on these complex challenges.

Obstetric Health Care Delivery

The issue then shifts focus to the delivery of obstetric health care, where advancements in both surgical techniques and pain management are transforming maternal care. A standout innovation in this field is the Enhanced Recovery After Cesarean Surgery (ERAS) protocol, which has led to a remarkable 94% reduction in opioid use following cesarean deliveries. This protocol incorporates intrathe-

• • •

Author Affiliations: Dr Aziz is *WMJ* editor in chief; Drs Mallinson, Petersen, Denson, and Klatt are members of the Advisory Board for this issue.

cal morphine and other best practices, resulting in lower pain scores and a decrease in the number of patients needing opioid medication after surgery.[12]

Despite these advancements, challenges persist in obstetric care, particularly when it comes to accurately measuring blood loss during cesarean births. Research has shown that traditional methods, such as estimated blood loss and quantitative blood loss, lack the sensitivity to accurately assess blood loss. A study by Kram et al highlights the need for improved measurement tools to better guide clinical decisions and improve patient outcomes in obstetrics.[13]

The articles in this section also explore environmental and iatrogenic risks to pregnancy outcomes. One study reports both a concerning lack of follow-up and reassuring results among those who completed testing within a population at high risk for lead exposure from their water lines,[14] and a thoughtful commentary also asks us to reconsider the benefits of folic acid food fortification.[15]

Beyond clinical advancements, this special issue also explores the emotional and ethical complexities of obstetric care and underscores the deep connection between medical practice, ethics, and the often underrecognized frequency and impact of loss. An insightful commentary discusses the mental health challenges that can result from even successful pregnancy outcomes.[16] The challenges clinicians, including trainees, often face are highlighted by a medical's students experience in a fetal anomalies clinic where patients, families, and clinicians deal with life-changing diagnoses, and a resident's thoughtful reflection on struggling to cope with a fetal death.[17,18] This issue also features a case report detailing the challenging decision-making process, including legal aspects, involved in terminating a pregnancy complicated by placenta increta through hysterectomy at the end of the first trimester.[19]

Health Behaviors and Practices

The next section explores the health behaviors and practices that influence maternal and child health. Factors such as access to reliable information, social support, and health crises like COVID-19 shape the choices of pregnant and postpartum individuals. A study in Milwaukee revealed a significant knowledge gap among pregnant women about the risks of tetrahydrocannabinol (THC) and cannabidiol (CBD) use, with over half unaware of the potential harm to fetal development.[20] This highlights the need for clear, evidence-based communication from health care providers. The COVID-19 pandemic further complicated maternal health, particularly breastfeeding, due to challenges like limited lactation support and increased isolation.[21] The pandemic also intensified loneliness among perinatal individuals, leading to higher rates of depression, anxiety, and poorer pregnancy outcomes.[22] Addressing these mental health issues remains crucial for improving maternal and child health.

Concerns about dietary health risks, such as excessive fish consumption beyond safety recommendations, were found among diverse populations including women of Asian descent in Milwaukee.[23,24] This underscores the need for culturally tailored education to reduce health risks from food contaminants. The issue also examines perceptions of patients experiencing infertility toward the COVID-19 vaccine, with a study showing that those with higher education levels and more fertility treatment experience were more likely to get vaccinated.[25] These findings highlight the importance of accessible information and building trust in medical advice, emphasizing the need for interventions that address the unique needs of different populations to improve health outcomes.

Pediatric Health

Finally, the issue transitions to pediatric health, addressing a range of critical topics affecting children's health in Wisconsin and across the country. The section opens with a commentary by Snooks et al that highlights a pressing public health crisis: pediatric gun violence, which has become the leading cause of death among American youth, even surpassing motor vehicle accidents as of 2020.[26] The authors highlight a significant increase in gun-related injuries and deaths at the Children's Wisconsin Pediatric Trauma Center since the pandemic, affecting not just physical health but also mental well-being across communities, and they call for a robust public health approach, including safe gun storage, community and hospital interventions, and legislative measures to shield mothers and children from gun violence.

A link between elevated blood lead levels to poorer academic performance is the focus of a study by Anguzu et al, which highlights the need for stronger prevention.[27] Research on mental health services includes a school-based program that improved both behavioral and academic outcomes, though challenges remain in optimizing outpatient care after ED visits.[28,29] The issue also explores adolescent mental health, particularly the link between social media use and higher rates of depression and anxiety, especially in females.[30] The PATCH program demonstrates the effectiveness of youth-led health initiatives,[31] while additional insights include the benefits of deferring antibiotics for febrile infants to reduce unnecessary interventions and the role of school-based rapid antigen testing in managing infectious disease outbreaks during the COVID-19 pandemic.[32,33]

Case studies on pediatric conditions, such as parechovirus infections and neonatal femur fractures, emphasize the need for early diagnosis and intervention.[34,35] The University of Wisconsin's Undiagnosed Disease Program highlights the potential of whole-genome sequencing in diagnosing rare neurodevelopmental disorders.[36] Family engagement in pediatric research is a key theme, with tools like the "Travel Passport" fostering collaboration between families and researchers.[37]

As you read through this special issue, we encourage you to reflect on the complexity and depth of the topics at hand. The manuscripts – and artwork – featured represent a wide array of perspectives and experiences, highlighting the diverse ways in which health care providers, patients, and communities have navigated the ever-present challenges in the field of maternal and child health. From overcoming access barriers to addressing emerging health crises, each piece contributes to a deeper understanding of the current state of care and the ongoing need for innovation, advocacy, and compassion.

We would like to express our sincere gratitude to the *WMJ* Publishing Board for its unwavering support throughout the editorial process and our esteemed advisory board members for their invaluable guidance and contributions. Their expertise and commitment have been crucial in bringing this issue to fruition. Together, these collective efforts have helped create a special edition that informs and inspires positive change. It is our hope that this work will spark further action, driving innovation and improvements in maternal and child health for years to come.

REFERENCES

1. Hipke KN. Maternal adverse childhood experiences and perinatal mental health: beyond postpartum depression. *WMJ*. 2024;123(6):451-459.

2. Sarawagi A, Vang M, Yan K, Piacentine LB, et al. Intimate partner violence screening in an obstetrics clinic: a retrospective study. *WMJ*. 2024;123(6):441-445.

3. Kamenetsky K, Bailey E, Lowry A, Gangnon R, Stafeil B, Hoppe K. The Role of Neighborhood in Individual and Disparity-Level Factors and Birth Weight in Dane County, Wisconsin. *WMJ*. 2024;123(6):422-426

4. Mersky JP, Janczewski C, Hami D. Addressing maternal and child health disparities through perinatal home visiting. *WMJ*. 2024;123(6):427-433.

5. Jenkins MC, Piette Durrance C, Ehrenthal DB. Medicaid enrollment gaps before, during, and after pregnancy: evidence from administrative data. *WMJ*. 2024;123(6):434-440.

6. *Roe v Wade*, 410 US 113 (1973).

7. *Dobbs v Jackson Women's Health Organization*, 597 US 215 (2022).

8. Mackinnon JC, Lynch W. An internist's action plan to reduce morbidity and mortality under abortion restrictions. *WMJ*. 2024;123(6):471-472.

9. Phillips C, Larson J, Godecker A, Jacques L, Hanks L. Sterilization rates for pregnancy-capable people at a single institution in Wisconsin before and after the Dobbs decision. *WMJ*. 2024;123(6):446-450.

10. Cox Bauer CM, Anschutz P, Safi L, Malloy E. Permanent contraception and the federal consent process: barriers to access. *WMJ*. 2024;123(6):464-465,470.

11. Higgins J, Seymour SW, Green T. Abortion access and birth-related outcomes and inequities: A call to dismantle abortion restrictions in Wisconsin to improve health and wellbeing). *WMJ*. 2024;123(6):466-467.

12. Antony KM, Anderson-Carter I, Broman AT, et al. Association of an enhanced recovery after cesarean surgery protocol with postpartum opioid utilization: a pre-post analysis of a quality improvement project. *WMJ*. 2024;123(6):474-481.

13. Kram JJF, Zermeno Y, Adefisoye JO, Dickson Michelson E, Malloy E, Salvo N. Assessing accuracy of blood loss measurements during cesarean birth in a diverse patient population: A quality improvement study. *WMJ*. 2024;123(6):483-486.

14. Getzin A, Kram JJF, Adefisoye JO, Kleber D, Oberbroeckling L. Lead exposure risk and testing for pregnant people in Milwaukee. *WMJ*. 2024;123(6):487-492.

15. Westmark C. Prophylactic or poison: the folic acid debate. *WMJ*. 2024;123(6):495-496,501.

16. Sangtiani AK, Mubeen M, Irfan A. Insights into perinatal mood and anxiety disorders: addressing treatment gaps, risk factors, and health outcomes. *WMJ*. 2024;123(6):497-498.

17. Jentsch A. Development of a doctor: a medical student's year training in a fetal anomalies clinic. *WMJ*. 2024;123(6): 498-501.

18. Stevenson Wyszewianski M. The emptiness of fetal death – a resident physician's struggle to cope with ongoing loss and disappointment in modern medicine. *WMJ*. 2024;123(6):499,501.

19. Neuburg B, Dielentheis K, Darrah E. Gravid Hysterectomy in the setting of placenta increta at 12 weeks gestation. *WMJ*. 2024;123(6):492-494.

20. Marion E, Matthew J. Dellinger MJ, PhD; Enriquez FJ, et al. Attitudes and knowledge of THC and CBD use during pregnancy in Milwaukee, Wisconsin. *WMJ*. 2024;123(6):503-507.

21. Regner C, Zgierska A, Lennon RP, Goldstein E. Enablers and challenges of breastfeeding during the COVID-19 pandemic. *WMJ*. 2024;123(6):508-514.

22. Allen EC, Goldstein E, Lennon RP, et al. COVID-19 pandemic-related perceived loneliness as a potential risk factor for worse outcomes among pregnant and postpartum people. *WMJ*. 2024;123(6):515-520.

23. Polter EJ, Schinwald M, Haban A, Meiman J, Tomasallo C. Fish consumption advisory awareness and behavior among Asian women of childbearing age — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023. *WMJ*. 2024;123(6):521-526.

24. Polter EJ, Haban A, Meiman J, Tomasallo C. Effectiveness of educational and psychological messaging interventions to improve safe fish consumption knowledge and behaviors among Asian women of childbearing age—Milwaukee, Wisconsin, June 7, 2023–February 24, 2023. *WMJ*. 2024;123(6):537-541.

25. Eggert D, Pan A, Krier CR, Schoyer K, Kaljo K, Gunderson S. The perceptions of infertility patients regarding the COVID-19 vaccine: a mixed methods analysis of patient readiness. *WMJ*. 2024;123(6):528-532.

26. Snooks KC, Levas M, Schultz ML. Gun violence in children: a public health crisis and an upstream approach to our response. *WMJ*. 2024;123(6):643-545.

27. Anguzu R, Rein LE, Tarima S, et al. Association between lead poisoning and third-grade academic performance of children in Milwaukee. *WMJ*. 2024;123(6):569-577.

28. Cipriano DJ, Maurice SA. Impact of a school-based mental health program on academic outcomes. *WMJ*. 2024;123(6):550-555.

29. Khan NI, Jaafar H, Wawrzyniak SE. Optimizing pediatric patients' attainment of outpatient mental health services following emergency department care. WMJ. 2024;123(6):556-561.

30. Alfredson Q. Systematic review of studies measuring social media use and depression, anxiety, and psychological distress in adolescents: 2018-2020. *WMJ*. 2024;123(6):578-588.

31. Jewell TI, Sabgir AR, Aeschbach CJ. What aspects of youth programming have lasting effects?: perspectives from Wisconsin PATCH alumni. *WMJ*. 2024;123(6):593-596.

32. Willey E, Zembles T, Segar E, Kuhn E, Mayer B. Outcomes among well-appearing infants initially deferred antibiotics for fever. *WMJ*. 2024;123(6):546-549.

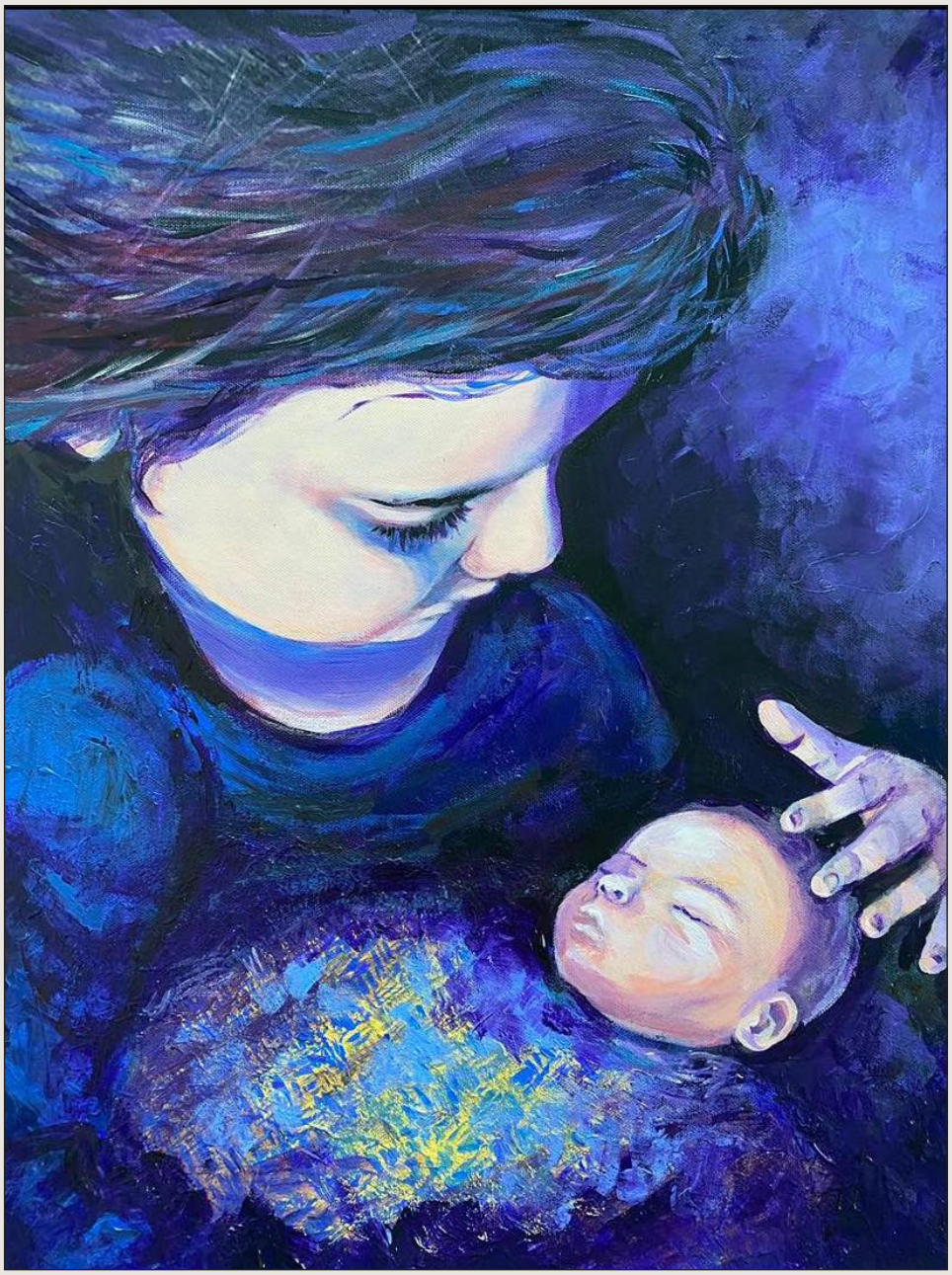
33. Goss MD, He C, Sabry A, et al. Utility and acceptability of rapid antigen testing for influenza and SARS-CoV-2 in K-12 school health offices during and after the COVID-19 pandemic. *WMJ*. 2024;123(6):597-600.

34. Bracken ZK, McConnaha KR, Mastey RR, Prakash PB, Koeppl D. Human Parechovirus infection in an infant presenting with hyperferritinemia. *WMJ*. 2024;123(6):619-624.

35. Aggarwal S, Chandra S. Perinatal femur fracture following difficult cesarean delivery: a case report. *WMJ*. 2024;123(6):610-613.

36. Heilmann JM, Hall AL, Legare JM, et al. The University of Wisconsin Undiagnosed Disease Program: Unveiling rare neurodevelopmental disorders in exome-negative patients. *WMJ*. 2024;123(6):619-624.

37. Mak V, Schiller J, Grimaldo A, Sutter EN, Collins KM, Gillick BT. 'Passport' to inclusive research participant engagement: integrating families in a research journey. *WMJ*. 2024;123(6):625-626.



Night Magic

Ronna Trapanese

Acrylic, 16 x 20”

About the Artist:

Ronna is a Wisconsin artist, working in painting (acrylics and oils), and sculpture (assemblage and found object). She is also an actress who has appeared in film and on stage, and occasionally works as such for the University of Wisconsin School of Medicine and Public Health Standardized Patient Program.

The Role of Neighborhood in Individual and Disparity-Level Factors and Birth Weight in Dane County, Wisconsin

Maria Kamenetsky, PhD, MS; Erin Bailey, MD, MS; Alexa Lowry, MD; Ronald Gangnon, PhD; Brian Stafeil, MD; Kara Hoppe, DO, MS

ABSTRACT

Introduction: There are significant disparities in the rates of maternal and infant morbidity and mortality in the United States—a discrepancy of particular importance in Wisconsin, where Non-Hispanic Black women experience the highest mortality rates in the country. The adverse effects of neighborhood socioeconomic status and geographical distance to obstetrical care outcomes have been demonstrated previously, with poor neighborhood socioeconomic status having been linked to higher rates of preterm births and low birth weight infants, which both increase the risk of neonatal morbidity and mortality. The objective of this study was to investigate the contributions of Area Deprivation Index and geographic location on age-matched birth weight z-scores.

Methods: We conducted a retrospective cohort study of all singleton births >22 weeks' gestation in Dane County, Wisconsin, from January 2016 through June 2018. Generalized additive models were adjusted for race/ethnicity, cigarette use, delivery route, pregnancy-related or chronic hypertension, pregestational and gestational diabetes, number of prenatal visits, maternal age, total weight gain, and pre-pregnancy body mass index.

Results: There is evidence of an association between birth weight z-score and spatial location (median *P* value 0.006). With area deprivation, we found no evidence of an association with birth weight z-score (-0.01; 95% CI, -0.03 to 0.01; *P* = 0.109). Mean birth weight z-scores were lowest (-0.72) in the urban center of Madison, while mean birth weight z-score was highest (0.18) in rural areas near the northeast, southeast, and southwest county borders. We found an effect of race/ethnicity on birth weight.

Conclusions: We identified geographic variations in birth weight at a granular level using census block groups and a holistic measure of deprivation, which can inform targeted public health interventions. The lack of evidence of area deprivation on birth outcomes but significant spatial trends demonstrated continued geographic disparities in our health care systems.

• • •

Author Affiliations: Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health (UW SMPH), Madison, Wisconsin (Kamenetsky, Gangnon); Department of Obstetrics and Gynecology, UW SMPH, Madison, Wisconsin (Bailey, Lowry, Hoppe); Department of Biostatistics and Medical Informatics, UW SMPH, Madison, Wisconsin (Gangnon); Dean Medical Group, SSM Health, Madison, Wisconsin (Stafeil).

Corresponding Author: Maria Kamenetsky, PhD, MS, 610 Walnut St, 707 WARF Building, Madison, WI 53726; phone 240.620.0611; email maria.kamenetsky@nih.gov; ORCID ID 0000-0002-5401-7786

INTRODUCTION

Maternal and infant morbidity and mortality is higher in the United States than other developed countries.[1] Additionally, there are significant disparities noted by race and ethnicity. This discrepancy is of particular importance in the state of Wisconsin, where the highest mortality rates in the country have been seen in non-Hispanic Black women at 14.28 per 1000 births, which is 3 times higher than rates quoted for White infants.[2-4] Looking at health disparities with a particular focus on modifiable risk factors for neonatal morbidity, a birth person's location of residence during pregnancy matters. The adverse effects of neighborhood socioeconomic status and geographical distance to obstetrical care outcomes have been demonstrated in previous literature.[2,5-6] Poor neighborhood socioeconomic status has been linked to higher rates of preterm births and low birth weight infants, both outcomes which increase the risk of neonatal morbidity and mortality.[5,7]

Though previous studies have pointed to both individual-level factors[8] and area-level factors,[9] birth and obstetric outcomes have not been explored previously at fine spatial resolution using the Area Deprivation Index (ADI).[10] ADI ranks census block groups by socioeconomic disadvantage at the state or national level. The index is a composite measure comprised of factors across the domains of income, education, employment, and housing quality. The objective of this study was to investigate the association between birth weight and ADI after accounting for known individual-level covariates.

We sought to identify and map spatial differences in Dane County, Wisconsin associated with poorer neonatal outcomes. We hypothesized that there would be an association between birth weight and ADI after accounting for known individual-level confounders. We use a generalized additive model with tensor product smooths to account for spatial dependence and adjust for individual-level covariates. We show that while area deprivation is not related to birth weight, we do still identify a significant spatial trend that is not explained by area-level factors.

METHODS

Study Population

Dane County is the second most populous county in Wisconsin and is where the state capitol of Madison is located. It has an area of 3100.84 km^2 and has an estimated population of 568 203 as of 2022. Residents in the county are mostly White (84.1%), over half (53%) have a bachelor's degree or higher, and approximately 11.3% of the county population is estimated to be living in poverty.[11] According to the 2017 Wisconsin Public Health Profiles, Dane County had a crude live birth rate of 11.3 per 1000, and approximately 7% of infants were born as low birth weight (< 2499 gm) regardless of gestational age.[12]

Peridata, a web-based prospective database available to hospitals in Wisconsin, was used to obtain birth record data and birth outcomes from the 2 delivering hospitals in Dane County, Wisconsin. Patients giving birth at 2 tertiary care centers, St Mary's Hospital Medical Center (n = 4927) and UnityPoint Health - Meriter Hospital (n = 8345), from January 2016 to June 2018 were included. These hospitals are the only 2 designated birthing centers in the county. For inclusion into our study, patients must have been (1) pregnant people > 15 years old and (2) carrying a singleton pregnancy. Analysis was limited to singletons because the etiology of preterm birth is different in multiple pregnancies. Exclusion criteria included (1) multiple gestations, (2) gestational age at delivery < 22 weeks, (3) residence outside of Dane County, and (4) maternal age < 15 years. The populations were pooled for the remaining data analysis, with a goal of capturing data from deliveries in Dane County, rather than comparing outcomes at the 2 locations. This study was approved by the Institutional Review Board at UnityPoint Hospital (IRB # 2018-017).

Primary Outcome and Covariates

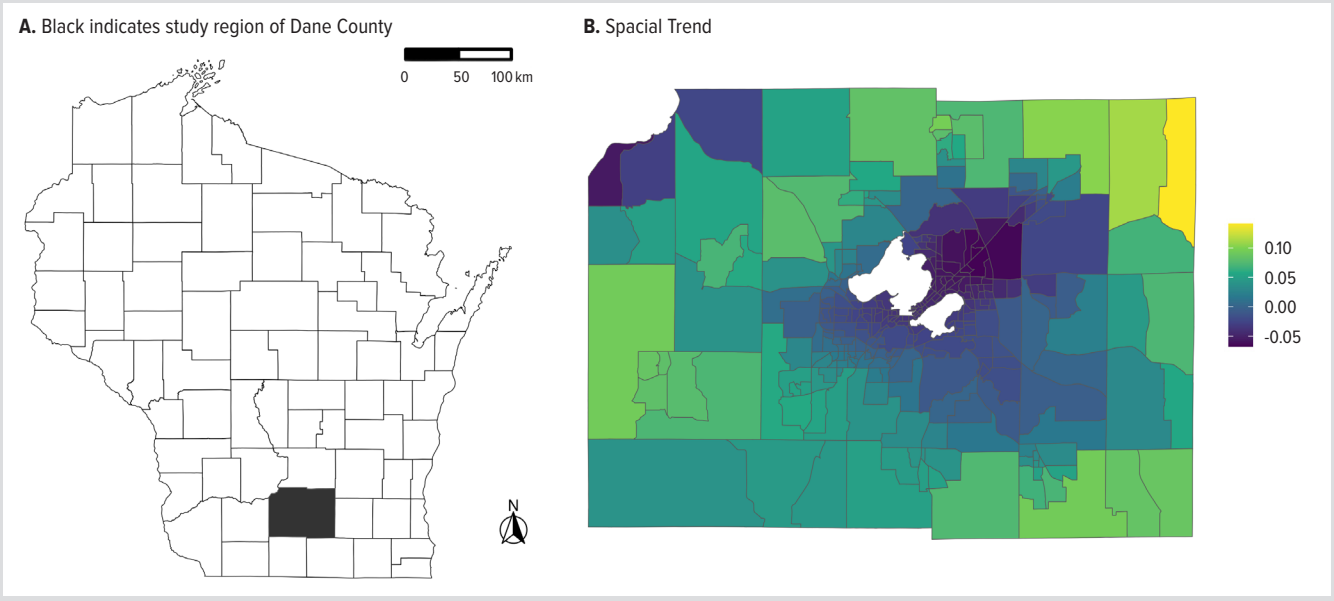
The primary outcome was birth weight, which was adjusted for by infant sex and gestational age based on Fenton growth charts (in grams) and converted to z-scores (standardized units).[13] The primary exposure is ADI. For analysis, the ADI was operationalized as the rank of the census block group at the state level (higher ranks indicate greater socioeconomic disadvantage). We also included the following covariates: cigarette use (yes/no [referent]), delivery route (spontaneous vaginal [referent], operative vaginal,

Table 1. Analytic Sample Demographics

	Mean (SD) or %	Missing (%)
Birth place facility (%)		0.00%
St Mary's Hospital Medical Center	4927 (37.1)	
Meriter	8345 (62.9)	
ADI-State rank (mean [SD])	3.16 (2.42)	0.13%
Mother's age (mean [SD])	31.13 (5.00)	0.00%
Pre-pregnancy BMI (mean [SD])	26.60 (8.46)	0.00%
Total weight gain (mean [SD])	30.48 (14.19)	1.88%
Gestational age (mean [SD])	39.15 (1.86)	0.00%
Infant sex (%)		8.79%
Female	5945 (44.8)	
Male	6161 (46.4)	
Birth weight (g) (mean [SD])	3366.83 (557.80)	0.05%
Race/ethnicity (%)		0.00%
White	9337 (70.4)	
Black	1245 (9.4)	
Latinx	1108 (8.3)	
Asian/Pacific Islander	1250 (9.4)	
Multiracial/other races	139 (1.0)	
Unknown	193 (1.45)	
Mother's education (%)		1.48%
No high school diploma	762 (5.7)	
High school diploma	1849 (13.9)	
Some college or associate degree	2678 (20.2)	
Bachelor's degree	4547 (34.3)	
Master's degree or higher	3239 (24.4)	
Cigarette use (%)		0.85%
No	12 386 (93.3)	
Yes	773 (5.8)	
Insurance		0.04%
Private/government insurance	10 129 (76.3)	
Medicaid	3119 (23.5)	
Self pay	19 (0.1)	
Number of prenatal visits (mean [SD])	12.68 (3.26)	3.16%
Pregnancy-related hypertension (%)		0.01%
No	12 304 (92.7)	
Yes	967 (7.3)	
Chronic hypertension (%)		0.01%
No	13 120 (98.9)	
Yes	151 (1.1)	
Gestational diabetes (%)		0.01%
No	12 818 (96.6)	
Yes	453 (3.4)	
Pregestational diabetes (%)		0.01%
No	12 673 (95.5)	
Yes	598 (4.5)	
Delivery route (%)		0.05%
Vaginal spontaneous	9280 (69.92)	
Cesarean	3312 (24.95)	
Operative vaginal	673 (5.07)	

Abbreviation: ADI, area deprivation index.

Figure 1. County-level Map of Wisconsin (A) and Map of the Predicted Spatial Trend in Birth Weight (B)



cesarean), pregestational diabetes (yes/no [referent]), gestational diabetes (yes/no [referent]), total weight gain (continuous), race/ethnicity (White [referent], Black, Latinx, Asian/Pacific Islander, multiracial/other), patient's education (no high school diploma, high school diploma, some college or associate degree, bachelor's degree [referent], master's degree or higher), and payment type (private/government insurance [referent], Medicaid/BadgerCare, self-pay).

Statistical Analysis

Patients were geocoded and aggregated to a census block group, then linked to the neighborhood ADI. Multiple imputation using additive regression, bootstrapping, and predictive mean matching as implemented in the aregImpute function in the Hmisc[14] package in R was used to account for potential biases due to missing data and is valid under a missing-at-random assumption. Associations between ADI and birth weight adjusted for spatial location and other covariates were assessed using generalized additive regression models (GAM),[15] which allow for parsimonious representations of potentially nonlinear effects of quantitative predictors, including spatial trends and/or autocorrelation.

Quantitative predictors (number of prenatal care visits, maternal age at birth, total weight gain during pregnancy, and pre-pregnancy body mass index [BMI]) were modeled using penalized cubic regression spline smooths. The effect of spatial location was modeled using a tensor product smooth of the census block group centroid coordinates (using the Wisconsin Transverse Mercator [WTM] coordinate system[16]). Point estimates and standard errors were pooled across analyses of the 38 imputed datasets using Rubin's method.[17] Median *P* values across imputations were used for multiparameter hypothesis tests.[18] Statistical analysis was performed using the mgcv[19] package in R version 4.0.2.[20]

RESULTS

A total of 13 272 patients were included in this study. Both mean and median state-ranked ADI did not differ across the 2 hospitals, nor did all other demographic variables (Table 1). Individual socioeconomic and prenatal factors were then explored for our outcomes. In the sample (Table 1), patients were, on average, in their early thirties, slightly overweight (BMI 26.60 m^2), had gained about 30 pounds throughout their pregnancy, and had birthed infants at approximately 39 weeks. Most patients were White (70.4%), had attained a bachelor's degree (34.3%), were on private or government insurance (76.3%), and had spontaneous vaginal births (69.92%).

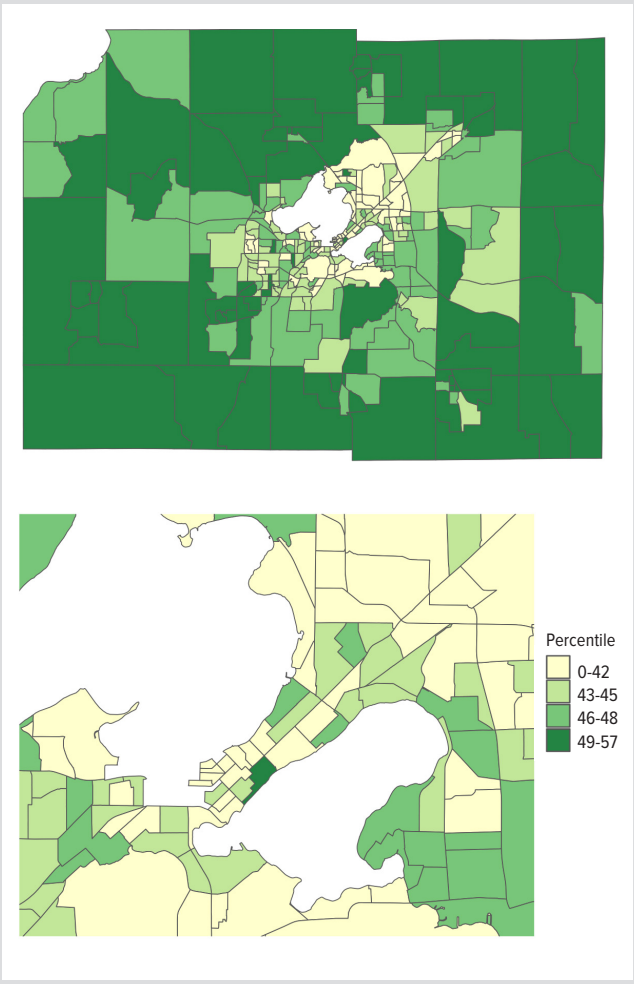
Though we found no evidence of an association between birth weight and ADI (adjusted estimate [adj est] -0.01; 95% CI, -0.01 to 0.00), we did find evidence of a statistically significant spatial trend ($P = 0.006$) indicating other spatial information not captured by ADI or covariates. The smoothness of the spatial trend indicates spatial dependence in birth weight not captured by any of the factors explored in our model (Figure 1). The spatial trend was lowest near the center of the county and along the isthmus (between the 2 lakes) near the capitol. Further from the county center, the spatial trend was increasing and highest in the top right corner along the border with the neighboring county (Dodge County), indicating stronger spatial dependence in this area. Interestingly, the top left corner had some of the lowest trend values near the border with Sauk County, indicating lower spatial dependence. Overall, we observed less spatial dependence in birth weight in the more

urban county center and stronger dependence along the county border in the more rural cities.

We used our model to predict birth weight in standardized units for each participant. We then aggregated those predicted values by taking the mean birth weight in each census block group. For ease of interpretation, we converted the predicted mean birth weights from z-scores to percentiles (Figure 2). The predicted birth weight percentiles ranged from 24th to 57th percentile (mean 45th percentile, SD 5). The spatial trend from Figure 1B can be seen in the predicted birth weight percentiles. Most of the lower percentile birth weights were found in the center of the county near the downtown area and state capitol between the 2 lakes (0%-42% range). Higher predicted mean birth weight percentiles were found further outside the center of the county nearer the county border.

We also found that Black (adj est -0.31; 95% CI, -0.37 to -0.25) and Asian/Pacific Islander (adj est -0.26; 95% CI, -0.32 to -0.21) patients had lower birth weights compared to White patients after adjusting for known covariates (Supplemental Table 1). Nonlinear relationships with maternal age, number of prenatal care visits, pre-pregnancy BMI, and total weight gain are visualized in Supplemental Figure 2.

Figure 2. Predicted Percentiles for Birth Weight in Dane County (top); Zoomed-in View of Predicted Percentiles Along the Downtown Area (bottom)



DISCUSSION

In our study, we found no association between ADI and birth weight. Dane County is an overall affluent county (mean ADI of 3.16) with variability within census blocks, so it is possible that we are not able to detect the effect of area deprivation. Given the relationship between low socioeconomic status and adverse neonatal outcomes demonstrated in previous literature,[21-24] we hypothesize that investigating ADI in a larger population would possibly highlight a relationship between ADI and these maternal and neonatal outcomes. We found a statistically significant spatial trend in birth weight. This may be driven by other socioeconomic factors not encompassed in the ADI index or other spatially dependent variables that we did not have available in our data. We also found a consistent association between these birth outcomes and patients' race, despite the relative affluence of the county. This may be driven by racial disparities at the individual level that are independent of socioeconomic status. This speaks to the need for continued investigation into the systemic drivers of these disparities.

This study has several limitations. Our ADI measure is at the census block group level which, though very small, may still be masking some spatial effects due to data aggregation. This may be why we observed spatial trends in birth weight but no association with ADI. There also may be other aspects of socioeconomic disadvantage not captured by the ADI that we did not explore. Though our sample size is large, our data are limited to a window of 2016 to 2018, so it may be possible that we need a longer time period and larger sample size to identify effects of ADI. Finally, our analysis is limited to Dane County, Wisconsin, which has a relatively high socioeconomic status and may not be generalizable to other counties that differ in their populations, demographics, and health care services.

Despite these limitations, this study has several strengths. First, the 2 hospitals explored are the only birthing hospitals in the county. Aside from home births or other alternative births, we captured the population of Dane County birthing patients from January 2016 to June 2018. Second, we use a flexible modeling strategy that allowed for nonlinearity in certain continuous covariates and, importantly, allowed for flexibility in capturing the spatial patterns in the data. Finally, we used multiple imputation to impute missing data instead of deleting those individuals from the data, reducing bias and improving precision in our estimates.

CONCLUSIONS

This exploratory study identified the feasibility of using a spatial model to examine neonatal outcomes. Assessments such as this could be used on a larger spectrum to identify areas in need of

improved access to high quality obstetrics care and to create a model for reallocation of prenatal services. Furthermore, we found a consistent association between race and birth outcomes even after adjustment for area deprivation and other individual-level factors. This indicates a continued need to investigate health disparities as well as promote the education of health care providers regarding bias to improve maternal and neonatal outcomes. In future work, this approach could be taken across a larger geographic area, such as multiple neighboring counties. This could help highlight locations that would benefit most from targeted public health interventions or even targeted physician recruitment, ultimately improving neonatal outcomes.

Funding/Support: This work was supported by Research and Development Funds from the University of Wisconsin School of Medicine and Public Health Department of Obstetrics and Gynecology.

Financial Disclosures: None declared.

Appendix: Visit www.wmjonline.org to access supplemental materials.

REFERENCES

1. Chinn JJ, Eisenberg E, Artis Dickerson S, et al. Maternal mortality in the United States: research gaps, opportunities, and priorities. A*m J Obstet Gynecol.* 2020;223(4):486-492.e6. doi:10.1016/j.ajog.2020.07.021

2. Infant mortality. Centers for Disease Control and Prevention. Updated September 16, 2024. Accessed April 30, 2020. https://www.cdc.gov/maternal-infant-health/infant-mortality/

3. Matthews TJ, Ely DM, Driscoll AK. State variations in infant mortality by race and Hispanic origin of mother, 2013-2015. N*CHS Data Brief.* 2018;(295):1-8. https://www.cdc.gov/nchs/data/databriefs/db295.pdf

4. Byrd DR, Katcher ML, Peppard P, Durkin M, Remington PL. Infant mortality: explaining Black/White disparities in Wisconsin. *Matern Child Health J.* 2007;11(4):319-326. doi:10.1007/s10995-007-0183-6

5. Ncube CN, Enquobahrie DA, Albert SM, Herrick AL, Burke JG. Association of neighborhood context with offspring risk of preterm birth and low birthweight: a systematic review and meta-analysis of population-based studies. *Soc Sci Med.* 2016;153:156-164. doi:10.1016/j.socscimed.2016.02.014

6. Grzybowski S, Stoll K, Kornelsen J. Distance matters: a population based study examining access to maternity services for rural women. *BMC Health Serv Res.* 2011;11:147. doi:10.1186/1472-6963-11-147

7. Giurgescu C, Zenk SN, Templin TN, Engeland CG, Kavanaugh K, Misra DP. The impact of neighborhood conditions and psychological distress on preterm birth in African-American women. *Public Health Nurs.* 2017;34(3):256-266. doi:10.1111/phn.12305

8. Nagahawatte NT, Goldenberg RL. Poverty, maternal health, and adverse pregnancy outcomes. *Ann N Y Acad Sci*. 2008;1136:80-85. doi:10.1196/annals.1425.016

9. DeFranco EA, Lian M, Muglia LA, Schootman M. Area-level poverty and preterm birth risk: a population-based multilevel analysis. *BMC Public Health.* 2008;8:316. doi:10.1186/1471-2458-8-316

10. Kind AJH, Buckingham WR. Making neighborhood-disadvantage metrics accessible - the Neighborhood Atlas. *N Engl J Med.* 2018;378(26):2456-2458. doi:10.1056/NEJMp1802313

11. QuickFacts: Dane County, Wisconsin. United States Census Bureau. Updated June 27, 2024. Accessed July 13, 2023. https://www.census.gov/quickfacts/danecountywisconsin

12. Wisconsin Department of Health Services. Wisconsin Public Health Profiles 2017. Wisconsin Department of Health Services; 2021. P-45358-21. February 2021. Accessed July 13, 2023. https://www.dhs.wisconsin.gov/publications/p45358-21.pdf

13. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. *BMC Pediatr.* 2013;13:59 doi:10.1186/1471-2431-13-59

14. Harrell FE Jr. Harrell Miscellaneous, version 5.1.1. CRAN; 2020. Accessed July 15, 2024. https://hbiostat.org/R/Hmisc/

15. Hastie T, Tibshirani R. Generalized additive models for medical research. Stat Methods Med Res. 1995;4(3):187-196. doi:10.1177/096228029500400302

16. Danielsen, D, Kock, T, ed. *Wisconsin: Coordinate Reference Systems*. 2nd ed. Wisconsin State Cartographer's Office; 2009. Updated June 2015. Accessed July 15, 2024. https://www.sco.wisc.edu/wp-content/uploads/2017/07/WisCoordRefSys_June2015.pdf

17. Rubin, D. *Multiple Imputation for Nonresponse in Surveys*. John Wiley & Sons, Inc; 1987.

18. Eekhout I, van de Wiel MA, Heymans MW. Methods for significance testing of categorical covariates in logistic regression models after multiple imputation: power and applicability analysis. *BMC Med Res Methodol*. 2017;17(1):129. doi:10.1186/s12874-017-0404-7

19. Wood, S. Mixed GAM Computation Vehicle with Automatic Smoothness Estimation, version 1.9.0. CRAN; 2018. Accessed July 15, 2024. https://cran.r-project.org/web//packages//mgcv/index.html

20. R Core Team. *R: A Language and Environment for Statistical Computing*. Version 4.0.2. The R Foundation; 2021. Accessed July 15, 2024. https://www.r-project.org/

21. Ruth CA, Roos N, Hildes-Ripstein E, Brownell M. The influence of gestational age and socioeconomic status on neonatal outcomes in late preterm and early term gestation: a population based study. *BMC Pregnancy Childbirth.* 2012;12:62. doi:10.1186/1471-2393-12-62

22. Bohanon FJ, Nunez Lopez O, Adhikari D, et al. Race, income and insurance status affect neonatal sepsis mortality and healthcare resource utilization. *Pediatr Infect Dis J*. 2018;37(7):e178-e184. doi:10.1097/INF.0000000000001846

23. Pabayo R, Cook DM, Harling G, Gunawan A, Rosenquist NA, Muennig P. State-level income inequality and mortality among infants born in the United States 2007-2010: a cohort study. *BMC Public Health.* 2019;19(1):1333. doi:10.1186/s12889-019-7651-y

24. Kim MK, Lee SM, Bae SH, et al. Socioeconomic status can affect pregnancy outcomes and complications, even with a universal healthcare system. *Int J Equity Health*. 2018;17(1):2. doi:10.1186/s12939-017-0715-7

Addressing Maternal and Child Health Disparities Through Perinatal Home Visiting

Joshua P. Mersky, PhD; Colleen Janczewski, PhD; Davin Hami, BS

ABSTRACT

Introduction: Perinatal home visiting is a popular strategy for promoting maternal and child health in the United States. Despite considerable research on home visiting programs, little is known about the extent to which they engage populations that are disproportionately affected by health inequalities and their social determinants.

Methods: Administrative data were obtained for 6327 households served by Wisconsin's Family Foundations Home Visiting (FFHV) program from October 1, 2016, to September 30, 2023. Analyses were performed to calculate the proportion of households representing priority populations at risk of poor maternal and child health outcomes, yielding comparisons with similar estimates in the general population. A service saturation analysis also was performed to explore the extent to which evidence-based home visiting services reach low-opportunity communities across Wisconsin.

Results: The findings confirmed that the FFHV program largely directs resources toward disadvantaged and marginalized populations. For instance, nearly two-thirds of the households served were below the federal poverty level, more than a third had a history of substance misuse, and more than half had a current tobacco user – exceeding comparative estimates in the general population by roughly 3-fold to 5-fold. Primary caregivers served were twice as likely to be Black or Hispanic and 5 times as likely to be American Indian or Alaska Native as they were to be White. Whereas 36.5% of Wisconsin ZIP codes were categorized as low-opportunity areas, 69.1% of families served were living in a low-opportunity ZIP code.

Conclusions: The FFHV program targets services to populations and communities at risk of maternal and infant health disparities. Additional strategies should be considered to bring home visiting to scale in Wisconsin and nationwide.

INTRODUCTION

Perinatal home visiting is a popular strategy for promoting maternal and child health in the United States, as evidenced by strong bipartisan support for the federal Maternal, Infant, and Early Childhood Home Visiting (MIECHV) Program that subsidizes evidence-based home visiting programs nationwide.[1,2] While there are many home visiting models with different curricula, most programs offer voluntary, comprehensive, and flexible services that can be tailored to suit the diverse needs of expectant and new parents. In aggregate, these programs have been linked to modest but measurable benefits, including improved outcomes in maternal and infant health, parenting, and child development.[3,4] Yet, despite their impact and wide reach, little is known about the extent to which these programs foster health equity at scale.

Home visiting programs may reduce health disparities, in part, because they typically take a selective approach to prevention. That is, they often target services to populations that are at risk of poor maternal and child health outcomes. For example, around two-thirds of families that are served by MIECHV-subsidized programs are at or below 100% of the federal poverty level.[5] Home visitors help these families achieve a wide range of goals by offering education, guidance, and encouragement. Home visitors also strengthen family connections to health care providers, human service agencies, and economic resources, thereby addressing modifiable conditions associated with structural social determinants of health that are believed to be root causes of health inequities.[6]

• • •

Author Affiliations: Institute for Child and Family Well-being, Helen Bader School of Social Welfare, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin (Mersky, Janczewski); University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Hami).

Corresponding Author: Joshua P. Mersky, PhD, 2400 E Hartford Ave, Milwaukee, WI 53211; phone 414.388.7512; email mersky@uwm.edu; ORCID ID 0000-0002-8803-8702

Since 2011, Wisconsin has used MIECHV funds to sustain the Family Foundations Home Visiting (FFHV) program, a robust home visiting network administered by the state Department of Children and Families in partnership with the Department of Health Services. The FFHV program supports 4 evidence-based home visiting models: Healthy Families America, Nurse-Family Partnership, Parents as Teachers, and Early Head Start. Each of these programs provides services that can begin prenatally and last for multiple years after a child is born. As of this writing, the FFHV program's local implementing agencies deliver these programs across more than half of Wisconsin's 72 counties and 11 federally recognized tribal regions. In accordance with MIECHV policy,[7] a statewide home visiting needs assessment was completed with the aim of directing the FFHV program's resources toward communities with high levels of adverse perinatal outcomes and other risk indicators, such as poverty and substance abuse.[8] Among its key findings, the needs assessment confirmed that there are significant racial/ethnic differences in perinatal outcomes and sizeable service gaps in certain communities. To the extent that these disparities in access and outcomes can be addressed, the FFHV program may act as a lever for promoting maternal and child health equity.

Despite considerable research on the impact of home visiting programs, little is known about the extent to which they reach populations that are disproportionately affected by health inequalities and their social determinants. Therefore, the current study uses household- and community-level data to assess the FFHV program's capacity and whether it serves priority populations and communities. By making comparisons to the general population of families with children, we are able to draw inferences about the extent to which program resources have been distributed equitably.

METHODS

Data and Sample

The current study was conducted as part of a MIECHV-coordinated state evaluation focused on family engagement and health equity. In alignment with a federally approved evaluation plan, an analysis was completed to explore whether Wisconsin's FFHV program is working effectively toward health equity goals by enrolling disadvantaged and marginalized families and communities. Administrative data housed at the Wisconsin Department of Children and Families were obtained for all families served by the FFHV program from October 1, 2016, through September 30, 2023. The begin date corresponds with a transition to the use of DAISEY (Data Application and Integration Solutions for the Early Years), a dedicated FFHV database that records standard performance indicators for each family served. Access to these data was granted by the Wisconsin Department of Children and Families pursuant to a data sharing agreement and approval of study protocols by the institutional review board at the University of Wisconsin-Milwaukee (protocol 14.286).

The primary study sample includes 6327 primary caregivers, with 96.2% identifying as women and 3.8% as men (nonbinary gender data were unavailable). At the point of enrolling in a home visiting program, more than half the participants (56.7%) were single and had never married, and more than a quarter (25.2%) had less than a high school diploma or GED equivalent. Statewide ZIP code-level data representing variation in levels of community opportunity were obtained from public records and matched to household address records for 4490 participants served from October 1, 2021, through September 30, 2023, with valid ZIP codes. The community-level analysis was restricted to this 2-year period to minimize the influence of changes to the composition of the FFHV program due to the occasional discontinuation of local implementing agencies and onboarding of new local implementing agencies.

Measures

Priority Populations: Program data housed in DAISEY were used to create indicators that correlate with maternal and infant health outcomes, including 4 measures that represent MIECHV priority populations: (1) low-income household (ie, < 100% of federal poverty guidelines), (2) primary caregiver under 20 years of age at the birth of the child associated with the home visiting service episode (ie, index child), (3) household member with a history of substance misuse or need for treatment, and (4) household tobacco use. Although race and ethnicity are not explicit priority population categories for the MIECHV Program, we also examined the FFHV program's engagement of different racial/ethnic groups given that many health disparities in the US fall along racial/ethnic lines. Primary caregivers associated with a service episode were coded as Hispanic/Latino or one of the following non-Hispanic categories: American Indian or Alaska Native, Asian, Black or African American, White, and Other.

Comparative data indicating the statewide prevalence of different priority populations were obtained from multiple sources, including the US Census, Centers for Disease Control and Prevention, and Wisconsin Department of Health Services.[9-11] State-level data were unavailable for household substance use; these data points were obtained from the National Surveys on Drug Use and Health.[12]

Priority Communities: Publicly available ZIP code-level information for participating households was obtained from the Child Opportunity Index 2.0 (COI 2.0), which indexes variation in community resources and conditions on a 5-point scale ranging from very low to very high child opportunity.[13] The COI 2.0 captures 29 indicators in 3 domains: (1) Education, (2) Health and Environment, and (3) Social and Economic. For this study, the total COI 2.0 score for each ZIP code in Wisconsin

Figure 1. Child Opportunity Levels by Wisconsin ZIP Code

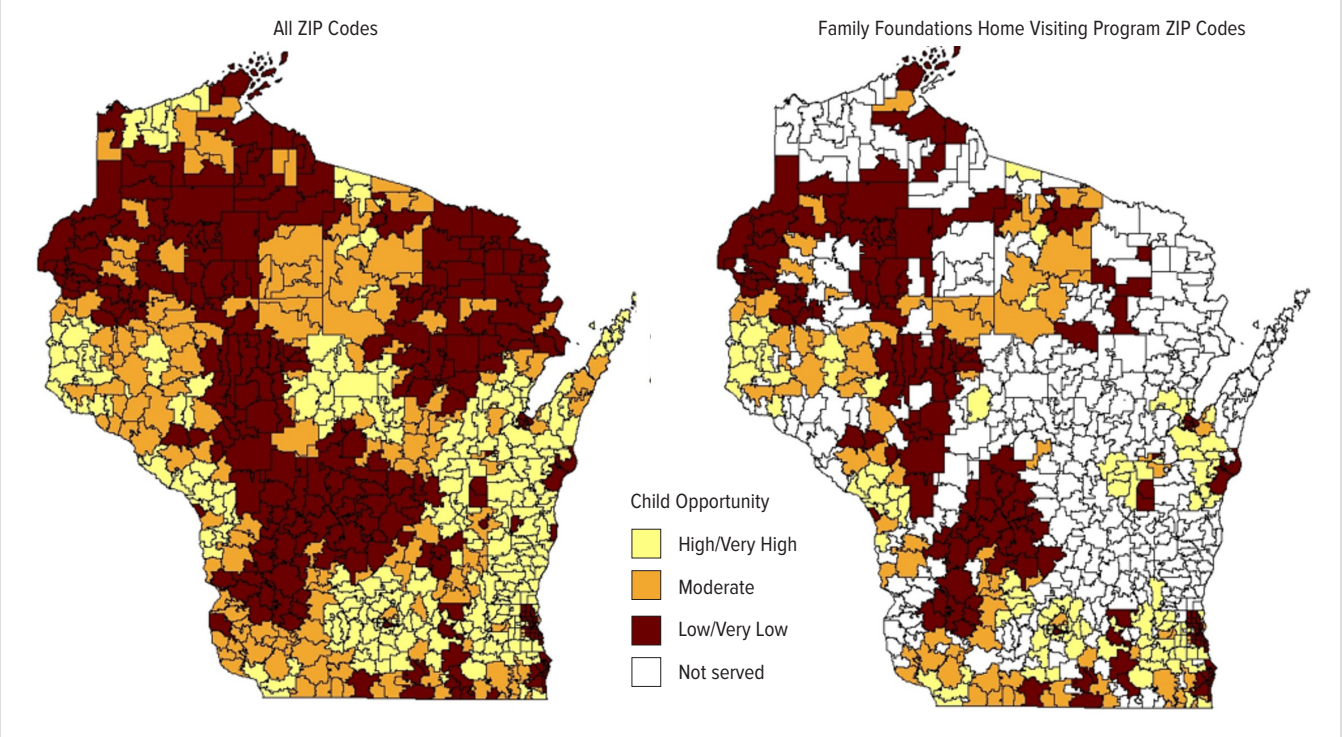


Figure displays variation in community resources and conditions at the ZIP code level according to data from the Child Opportunity Index 2.0. The map on the left distinguishes opportunity levels across all ZIP codes in Wisconsin, and the map on the right distinguishes opportunity levels across ZIP codes where families were served by the Family Foundations Home Visiting Program (FFHV). ZIP codes shown in white were not served by the FFHV program between October 1, 2021, and September 30, 2023.

was ranked initially into quintiles representing different levels of opportunity (very low, low, moderate, high, very high). To avoid small cell sizes, the ZIP codes were then recoded into 3 categories of community opportunity: (1) low (ie, low or very low), (2) moderate, (3) high (ie, high or very high). The maps shown in Figure 1 present the distribution of opportunity levels across all ZIP codes in Wisconsin and the ZIP codes served by the FFHV program.

Analysis Plan

Descriptive analyses were performed to calculate the proportion of the FFHV sample composed of different priority populations (eg, living in poverty, substance misuse). Similar rates were obtained from public data sources to facilitate descriptive comparisons with the general population statewide or nationally.[9-12] Cross-tabulations were performed to produce a risk ratio (RR) for each metric, with an RR above 1.00 indicating that a priority population is overrepresented in the FFHV sample. Separate cross-tabulations were performed to explore the distribution of MIECHV priority population categories among racial/ethnic groups in the FFHV sample. Chi-square tests were conducted to produce RR estimates, indicating whether these priority categories were overrepresented or underrepresented among racial/ethnic minority participants compared to non-Hispanic White

Table 1. Demographic Comparison of Families Served by the Family Foundations Home Visiting (FFHV) Program to the General Population (N = 6327)

	FFHV Program	General Population	Risk Ratio
Low-income household	65.0%	12.9%[a]	5.0
Under age 20 at child's birth[a]	20.9%	7.8%[d]	2.7
History of substance misuse or treatment needs	36.9%	12.3%[c]	3.0
Tobacco use	50.9%	10.1%[d]	5.2
Race and ethnicity			
American Indian or Alaska Native	5.6%	1.1%[b]	5.1
Asian	4.7%	4.4%[b]	1.1
Black/African American	20.3%	10.1%[b]	2.0
Hispanic/Latino	22.8%	11.2%[b]	2.0
Other	3.3%	2.7%[b]	1.2
White	43.3%	71.5%[b]	0.6

[a]The federal MIECHV Program prioritizes serving individuals who give birth before age 21. This study uses a lower age threshold for early childbearing (< 20) because comparable state-level data are available. The prevalence of early childbearing among FFHV participants is underestimated because some participants who gave birth to the index child after age 20 also gave birth previously before age 20.

[b]Source: US Census, American Community Survey.[9]

[c]Source: Centers for Disease Control and Prevention.[10]

[d]Source: Comparative estimate unavailable for Wisconsin population. Estimate from the US population was calculated using data from National Surveys on Drug Use and Health.[12]

[e]Source: Wisconsin Department of Health Services, Wisconsin Interactive Statistics on Health.[11]

Table 2. Priority Populations Served by the Family Foundations Home Visiting Program, Variation by Race/Ethnicity (N = 6314)

Priority Population Indicators	American Indian/ Alaska Native, n = 353 % RR (95% CI)	Asian n = 295 % RR (95% CI)	Black/African American, n = 1281 % RR (95% CI)	Hispanic n = 1441 % RR (95% CI)	Other n = 207 % RR (95% CI)	White n = 2737 % RR
Low-income household	72.6% **1.21 (1.12–1.30)**	64.6% 1.07 (0.98–1.18)	76.4% **1.27 (1.21–1.33)**	61.7% 1.03 (0.97–1.08)	71.2% **1.18 (1.08–1.30)**	60.1%
< Age 20 at child's birth	17.8% 0.90 (0.71–1.13)	8.8% **0.44 (0.30–0.64)**	23.6% **1.19 (1.05–1.34)**	23.4% **1.18 (1.04–1.33)**	22.0% 1.10 (0.84–1.44)	19.9%
Substance misuse or treatment needs	65.8% **1.33 (1.22–1.45)**	7.8% **0.16 (0.11–0.23)**	25.3% **0.51 (0.46–0.57)**	21.6% **0.44 (0.39–0.49)**	38.2% **0.77 (0.65–0.92)**	49.5%
Tobacco use	68.8% 1.07 (0.99–1.15)	33.9% **0.53 (0.45–0.62)**	45.3% **0.71 (0.66–0.75)**	29.2% **0.45 (0.42–0.50)**	55.1% **0.86 (0.76–0.97)**	64.3%

A risk ratio (RR) and CI is listed below each prevalence estimate (%). RRs compare the prevalence of priority population indicators reported by White caregivers to the prevalence reported by caregivers of other racial/ethnic groups served by the FFHV program. RRs in bold denote statistically significant contrasts ($P < .05$). Sample sizes are reduced due to missing data for race/ethnicity (n = 13).

participants. Missingness for priority populations ranged from 0.2% (under age 20 at child's birth) to 6.6% (low-income household); 0.2% of the sample (n=13) were missing race/ethnicity. Missing cases were omitted from corresponding analyses via listwise deletion.

Table 3. ZIP Codes Served by Child Opportunity Level, Family Foundations Home Visiting Program (FFHV), 2021-2023

ZIP Code Categories	Child Opportunity Level: Low % (N)	Moderate % (N)	High % (N)	Total % (N)
FFHV service area, ZIP codes served	42.8% (154)	26.9% (97)	30.3% (109)	100.0% (360)
FFHV service Area, ZIP codes not served	37.5% (93)	21.4% (53)	41.1% (102)	100.0% (248)
ZIP codes outside FFHV service area	26.6% (68)	25.4% (65)	48.0% (123)	100.0% (256)
Total	36.5% (315)	24.9% (215)	38.7% (334)	100.0% (864)

A service saturation analysis was conducted to explore whether the FFHV program reaches priority communities across Wisconsin. To operationalize service saturation—or the extent to which the FFHV program penetrated different communities—we calculated the number of families served in all 864 Wisconsin ZIP codes and classified each ZIP code into 1 of 3 categories: (1) FFHV service area, families served; (2) FFHV service area, no families served; and (3) non-FFHV service area. Across all 3 service area categories, we described the proportion of ZIP codes that were low-opportunity, moderate-opportunity, and high-opportunity areas. We then used household-level data to conduct a within-group analysis of FFHV-served families to determine the proportion that lived in low-, moderate-, and high-opportunity areas. The analysis was conducted in SPSS version 28.0, and corresponding maps were generated using ArcGIS 10.8.

RESULTS

Priority Populations Served

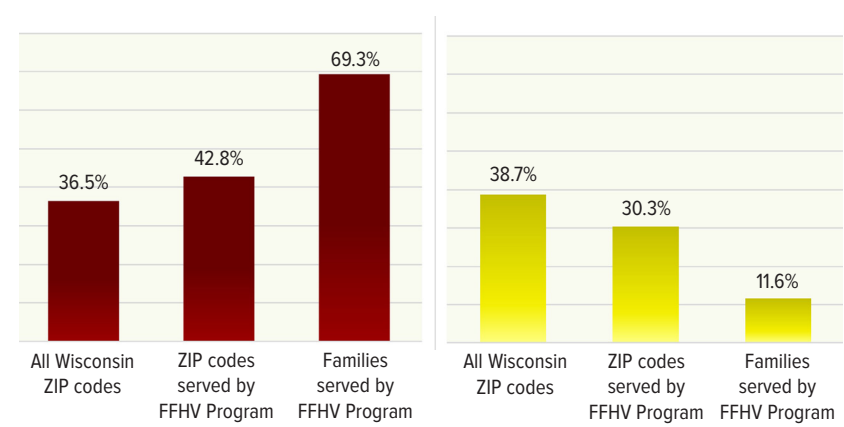
Table 1 presents household demographics for FFHV program participants along with comparative population estimates. Nearly two-thirds (65.0%) of FFHV households served were below the federal poverty level, which is about 5 times higher than the poverty rate among all Wisconsin households with children under age 18 (12.9%; RR 5.0). More than 1 out of 5 (20.9%) index children served by the FFHV program had a primary caregiver under the age of 20, which is nearly 3 times the rate of teen childbearing in Wisconsin (7.8%; RR 2.7). Over a third of FFHV households had an identified history of substance misuse or need for treatment (36.9%), which is roughly 3 times the estimated proportion of US children who live with a parent who has a substance use disorder (12.3%; RR 3.0). Signs of tobacco use were present in over half of FFHV households (50.9%), which is more than 5 times the estimated proportion among all Wisconsin households with children (10.1%; RR 5.2). The racial/ethnic composition of primary tablecaregivers in the FFHV sample was 43.3% White, 22.8% Hispanic/Latino, 20.3% Black/African American, 5.6% American Indian/Alaska Native, 4.7% Asian, and 3.3% Other. Compared to the general Wisconsin population of adults with children, the FFHV program was 1.1 times as likely to serve Asian adults, 1.2 times as likely to serve adults classified as Other race, 2.0 times as likely to serve both Black/African American and Hispanic/Latino adults, and 5.1 times as likely to serve American Indian/Alaska Native adults.

Racial/Ethnic Comparison of Priority Populations Served

Table 2 displays how priority populations are distributed among racial/ethnic groups. Compared to the 60.1% of White primary caregivers from households living below the poverty level, Black/African American caregivers were more likely to be poor (76.4%; RR 1.27), as were American Indian/Alaska Native caregivers (72.6%; RR 1.21). Compared to the 19.9% of White caregivers who were less than age 20 at the index child's birth, teen child-

bearing was more prevalent among Black/African American caregivers (23.6%; RR 1.19) and Hispanic/Latino caregivers (23.4%; RR 1.18), and less prevalent among Asian caregivers (8.8%; RR 0.44). Substance misuse was more prevalent in households with American Indian/Alaska Native caregivers compared to White caregivers (65.8% vs 49.5%; RR 1.33). Conversely, lower rates of substance misuse were present among households with caregivers who were Asian (7.8%; RR 0.16), Hispanic/Latino (21.6%; RR=0.44), Black/African American (25.3%; RR 0.51), and Other race (38.2%; RR 0.77). Compared to the 64.3% of White caregivers living in a household with tobacco use, lower rates of tobacco use were present in households with caregivers who were Hispanic/Latino (29.2%; RR 0.45), Asian (33.9%; RR 0.53), Black/African American (45.3%; RR 0.71), and Other (55.1%; RR 0.86).

Figure 2. Variation in Child Opportunity Levels



In each panel, the first two bars denote the proportion of ZIP codes that were classified as low opportunity and high opportunity. The third bar in each panel denotes the proportion of families served by the Family Foundations Home Visiting (FFHV) program that resided in low-opportunity and high-opportunity areas.

Service Saturation Analysis

Out of 864 Wisconsin ZIP codes, 608 (70.4%) were within the service coverage area of the FFHV program (see Table 3). Among these 608 ZIP codes, 360 (59.2%) had at least 1 family served during the 2-year analysis period. Out of the 360 ZIP codes that were actively served by the FFHV program, 154 (42.8%) were a low-opportunity area, 97 (26.9%) were a moderate-opportunity area, and 109 (30.3%) were a high-opportunity area. Out of the 256 ZIP codes that were outside the FFHV Program's coverage area, 68 (26.6%) were a low-opportunity area, 65 (25.4%) were a moderate-opportunity area, and 123 (48.0%) were a high-opportunity area.

There were 4490 families served by the FFHV program during the analysis period, 69.3% of whom resided in a low-opportunity area (see Figure 2, Panel 1). By comparison, 36.5% of all Wisconsin ZIP codes were low-opportunity areas. Among all FFHV-served families, 11.6% lived in a high-opportunity area, whereas 38.7% of all Wisconsin ZIP codes were high-opportunity areas (see Figure 2, Panel 2).

DISCUSSION

Demonstrating Wisconsin's evidence-based home visiting service capacity, agencies supported by the FFHV program enrolled more than 6300 families over a 7-year period ending in September 2023. Nearly two-thirds of the households served were at or below the federal poverty level, more than a third had a history of substance misuse, and more than half had a current tobacco user—these figures exceed comparative estimates in the general population by roughly 3-fold to 5-fold. Primary caregivers served by the FFHV program were twice as likely to be Black or Hispanic and 5 times as likely to be American Indian/Alaska Native as they were to be White. Compared to their White counterparts, Black and Indigenous caregivers were more likely to be poor, while Black and Hispanic caregivers were more likely to be a teen parent at enrollment. Taken together, these findings signal that the FFHV program largely directs resources toward disadvantaged and marginalized populations at an elevated risk of maternal and infant health disparities.

It is also notable that rates of substance misuse and tobacco use were higher among low-income White and Indigenous households than among low-income Black and Hispanic households. These results reinforce research indicating that health disparities and their upstream correlates do not cleave neatly along racial/ethnic lines within the FFHV service population.[14,15] Variability in racial/ethnic disparities may be partly related to differences between urban environments, where most of Wisconsin's Black and Hispanic families receive home visiting services, and more rural environments, where most White and Indigenous families are served. Supporting this hypothesis, prior research has documented rural-urban discrepancies in health behaviors and health outcomes.[16-18]

We performed a service saturation analysis to evaluate the extent to which the FFHV program reaches families and communities at risk of poor maternal and child health outcomes. At present, 70% of Wisconsin's ZIP codes lie within the FFHV coverage area, although only 42% of the state's ZIP codes had at least 1 family served from October 2021 through September 2023. As expected, the FFHV program dedicated much of its resources to less advantaged community areas. Less than 27% of ZIP codes outside the FFHV program's coverage area were classified as low-opportunity, whereas nearly 43% of the ZIP codes actively ser-

viced by the program were low-opportunity. Moreover, 69% of all families that received services from one of the FFHV program's local implementing agencies were living in a low-opportunity ZIP code. These findings suggest that the state FFHV program supports agencies that disproportionately serve low-opportunity ZIP codes and that these agencies further redistribute resources toward families residing in more disadvantaged ZIP codes within their service area.

Limitations

This study has multiple limitations. Chief among them is our reliance on available public records with inconsistent operational definitions for drawing comparisons between the FFHV sample and the general population. Although we are reasonably confident in the overall accuracy of our conclusions, the risk ratio estimates presented are imprecise. Additionally, inferences related to variations in community opportunity should be interpreted with caution, as ZIP codes are coarse geographic designations that have shortcomings for investigations of spatial and demographic variation.[19]

Implications and Future Directions

Perinatal home visiting programs occupy a special position in the health and human services landscape because they engage families in their natural environments during a sensitive period of the life course. These programs may promote health equity by enhancing maternal and child health outcomes among some of society's most disadvantaged families and communities. Results from this study suggest that the FFHV program successfully targets resources toward priority populations, including low-income households, racial/ethnic minority groups, and low-opportunity community areas. Given their broad and flexible service array, home visiting programs can address a variety of health inequities that manifest in these different subpopulations.

While there are reasons for optimism, caution should be exercised when projecting the net impact of home visiting programs on health disparities. Program effects tend to be heterogeneous and small in aggregate.[3,4] Additionally, most programs employ a targeted prevention approach whereby services are directed toward a small segment of the population. For instance, the FFHV program typically enrolls less than 1000 families with newborns per year, representing less than 2% of births statewide.[20] Moving the needle on population-level health disparities may require achieving larger effect sizes, reaching more families, or both.

Efforts to promote maternal and child health equity in Wisconsin may be advanced by expanding the FFHV program statewide. At the same time, there is a need to understand which strategies are most effective for specific populations, an approach known as precision home visiting.[21] One way to increase precision is by investing in innovative models that engage underserved populations. For instance, the Milwaukee Health Department supports the Direct Assistance for Dads Project, which serves expecting fathers and men with children up to age 3. Another example is the Family Spirit model, which provides culturally aligned education and services to tribal communities[22] and has been piloted in Wisconsin by the Ho-Chunk Nation Department of Health.

Greater precision also may be achieved by combining targeted interventions with more universal strategies, as recommended by the World Health Organization's Commission on Social Determinants of Health.[23] Exemplifying progress on this front in Wisconsin, Racine and Walworth counties recently adopted the Hello Baby program, a postpartum nurse home visiting initiative. Once fully implemented, this program will offer services countywide to all families with a newborn. Although Hello Baby is offered to families across the socioeconomic spectrum, the level of support they receive varies based on their assessed need. This prevention strategy, known as targeted universalism, balances equality of access with equity of resource allocation. By increasing access to home visiting and allocating resources proportionate to the needs of different families and communities, Hello Baby is well aligned with national health equity goals articulated in the Healthy People 2030 framework.[24]

CONCLUSIONS

Since 2011, Wisconsin has used federal Maternal, Infant, and Early Childhood Home Visiting dollars to develop and sustain a robust network of evidence-based home visiting programs. Our findings suggest that the Family Foundations Home Visiting program is successfully reaching priority populations and communities at risk of poor maternal and child health outcomes. More fully realizing the program's potential to promote health equity at scale may require additional investments to extend services to unserved and underserved populations and communities.

Acknowledgement: The authors would like to acknowledge Meghan Majors, MPH, MSW, whose work was essential for the development of this article.

Funding/Support: This work was supported with funding from the Maternal Infant and Early Childhood Home Visiting Program, US Department of Health and Human Services, Health Resources and Services Administration (X10MC43618).

Financial Disclosures: None declared.

REFERENCES

1. Jackie Walorski Maternal and Child Home Visiting Reauthorization Act of 2022, H.R. 8876, 117th Cong. (2021-2022). Accessed June 25, 2024. https://www.congress.gov/bill/117th-congress/house-bill/8876

2. Congressional Research Service. In focus: Maternal, Infant, and Early Childhood Home Visiting Program. Updated August 29, 2023. Accessed June 25, 2024. https://crsreports.congress.gov/product/pdf/IF/IF10595

3. Filene JH, Kaminski JW, Valle LA, Cachat P. Components associated with home visiting program outcomes: a meta-analysis. *Pediatrics*. 2013;132(suppl 2):S100-S109. doi:10.1542/peds.2013-1021H

4. Sweet MA, Appelbaum MI. Is home visiting an effective strategy? a meta-analytic

review of home visiting programs for families with young children. *Child Dev.* 2004;75(5):1435-1456. doi:10.1111/j.1467-8624.2004.00750.x

5. The Maternal, Infant, and Early Childhood Home Visiting Program. Health Resources and Services Administration, Maternal and Child Health Bureau. June 2024. Accessed June 25, 2024. https://mchb.hrsa.gov/sites/default/files/mchb/about-us/program-brief.pdf

6. Braveman P, Gottlieb L. The social determinants of health: it's time to consider the causes of the causes. *Public Health Rep*. 2014;129(suppl 2):19-31. doi:10.1177/00333549141291S206

7. Mitchell A, Heisler, EJ. Bipartisan Budget Act of 2018 (P.L. 115-123): CHIP, public health, home visiting, and Medicaid provisions in Division E. Congressional Research Service. Report R45136. March 20, 2018. Accessed June 25, 2024. https://sgp.fas.org/crs/misc/R45136.pdf

8. Wisconsin Maternal, Infant, and Early Childhood Home Visiting: statewide needs assessment update. Wisconsin Department of Children and Families. 2020. Accessed June 25, 2024. https://dcf.wisconsin.gov/files/cwportal/prevention/wi-update-narrative.pdf

9. American Community Survey: ACS 5-year estimates detailed tables. Table B05010: ratio of income to poverty level in the past 12 months by nativity of children under 18 years in families and subfamilies by living arrangements and nativity of parents. United States Census Bureau. 2021. Accessed June 25, 2024. https://data.census.gov/table/ACSDT5Y2021.B05010?q=B05010&y=2021

10. CDC WONDER: natality information. Centers for Disease Control and Prevention. Updated September 18, 2024. Accessed December 18, 2024. https://wonder.cdc.gov/natality.html

11. Wisconsin Interactive Statistics on Health (WISH) query system: birth counts module. Wisconsin Department of Health Services. Updated May 10, 2023. Accessed June 25, 2024. https://www.dhs.wisconsin.gov/wish/birth/index.htm

12. Lipari RN, Van Horn SL. Children living with parents who have a substance use disorder. In: *The CBHSQ Report.* Substance Abuse and Mental Health Services Administration (US); August 24, 2017.1-7. Accessed June 25, 2024. https://www.ncbi.nlm.nih.gov/books/NBK464590/

13. Noelke C, McArdle N, Baek M, et al. *Child Opportunity Index 2.0 Technical Documentation.* diversitydatakids.org; January 15, 2020. Accessed June 25, 2024. https://www.diversitydatakids.org/sites/default/files/2020-02/ddk_coi2.0_technical_documentation_20200212.pdf

14. Mersky JP, Jeffers NK, Lee CP, Shlafer RJ, Jackson DB, Gómez A. Linking adverse experiences to pregnancy and birth outcomes: a life course analysis of racial and ethnic disparities among low-income women. *J Racial Ethn Health Disparities.* 2024;11(3):1741-1753. doi:10.1007/s40615-023-01647-w

15. Mersky JP, Janczewski CE. Racial and ethnic differences in the prevalence of adverse childhood experiences: findings from a low-income sample of U.S. women. *Child Abuse Negl.* 2018;76:480-487. doi:10.1016/j.chiabu.2017.12.012

16. Parker MA, Weinberger AH, Eggers EM, Parker ES, Villanti AC. Trends in rural and urban cigarette smoking quit ratios in the US from 2010 to 2020. *JAMA Netw Open.* 2022;5(8):e2225326. doi:10.1001/jamanetworkopen.2022.25326

17. Probst JC, Zahnd WE, Hung P, Eberth JM, Crouch EL, Merrell MA. Rural-urban mortality disparities: variations across causes of death and race/ethnicity, 2013-2017. *Am J Public Health*. 2020;110(9):1325-1327. doi:10.2105/AJPH.2020.305703

18. Zeng D, You W, Mills B, Alwang J, Royster M, Anson-Dwamena R. A closer look at the rural-urban health disparities: insights from four major diseases in the Commonwealth of Virginia. *Soc Sci Med*. 2015;140:62-68. doi:10.1016/j.socscimed.2015.07.011

19. Grubesic TH. Zip codes and spatial analysis: problems and prospects. *Socioecon Plan Sci.* 2008;42(2):129-149. doi:10.1016/j.seps.2006.09.001

20. Wisconsin Interactive Statistics on Health (WISH) query system: annual number of Wisconsin births, 1990-2022. Wisconsin Department of Health Services. Updated February 15, 2024. Accessed August 26, 2024. https://www.dhs.wisconsin.gov/wish/birth/data.htm

21. Supplee LH, Duggan A. Innovative research methods to advance precision in home visiting for more efficient and effective programs. *Child Dev Perspect.* 2019;13(3):173-179. doi:10.1111/cdep.12334

22. Haroz EE, Ingalls A, Kee C, et al. Informing precision home visiting: identifying meaningful subgroups of families who benefit most from family spirit. *Prev Sci.* 2019;20(8):1244-1254. doi:10.1007/s11121-019-01039-9

23. World Health Organization. Closing the gap in a generation: health equity through action on the social determinants of health – final report of the Commission on Social Determinants of Health. August 27, 2008. Accessed August 26, 2024. https://www.who.int/publications/i/item/WHO-IER-CSDH-08.1

24. US Department of Health and Human Services. Healthy People 2030 framework. Accessed August 26, 2024. https://health.gov/healthypeople/about/healthy-people-2030-framework

Medicaid Enrollment Gaps Before, During, and After Pregnancy: Evidence from Administrative Data

Marina C. Jenkins, PhD; Christine Piette Durrance, PhD; Deborah B. Ehrenthal, MD, MPH

ABSTRACT

Introduction: Consistent access to health care before, during, and after pregnancy is critical in the United States, where high rates of maternal morbidity and pregnancy-related mortality persist. Medicaid plays a critical role in financing health care coverage for pregnancy and childbirth in the US, including postpartum care.

Methods: We used Wisconsin birth certificate records linked to Medicaid enrollment files for 2009 through 2018 to determine maternal Medicaid coverage spanning the 12 months pre-pregnancy to 12 months postpartum. Covariates included age, race/ethnicity, parity, education, and marital status. Analysis included descriptive statistics and log-binomial regression to predict adjusted risk of postpartum Medicaid coverage loss.

Results: Of 267 416 Medicaid-covered births in our sample, 50.5% (n=134 970) were continuously enrolled while 33.1%, (n=88 425) were never enrolled during the 12 months pre-pregnancy. Most (97.9%, n=261 713) were enrolled at some time during the prenatal period, and a majority of mothers (86.1%, n=230 325) were enrolled consistently throughout the first postpartum year. Postpartum unenrollment peaked in month 3, when 34.2% of unenrollment occurred. Those younger, married, and with lower parity had higher risk of unenrollment. Notably, those reporting non-Hispanic Black were at the lowest risk, while non-Hispanic Asian/Pacific Islanders were at a higher risk of unenrollment.

Conclusions: The extension of postpartum coverage to 90 days may address one-third of the postpartum Medicaid loss observed, postponing coverage loss an additional month. A full 12-month postpartum Medicaid extension would support postpartum health by ensuring health care access during this critical period.

INTRODUCTION

Prenatal care is a central strategy to improve birth outcomes and reduce disparities in infant and maternal mortality. In 2006, recommendations for improvements in preconception care were made by the US Centers for Disease Control and Prevention and the American College of Obstetricians and Gynecologists.[1] Preconception care provides the opportunity to identify and address modifiable risk factors and improve maternal and infant health.[2] More recently, attention has focused on postpartum care, sometimes termed the fourth trimester, which provides follow-up care for delivery complications, family planning, and care for the management of chronic conditions.[3]

Ensuring consistent access to health care before, during, and after pregnancy is especially critical in the US, where high rates of maternal morbidity and pregnancy-related mortality persist.[4,5] Medicaid currently covers pregnancy-related health care for approximately 41% of the nearly 4 million annual births.[6] In addition to traditional Medicaid, the Children's Health Insurance Program (CHIP) is used for pregnancy coverage in some settings. Federal Medicaid requires minimum coverage to extend through the month that includes the 60th postpartum day. Following the passage of the Affordable Care Act (ACA), states that expanded Medicaid did so by expanding adult eligibility up to 138% of the federal poverty level (FPL), which is considerably lower than most states' pregnancy eligibility.[7] Children of mothers eligible for or receiving Medicaid during pregnancy automatically qualify for coverage through the first year of life.

• • •

Author Affiliations: Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Jenkins); La Follette School of Public Affairs, University of Wisconsin–Madison, Madison, Wisconsin (Durrance); Social Science Research Institute and Professor, Biobehavioral Health, The Pennsylvania State University, University Park, Pennsylvania (Ehrenthal).

Corresponding Author: Marina Jenkins, PhD, Johns Hopkins University, 615 N Wolfe St, Baltimore, MD 21205; phone 814.863.7563; email mjenki51@jh.edu; ORCID ID 0000-0002-5158-2894

Given that those with higher income levels can qualify for Medicaid during pregnancy but not after delivery, it is not surprising that enrollment changes and disruptions are common postpartum.[8] Analysis of the Medical Expenditure Panel Survey (pre-ACA) showed about half of those who had been uninsured during 9 months prior to pregnancy acquired Medicaid coverage for prenatal care; however, 5% of women with Medicaid reported coverage disruptions during the first 6 months postpartum.[8] Post-ACA, data from the National Health Interview Survey showed rates of uninsurance during pregnancy fell significantly, especially for low income mothers.[9] However, a study using the Pregnancy Risk Assessment Monitoring System (PRAMS) survey of postpartum mothers in 43 states found 22% of those with a Medicaid-covered live birth were uninsured after 3 months postpartum, and rates of coverage loss were 3 times higher in non-Medicaid expansion states than expansion states.[10] Another study using PRAMS data for 2015-2018 found that over half of mothers with Medicaid-covered births experienced uninsurance in the preconception and postpartum periods.[11]

Table 1. Characteristics of Individuals with Postpartum Medicaid Unenrollment Following a Live Birth, Wisconsin 2009-2018

	Overall N=267 416	Ever Unenrolled Postpartum N = 37 091	Continuous Coverage Postpartum N = 230 325
Variable	**% (n)**	**% (n)**	**% (n)**
Age (years)			
<19	5.7 (15 329)	8.7 (3229)	5.3 (12 100)
19 – 24	44.3 (118 481)	34.6 (12 833)	45.9 (105 648)
25 – 34	41.4 (110 612)	48.6 (18 011)	40.2 (92 601)
35+	8.6 (22 994)	8.1 (3018)	8.7 (19 976)
Race/ethnicity			
non-Hispanic White	54.6 (146 046)	59.0 (21 888)	53.9 (124 158)
non-Hispanic Black	19.4 (51 890)	14.7 (5468)	20.2 (46 422)
Hispanic	16.1 (43 176)	15.1 (5588)	16.3 (37 588)
non-Hispanic Asian/Pacific Islander	1.9 (5171)	2.8 (1036)	1.8 (4135)
non-Hispanic Other/multiple/unknown	2.9 (7727)	3.0 (1131)	2.9 (6596)
Parity			
First birth	55.9 (149 390)	65.2 (24 179)	54.4 (125 211)
Second or greater birth	44.0 (117 681)	34.7 (12 854)	45.5 (104 827)
Marital status			
Married	32.4 (86 774)	42.3 (15 695)	30.9 (71 079)
Unmarried	67.5 (180 625)	57.7 (21 390)	69.1 (159 235)
Completed education			
Not high school graduate	20.6 (55 071)	20.4 (7570)	20.6 (47 501)
High school graduate	41.0 (109 760)	35.8 (13 281)	41.9 (96 479)
Some college or more	37.7 (100 692)	43.1 (15 968)	36.8 (84 724)

Because of differences in state Medicaid eligibility criteria, the duration of postpartum coverage varies across the country.[9,11-13] Since 2014, some states extended postpartum coverage through Section 1115 Waivers.[14] Others shifted towards permanent policy pathways, including provisions in the American Rescue Plan Act (2021) to extend postpartum coverage to 12 months.[15]

In 2022, the State of Wisconsin submitted a 1115 Postpartum Coverage Demonstration Waiver to expand postpartum Medicaid coverage. However, Wisconsin requested a modest extension of coverage from 60 to 90 days.[16] It is of critical importance, therefore, to understand Wisconsin Medicaid insurance loss patterns in the postpartum period to better understand how this policy change may impact access to health care coverage during the postpartum period.

METHODS

Study Setting

We studied all Wisconsin residents delivering in-state live births from 2009 through 2018. Health disparities in Wisconsin are notable; the pregnancy-related maternal mortality ratio is 5 times higher for Black mothers than White mothers, and the Black infant mortality rate is among the highest in the US.[17,18] Though Wisconsin did not expand Medicaid, the state historically has had more generous eligibility thresholds for pregnant people (300% FPL) and adults (100% FPL, previously 200%) than all nonexpansion states, with a threshold for pregnancy coverage on par with the most generous expansion states.[19,20] In 2014, changes in the Wisconsin Medicaid program led to new premiums for some adults with incomes >100% FPL, as well as elimination of prior enrollment waitlists.[21]

During the study period, 3 Medicaid coverage plans were available to pregnant individuals through BadgerCare Plus (BC Plus). BC Plus provided coverage for low-income residents using funding from Medicaid and CHIP. The BC Plus Prenatal Program, funded through CHIP, provided prenatal coverage for those ineligible for BC Plus because of their immigration or incarceration status. BC Plus Emergency Services covered emergency care for those who did not qualify for either BC Plus due to their immigration status or the Prenatal Program. Only BC Plus included comprehensive postpartum coverage through the end of the month in which the 60th day occurs; those covered by the Emergency Services and Prenatal Programs qualify for emergency services coverage only.[22] Individuals not enrolled at the time of obstetrical delivery could receive coverage for delivery services only.

Data Sources and Study Sample

We used data from Big Data for Little Kids (BD4LK), an integrated data source that merges birth certificate records

of all Wisconsin resident in-state live births with the Institute for Research on Poverty's Wisconsin Administrative Data Core, which includes Medicaid claims and enrollment files. Files include coverage from both Medicaid and CHIP sources and, henceforth, coverage from either source is referred to as Medicaid coverage.[23]

This study was approved by the University of Wisconsin-Madison Institutional Review Board. "Mothers" is used throughout this study to align with terminology used in Medicaid policy and previous literature, but we recognize that health care and insurance during the perinatal period includes birthing people of all genders.

The study sample included all 2009-2018 birth records that linked to a paid Medicaid claim for delivery. For plural births, we selected the first delivery; if mothers had multiple live, Medicaid-covered deliveries during our sample period, each was represented as a separate observation. From a sample of 268 011 Medicaid-covered live births to 181 294 unique mothers, we excluded those missing both a clinical estimate of gestational age and last menstrual period (n = 577) because we could not determine the prenatal period and a small number (n=18) of mothers with multiple birth records and birth intervals between 4 and 240 days that were shorter than the gestational age of the later birth, as these records were considered to contain administrative errors. From the original sample (n = 267 416), 99.8% were included in the primary analysis. In the exploratory analysis of infant Medicaid/CHIP coverage, 98.9% of maternal enrollment records (n = 264 372) were linked to an infant enrollment record.

Table 2. Medicaid Enrollment Rates Among all Mothers with a Medicaid-Covered Live Birth, by Coverage Period, Wisconsin 2009-2018

Period	Continuous Coverage[a] % (n)	Some Coverage % (n)	No Coverage % (n)
Pre-pregnancy, 12 months			
All births	50.5 (134 970)	16.5 (44 021)	33.1 (88 425)
First live births	35.2 (52 562)	17.1 (25 573)	47.7 (71 255)
Prenatal			
All births	97.9 (261 713)	n/a[b]	2.1 (5703)
First live births	97.4 (145 467)	n/a[b]	2.6 (3923)
Postpartum, 12 months			
All births	86.1 (230 325)	12.6 (33 669)	1.3 (3422)
First live births	83.8 (125 211)	14.9 (22 213)	1.3 (1966)

[a]Continuous coverage allows for up to 2 months of enrollment gaps (or administrative missingness) during that period.

[b]There is presumptive eligibility for pregnant individuals; as such, we assume continuous coverage throughout the prenatal period once enrolled.

Table 3. Relative Risk of Postpartum Medicaid Unenrollment Following a Live Birth, Adjusted for All Covariates, Wisconsin 2009-2018

Variable	Adjusted Relative Risk (95% CI)[a]
Age Group, years	
<19	1.68 (1.62 – 1.74)
19 – 24	ref
25 – 34	1.12 (1.10 – 1.15)
35+	1.09 (1.04 – 1.13)
Race/ethnicity	
Non-Hispanic White	1.22 (1.18 – 1.25)
Non-Hispanic Black	ref
Hispanic	1.09 (1.05 – 1.13)
Non-Hispanic Asian/Pacific Islander	1.36 (1.29 – 1.43)
Non-Hispanic Other/multiple/unknown	1.18 (1.13 – 1.25)
Parity	
First live birth	1.57 (1.54 – 1.61)
Second or greater birth	ref
Marital status	
Married	1.61 (1.58 – 1.65)
Unmarried	ref

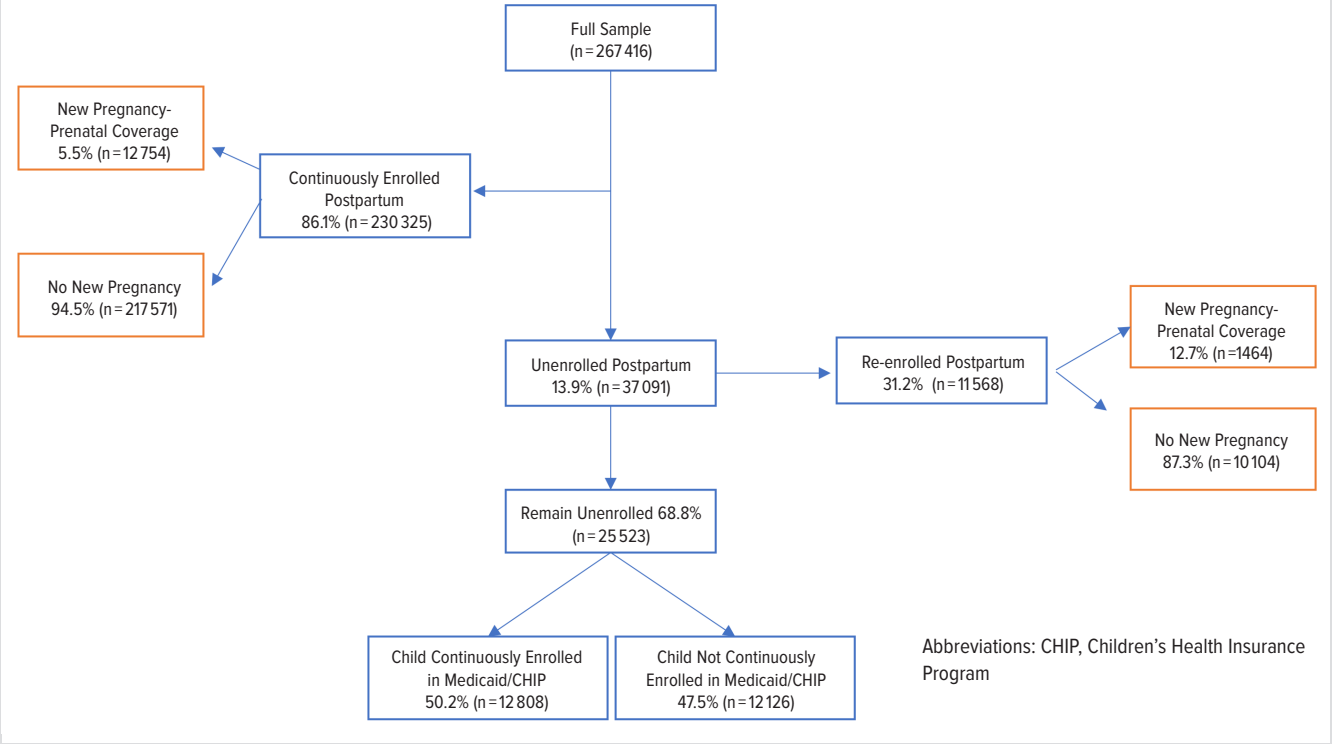
[a]Results from a log-binomial regression where the dependent variable is any postpartum unenrollment (regardless of reenrollment) adjusted for age group, race/ethnicity, parity, and marital status, clustered births from same mother using general estimating equations.

Variables

The preconception period was defined as the 12 months prior to the month of estimated date of conception (EDC); the prenatal period spanned the month of the EDC through the delivery month; and the postpartum period was the 12 months following the delivery month. Therefore, Medicaid enrollment data were extracted for 2008-2019 to represent the full observation period for all mothers. If the clinical estimate of gestational age was missing (n = 309), last menstrual period was used to determine the EDC month.

We used Medicaid enrollment data, which are intended for administrative – not research – purposes. As such, enrollees may have gaps in enrollment for reasons related to eligibility changes or switching plans, not actual disenrollment. We chose to consider a duration of 2 months as administrative missingness based on guidance of those familiar with the Wisconsin Medicaid enrollment data, both at the Institute for Research on Poverty and the Wisconsin Department of Health Services. This definition is more conservative than a 1-month gap, enabling better identification of true disenrollment in Medicaid during the postpartum period. During the 12-month preconception and postpartum periods, mothers were categorized as having continuous coverage if there were no enrollment gaps longer than 2 months, some coverage if unenrolled for 3 or more months, or no coverage if there was no enrollment. Because there is presumptive Medicaid eligibility during pregnancy if enrolled prior to delivery, we assumed continuous coverage throughout the prenatal period for the some

Figure 1. Medicaid Unenrollment During the Postpartum Period Among Mothers With Medicaid-Covered Live Births, Wisconsin 2009-2018



coverage group. We used medical status codes for the Medicaid plan to identify coverage for a subsequent pregnancy during the postpartum year.

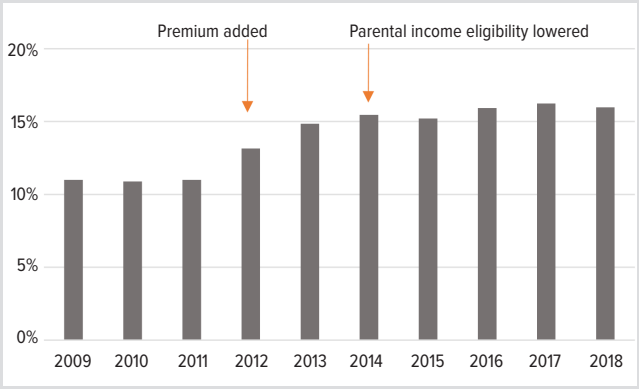
We considered reasons for mothers' changes in enrollment during the first postpartum year by considering their infants' enrollment in Medicaid/CHIP. In Wisconsin, infants are automatically eligible for CHIP coverage for 12 months following a Medicaid-covered delivery. An infant not enrolled in Medicaid/CHIP may have moved out of state or become covered by a parent's private insurance. We explored infant postpartum unenrollment among mothers who unenrolled postpartum as a proxy for a shift from Medicaid to private insurance.

Covariates provided by the birth records included age at delivery (<19, 19-24, 25-34, 35+), race/ethnicity (non-Hispanic White [hereafter White], non-Hispanic Black [hereafter Black], Hispanic, non-Hispanic Asian/Pacific Islander [hereafter Asian/Pacific Islander], and non-Hispanic Other race [hereafter Other], including multiple races), marital status (unmarried, married), completed education (no high school, high school, some college), and parity (first birth, second or greater birth).

Statistical Analysis

We used descriptive statistics to summarize each covariate and outcome. Main effects log-binomial regression models were used to estimate relative risk of postpartum unenrollment associated with maternal demographic characteristics, using generalized estimating equation to account for correlation between births from the same mother. We included parity and demographic characteristics as covariates based on known differences in Medicaid eligibility for childless adults and prior research.[8] We tested the association between birth year and postpartum unenrollment using a chi-square test for trend. All analyses were conducted using SAS software, Version 9.4 (SAS Institute Inc, Cary, North Carolina).

Figure 2. Postpartum Medicaid Unenrollment in Wisconsin by Birth Year, 2009-2018



RESULTS

Table 1 shows the characteristics of the overall sample (N=267 416), those unenrolled postpartum (n=37 091), and those continuously enrolled postpartum (n=230 325). On aver-

age, mothers in the sample were 26 years of age (SD 5.6) at delivery, 54.6% (n=146 046) were White, 55.9% (n=149 390) were primiparous, and 67.5% (n=180625) were unmarried.

Medicaid Enrollment

Mothers' enrollment varied by period (Table 2). During the 12 months pre-pregnancy, approximately half (50.5%, n = 134 970) were continuously enrolled, while a third (33.1%, n = 88 425) were never enrolled. Nearly all were enrolled at some time during the prenatal period (97.9%, n = 261 713), though some were never enrolled (2.1%, n = 5703) and a subset of these were covered for delivery services only, with no other coverage in the pre-pregnancy, prenatal, or postpartum period (0.8%, n = 2026). Enrollment patterns during the pre-pregnancy period varied by parity. Relative to all mothers, first-time mothers had lower continuous coverage during the 12 months prior to pregnancy (35%, n = 52 562) and a higher fraction (47.7%, n = 71 255) were not enrolled in Medicaid at any time during the year prior to conception. Most mothers (86.1%, n=230325) were consistently enrolled throughout the first postpartum year.

Postpartum Unenrollment

As shown in Table 1, of the 37091 mothers who unenrolled postpartum, 48.6% (n=18 011) were age 25 to 34; 14.7% (n = 5468) were Black, 15.1% (n = 5588) were Hispanic, and 59.0% (n = 21 888) were White. Younger age, lower parity, and being married were associated with a greater risk of postpartum Medicaid unenrollment in the adjusted, multivariable log-binomial regression model (Table 3). Notably, those reporting Black were at the lowest risk, while Asian/Pacific Islanders were at a higher risk of unenrollment.

The postpartum enrollment flow diagram (Figure 1) shows the majority of all 267 416 mothers (86.1%, n = 230 325) remained enrolled throughout the 12 months. This included a small number with a new pregnancy (5.5%, n = 12 754) during that year and who may have maintained enrollment because of more generous pregnancy eligibility. The balance, 13.9% (n = 37 091) unenrolled at some point during the postpartum year. A small percentage (1.3%, n = 3422) lost enrollment immediately following delivery. The peak of unenrollment occurred in month 3, when 34.2% of unenrollment occurred, likely reflecting Medicaid loss following the change in eligibility occurring 60 days postpartum. By the fourth postpartum month, more than half (54.3%) were no longer enrolled. Some (31.2%, n = 11568) re-enrolled before the end of the postpartum period, but a majority (68.8% , n = 25 523) remained unenrolled. A small percentage (12.7%, n = 1464) regained enrollment with subsequent pregnancy. On average, mothers who re-enrolled experienced a gap in Medicaid coverage of 5.3 months during the postpartum period.

Most of the 264 372 infants (89.9%, n = 237 575) were continuously enrolled in Medicaid/CHIP for the first year; only a small minority (1.94%, n = 5127) were never enrolled. Among all mothers who remained unenrolled during the postpartum period, 50.2% (n = 12 808) of their children were enrolled in Medicaid/CHIP through the first year of life and, therefore, had not been picked up by parental private insurance (Figure 1), suggesting that half of the women who remained unenrolled after losing Medicaid coverage were likely uninsured.

Postpartum enrollment patterns changed during the study period. As shown in Figure 2, the percentage of mothers who lost enrollment postpartum increased significantly from 11.0% in 2009 to 16.0% in 2018 ($P < .001$). Notable changes were an absolute increase of 4.5% between 2011 and 2014 and another increase of 1.0% between 2015 and 2017.

DISCUSSION

Using linked administrative data for 2009-2018, we described patterns of Wisconsin Medicaid enrollment during the preconception, prenatal, and postpartum periods. We identified significant enrollment gaps before and after pregnancy that may limit access to recommended health care during these critical periods. Our detailed analysis of postpartum enrollment found nearly 14% of mothers delivering a live birth were unenrolled in Medicaid during the first postpartum year. The peak of unenrollment occurred in month 3, when 34.2% of unenrollment occurred, likely reflecting Medicaid loss following the 60-day postpartum threshold.

Our estimates of insurance coverage gaps are consistent with studies using data from PRAMS.[11] While our observed rates of postpartum Medicaid insurance loss are lower than pooled national rates, they do closely mirror those of a state-level analysis of PRAMS that found a larger proportion of Wisconsin mothers reported having maintained postpartum coverage than the average across the 43 US states included in the study.[10] Based on self-reported coverage during 2015-2018, postpartum unenrollment rates in Wisconsin were among the lowest in the US, potentially explained by the state's more generous income limits. However, in contrast to improvements in postpartum coverage seen across Medicaid expansion states, the trend over this study period suggests postpartum coverage loss became more common following the state's 2014 changes in eligibility policies, which lowered adult coverage from 200% to 100% FPL.[21]

Our findings suggest that postpartum Medicaid loss was more likely following first births and among mothers who were younger or married and least common among those who identified as Black. Higher rates of Medicaid loss among younger and new mothers may result from inexperience navigating the benefit system. Additionally, mothers with prior live births likely have larger households, impacting FPL calculations and the possibility of Medicaid coverage. Married mothers may be more likely to move to spousal private insurance following delivery. Unenrollment among married mothers may represent a transition to spousal private insurance following delivery, rather than insurance loss. The

individual demographic factors (eg, race/ethnicity) we found associated with postpartum unenrollment differ somewhat from some prior research.[10,11] Wisconsin ranks 49th in Black-White income disparities, with 39% of Black Wisconsinites living in poverty in 2015.[24] Therefore, it is possible that Black mothers are more likely to maintain postpartum eligibility than non-Black mothers because they continue to meet the income-based eligibility criteria.

There are important limitations to this study. We accounted for 2-month administrative gaps to avoid overestimating preconception and postpartum Medicaid loss. However, it is possible our conservative measures excluded real 1- to 2-month coverage gaps in some cases for the approximately 3% of mothers with this level of missingness. Our definition of unenrollment also includes mothers who were not fully enrolled during the study period; however, as we were interested in examining postpartum coverage for all mothers with a Medicaid-covered delivery, we consider this small subset to be unenrolled postpartum for our purposes.

For both mothers and infants, lack of postpartum enrollment may reflect movement out of state, acquisition of private insurance coverage, or other missingness. Our estimates of postpartum Medicaid unenrollment likely overestimate the percentage of mothers without postpartum health insurance. We attempted to address this limitation by using infant enrollment data to estimate the fraction of mothers who were uninsured. However, our proxy for mother's uninsurance may be inaccurate, as mothers may choose to keep their infant on Medicaid for reasons including the comprehensiveness of Medicaid coverage, the window for newborn enrollment in commercial insurance, the disruption of switching insurance, and, perhaps most importantly, that Medicaid is free or very low cost for infants. Despite this limitation, our rate of maternal postpartum uninsurance is lower than other sources of self-reported uninsurance for Wisconsin new mothers, suggesting our estimate is not inflated.[25]

There are also important strengths. The unique level of granularity and data permits learning opportunities for Wisconsin and other states. Enrollment files permit observation of relevant enrollment patterns that are relevant to the state's recent Section 1115 Waiver. By using birth records and enrollment files, we have the full population—not a weighted sample—and are able to confirm deliveries were paid for by Medicaid. This also ensures that we are not considering limited coverage plans that women may report as comprehensive health insurance in some survey studies. Unlike cross-sectional studies, we can identify the timing of unenrollment and reenrollment during the postpartum period and reenrollment through a subsequent pregnancy.

Policy Implications

Pregnancy is a time when important short- and long-term health risks may be identified, creating opportunities for prevention. Without consistent access to health care, these opportunities for prevention are lost, and needed health care will be provided in expensive acute care settings, which are ill-equipped for follow-up care.

Currently, federal and state policy attention is focused on postpartum Medicaid expansion. Medicaid faced a federal maintenance of eligibility requirement, prohibiting programs from disenrolling Medicaid recipients during the COVID-19 crisis, effectively expanding Medicaid to postpartum individuals. To improve maternal and infant outcomes, as well as reduce racial disparities, the American Rescue Plan Act offered states the opportunity to expand Medicaid coverage through 12 months postpartum. As of January 2023, over half of states have implemented extensions, and Wisconsin has requested approval to increase coverage from 60 to 90 days postpartum.[16]

CONCLUSIONS

While 34% of the postpartum Medicaid loss we observed occurred between 60 and 90 days, the proposed Section 1115 Waiver would, in most cases, add only 1 additional month of coverage. A full 12-month postpartum Medicaid extension would support postpartum health by enabling greater continuity and quality of care over this critical period.

Funding/Support: This work was supported in part by a grant to Ehrenthal from the Eunice Kennedy Shriver National Institutes for Child Health and Human Development NIH R01 #HD102125-01).

Financial Disclosures: None declared.

Acknowledgements: Data were provided by the Wisconsin Department of Health Services. The content is solely the responsibility of the authors and does not necessarily represent the official views of supporting agencies. Additionally, supporting agencies do not certify the accuracy of the analyses presented. Portions of this work were presented virtually at the CityMatCH Leadership and MCH Epidemiology Conference December, 2021.

REFERENCES

1. Johnson K, Rosenbaum S, Handley M. The next steps to advance maternal and child health in Medicaid: filling gaps in postpartum coverage and newborn enrollment. *Health Affairs Blog*. January 9, 2020. Accessed June 23, 2023. https://www.healthaffairs.org/content/forefront/next-steps-advance-maternal-and-child-health-medicaid-filling-gaps-postpartum-coverage

2. Raghuraman N, Tuuli MG. Preconception care as an opportunity to optimize pregnancy outcomes. *JAMA*. 2021;326(1):79-80. doi:10.1001/jama.2020.27244

3. Tully KP, Stuebe AM, Verbiest SB. The fourth trimester: a critical transition period with unmet maternal health needs. *Am J Obstet Gynecol.* 2017;217(1):37-41. doi:10.1016/j.ajog.2017.03.032

4. D'Alton ME, Friedman AM, Bernstein PS, et al. Putting the "M" back in maternal-fetal medicine: a 5-year report card on a collaborative effort to address maternal morbidity and mortality in the United States. *Am J Obstet Gynecol.* 2019;221(4):311-317.e1. doi:10.1016/j.ajog.2019.02.055

5. Moaddab A, Dildy GA, Brown HL, et al. Health care disparity and pregnancy-related mortality in the United States, 2005-2014. *Obstet Gynecol.* 2018;131(4):707-712. doi:10.1097/AOG.0000000000002534

6. Births financed by Medicaid. Kaiser Family Foundation. Updated 2024. Accessed June 23, 2023. https://www.kff.org/8140f64/

7. Brooks T, Gardner A, Tolbert J, Dolan R, Pham O. Medicaid and CHIP eligibility and enrollment policies as of January 2021: findings from a 50-state survey. Kaiser Family Foundation; March 8, 2021. Accessed June 23, 2023. https://www.kff.org/report-section/

medicaid-and-chip-eligibility-and-enrollment-policies-as-of-january-2021-findings-from-a-50-state-survey-report/

8. Daw JR, Hatfield LA, Swartz K, Sommers BD. Women in the United States experience high rates of coverage 'churn' in months before and after childbirth. *Health Aff (Millwood*). 2017;36(4):598-606. doi:10.1377/hlthaff.2016.1241

9. Daw JR, Sommers BD. The Affordable Care Act and access to care for reproductive-aged and pregnant women in the United States, 2010-2016. *Am J Public Health.* 2019;109(4):565-571. doi:10.2105/AJPH.2018.304928

10. Daw JR, Kozhimannil KB, Admon LK. Factors associated with postpartum uninsurance among Medicaid-paid births. *JAMA Health Forum.* 2021;2(6):e211054. doi:10.1001/jamahealthforum.2021.1054

11. Johnston EM, McMorrow S, Alvarez Caraveo C, Dubay L. Post-ACA, more than one-third of women with prenatal Medicaid remained uninsured before or after pregnancy. *Health Aff (Millwood).* 2021;40(4):571-578. doi:10.1377/hlthaff.2020.01678

12. Gordon SH, Sommers BD, Wilson IB, Trivedi AN. Effects of Medicaid expansion on postpartum coverage and outpatient utilization. *Health Aff (Millwood).* 2020;39(1):77-84. doi:10.1377/hlthaff.2019.00547

13. McMorrow S, Dubay L, Kenney GM, Johnston EM, Caraveo CA. Uninsured new mothers' health and health care challenges highlight the benefits of increasing postpartum Medicaid coverage. Urban Institute. May 2020. Accessed June 23, 2023. https://www.urban.org/sites/default/files/publication/102296/uninsured-new-mothers-health-and-health-care-challenges-highlight-the-benefits-of-increasing-postpartum-medicaid-coverage_0.pdf

14. Eckert E. It's past time to provide continuous Medicaid coverage for one year postpartum. *Health Affairs Blog*. February, 6 2020. Accessed date?. https://www.healthaffairs.org/content/forefront/s-past-time-provide-continuous-medicaid-coverage-one-year-postpartum

15. American Rescue Plan Act of 2021. H.R. 1319, 117th Cong (2021-2022). Accessed June 23, 2023. https://www.congress.gov/bill/117th-congress/house-bill/1319/text#toc-HD0A062309C1143928EF82EC5845217C3/

16. Medicaid postpartum coverage extension tracker. Kaiser Family Foundation. Updated August 1, 2024. Accessed June 22, 2023. https://www.kff.org/medicaid/issue-brief/medicaid-postpartum-coverage-extension-tracker/

17. Matthews TJ, Ely DM, Driscoll AK. State variations in infant mortality by race and Hispanic origin of mother, 2013-2015. *NCHS Data Brief.* 2018;(295):1-8. https://www.cdc.gov/nchs/data/databriefs/db295.pdf

18. Maternal mortality and morbidity. Wisconsin Department of Health Services. Updated October 3, 2024. Accessed June 23, 2023. https://www.dhs.wisconsin.gov/mch/maternal-mortality-and-morbidity.htm

19. Haley JM, Johnston EM, Hill I, Kenney GM, Thomas TW. The public health insurance landscape for pregnant and postpartum women: state and federal policies in 2020. Urban Institute. January 29, 2021. Accessed June 23, 2023. https://www.urban.org/sites/default/files/publication/103561/the-public-health-insurance-landscape-for-pregnant-and-postpartum-women_0.pdf

20. Garfield R, Damico, A. The coverage gap: uninsured poor adults in states that do not expand Medicaid – an update. Henry J. Kaiser Family Foundation. October 2017. Accessed June 23, 2023. http://resource.nlm.nih.gov/101717244

21. Gates, A, Rudowitz, R. Wisconsin's BadgerCare program and the ACA. Kaiser Commission on Medicaid and the Uninsured. February 25, 2014. Accessed June, 23, 2023. https://www.kff.org/medicaid/fact-sheet/wisconsins-badgercare-program-and-the-aca/

22. BadgerCare Plus eligibility handbook. Wisconsin Department of Health Services. Release 21-02. August 30, 2021. Accessed June 23, 2023. https://www.dhs.wisconsin.gov/publications/p10171-21-02.pdf

23. Mallinson DC, Grodsky E, Ehrenthal DB. Gestational age, kindergarten-level literacy, and effect modification by maternal socio-economic and demographic factors. *Paediatr Perinat Epidemiol.* 2019;33(6):467-479. doi:10.1111/ppe.12588

24. Jones M. Significant changes in Wisconsin poverty: comparisons of the Census Bureau's American Community Survey 2010-2014 and 2005-2009 5-year estimates. Applied Population Lab, University of Wisconsin-Madison. December 9, 2015. Accessed June 23, 2023. https://apl.wisc.edu/data-briefs/acs-poverty-15

25. McMorrow S, Kenney G. Despite progress under the ACA, many new mothers lack insurance coverage. *Health Affairs Blog*. September 19, 2018. Accessed June 23, 2023. https://www.healthaffairs.org/content/forefront/despite-progress-under-aca-many-new-mothers-lack-insurance-coverage

Intimate Partner Violence Screening in an Obstetrics Clinic: A Retrospective Study

Ankita Sarawagi, MD; Mychoua Vang, MS; Ke Yan, PhD; Linda B. Piacentine, PhD; Kimberly Gecsi, MD; Gisela Chelimsky, MD; Colleen Galambos, PhD; Teresa Jerofke-Owen, PhD; Heidi Paquette, PhD; Erin Schubert, PhD; Nilanjan Lodh, PhD

ABSTRACT

Introduction: Intimate partner violence (IPV) is a serious public health and human rights issue affecting at least 324 000 pregnant women annually. It also occurs at any age, with 1 in 3 women experiencing IPV in their lifetime. Abuse during pregnancy leads to direct and indirect harm to both the mother and child. It also is associated with increased rates of depression, posttraumatic stress disorder, placental abruption, uterine rupture, and hemorrhage. Due to the possibility of such morbidity, it is vital to identify women at risk of abuse and act as early as possible.

Objective/Methods: The objective of this study was to evaluate the current IPV screening practices at Froedtert & Medical College of Wisconsin's obstetrics and gynecology (OB/GYN) clinic before and after the implementation of a standardized screening protocol for IPV using the Humiliation, Afraid, Rape, Kick (HARK) tool. Data were collected via a retrospective chart review during April-September 2019-2021, with the tool going into effect in 2020.

Results: A continuously increasing number of screens occurred in 2020 and 2021 after screening standardization. While more screenings were conducted, overall positive screening rates were lower in 2021 compared to 2019 and 2020 ($P = 0.0008$ and $P = 0.0004$, respectively). In addition, there were significantly fewer positive screens for patients who were married or those with significant others compared to those who were single or legally separated, divorced, and widowed ($P = 0.0001$).

Conclusions: There was no significant difference in the positive screening rate between 2019 and 2020, but with more screenings performed in 2020, additional positive screens were picked up that otherwise may have been missed before using the standardized protocol. Overall, the implementation of a standardized screening protocol using the HARK tool increased screenings in the OB/GYN clinic, which can be replicated in other health care settings.

• • •

Author Affiliations: Medical College of Wisconsin, Milwaukee, Wisconsin (Sarawagi, Vang, Yan, Gecsi); Marquette University, Milwaukee, Wisconsin (Piacentine, Jerofke-Owen, Paquette, Lodh); Virginia Commonwealth University, Richmond, Virginia (Chelimsky); University of Wisconsin – Milwaukee, Milwaukee, Wisconsin (Galambos); Sojourner Family Peace Center – Milwaukee, Wisconsin (Schubert).

Corresponding Authors: Ankita Sarawagi, MD, Medical College of Wisconsin, Milwaukee, WI; email asarawagi@mcw.edu; Nilanjan Lodh, PhD, Department of Medical Laboratory Science, 560 N 16th St, Schroeder Complex 274, Milwaukee, WI 53201; phone 414.288.3404; email nilanjan.lodh@marquette.edu; ORCID ID 0000-0002-0363-3538

INTRODUCTION

Intimate partner violence (IPV) was a serious public health and human rights issue in the United States even before the COVID-19 pandemic, with 1 in 3 women experiencing IPV in their lifetime.[1] IPV is described as physical, sexual, or emotionally abusive acts or threats carried out by an intimate partner, including current and past partners of the same or opposite sex.[2,3] Certain aspects of the COVID-19 pandemic, such as shelter-in-place orders, increased unemployment rates, and school closures, have led to increased IPV rates of up to 40%, leading to the portrayal of IPV as the shadow pandemic.[2-4] Some risk factors associated with higher rates of abuse include young age (< 25 years old), single relationship status, minority race and ethnicity, and poverty defined as annual household income <$25 000.[5,6] While IPV can be present at any point during an individual's life, research during the perinatal period is particularly important due to an increase in the prevalence of IPV during this time, as well as IPV's negative impact on pregnancy outcomes, which may have long-term physical and mental health implications for both infants and postpartum women.[4,7,8]

Previous research indicates that 3% to 9% of women experience abuse during pregnancy. Also, approximately 1.5 million women experience some sort of assault every year in the US, and approximately 324 000 are pregnant at the time.[2,8,9] Unintended pregnancies carry an increased prevalence of abuse compared to intended pregnancies.[9] However, these statistics are considered underestimates due to unreported, missed, or unmeasured cases.[8,9]

IPV victims—especially those who are pregnant—are often reluctant to report their experience due to stigma, fear of losing custody of their children, fear of retaliation from their abusive partner, distrust of the medical and criminal legal fields, economic dependence on the abuser, and so forth.[10] Few victims (34%) ever seek medical care for IPV-related issues, and even fewer disclose the cause of their injury or condition once accessing care.[11]

Experiencing abuse during pregnancy leads to direct and indirect harm to both the mother and child. Women abused during pregnancy are more likely to miss prenatal appointments or delay seeking care, often waiting until the third trimester. These women are also at higher risk for poor nutrition associated with inadequate gestational weight gain and participation in high-risk behaviors, including smoking, alcohol, and substance use. All of these behaviors directly impact both short-term and long-term fetal and neonatal health outcomes. IPV exposure during the perinatal period may be related to increased maternal rates of depression and posttraumatic stress disorder, as well as pregnancy-associated deaths from homicide and suicide.[12,13] In 1 study, pregnant women hospitalized after an assault demonstrated increased risks of placental abruption, uterine rupture, and hemorrhage.[3,14] Studies also have shown that IPV is associated with an increased risk of preterm birth and low birth weight at the time of delivery.[2,14,15]

In addition to increased risks of poor health outcomes for pregnant women and the fetus, research found that IPV was experienced by 28% of female subjects of all ages seen in primary care settings, prompting the researchers to suggest that routine IPV screening practices be adopted in clinics that include women of all ages and throughout the lifespan.[1,16]

Because of its grave consequences, women during their pregnancy who are experiencing IPV need to be identified and approached about the issue as early as possible. Several screening tools already exist to identify IPV, including the following: Abuse Assessment Screen; Partner Violence Screen; Woman Abuse Screening Tools; Hurt, Insult, Threaten, Scream; and Humiliation, Afraid, Rape, Kick (HARK) tools.[17,18] These tools provide a standardized framework to screen patients at risk of IPV, and all are most effective when used consistently and longitudinally at least once each trimester and in the postpartum period.[8] Moreover, universal screening for IPV is recommended in health care settings when screening can be conducted privately, safely, and comfortably, although there is no consensus on the optimal screening setting or method.[19] In addition, universal screening is not the standard practice in health care settings. However, prior studies demonstrate higher screening rates during pregnancy among women of color, those without a high school degree, those who have never been married, those who receive Women, Infants, and Children (WIC) benefits, and those who are publicly insured.[15] While these populations may be at higher risk of IPV, all women should be screened due to the pervasive risk of IPV across the general population.[9] The results of a chart review study of routine screening for IPV in obstetrics and gynecology (OB/GYN) clinics led to the recommendation that there is a need for IPV screening with all women patients receiving obstetrics and gynecology care.[20]

This study sought to evaluate current IPV screening practices at Froedtert & Medical College of Wisconsin's OB/GYN clinic by comparing overall screening and positive screens before and during the COVID-19 pandemic, as well as before and after the implementation of the HARK screening tool,[17] which was implemented as part of clinical care in November 2020 and standardized by 2021. Before implementation of the HARK screening tool, there was no standardized method of screening for IPV, and the method and timing of screening were left to each clinician's discretion. The EHR tool was implemented as a standardized process in which MAs routinely performed the IPV screening at this clinic for all pregnant patients during the new patient intake process, which was completed via telephone before the first prenatal visit.

Research questions for this study were: (1) How did overall screening of positive cases compare before and during the COVID-19 pandemic?; (2) How did general IPV and positive screen numbers compare before and after the implementation of the standardized protocol using the HARK tool in Epic?; (3) What are the demographic, ethnicity, and relationship differences in patients screening positive for IPV in an obstetrics clinic?; and (4) Do screening results change with screening on each subsequent visit? We hypothesized that general screening and positive screen numbers would increase after the implementation of a standardized protocol using the HARK tool and during the COVID-19 pandemic.

MATERIALS AND METHODS

Data Source

This study is a retrospective secondary data analysis. The use of clinical data was approved by the Institutional Review Board of the Medical College of Wisconsin (PRO00041036). The clinical data were accessed through the Clinical and Translational Science Institute of Southwest Wisconsin (CTSI)'s Clinical Research Data Warehouse. Using the Informatics for Integrating Biology and the Bedside (i2b2) Cohort Discovery Tool and the Honest Broker Data Extraction Tool, queries were created to access deidentified patient data. The data were downloaded from Epic (Epic Systems Corporation—an EHR software utilized by the Froedtert and Medical College of Wisconsin health system.

All downloaded patient data were sorted according to those who screened positive or negative for IPV, patients who refused to answer the screening questions, and those who were not screened. All patients who received IPV screening at the clinic over the 3 years mentioned were assigned a unique patient ID number and different visit ID numbers (multiple IDs for multiple screenings), and the corresponding data were uploaded into the REDCap database.

Three sets of data were collected: (1) April through September

2019 for data before the COVID-19 pandemic and prior to implementation of the HARK tool, (2) April through September 2020 for data during the peak of the pandemic and implementation and use of the HARK tool, and (3) April through September 2021 for data later in pandemic and after standardization of the HARK tool. These three 6-month periods were chosen to ensure manageability and with April as the starting month as it was during in the region's 2020 pandemic lockdown period.

The HARK tool has 4 yes/no close-ended questions specific to "humiliation," "afraid," "rape," and "kick" and refers to possible abuse within the past year. If a patient answered "yes" to any of the 4 questions, the screen was positive.

Table 1. Demographic Characteristics Compared by Year[a]

	2019 (N = 59)	2020 (N = 418)	2021 (N = 790)	*P* value
Age (mean and age range)	31.3 (26.2 – 44.0)	33.6 (28.9 – 42.2)	30.8 (26.4 – 34.5)	< 0.0001
Race				0.11
White	38 (64.4)	261 (62.4)	435 (55.1)	
Black	16 (27.1)	110 (26.3)	245 (31.0)	
Other	5 (8.5)	47 (11.2)	110 (13.9)	
Ethnicity[b]				0.049
Hispanic or Latino	2 (3.4)	26 (6.3)	76 (9.6)	
Not Hispanic or Latino	57 (96.6)	390 (93.7)	714 (90.4)	
Relationship status[b]				< 0.0001
Married/significant other	26 (44.8)	226 (54.1)	489 (61.9)	
Legally separated/divorced/widowed	6 (10.3)	28 (6.7)	12 (1.5)	
Single	26 (44.8)	164 (39.2)	289 (36.6)	

[a]Data presented are frequency (%) for categorical variables and median (IQR) for continuous variables.
[b]Variables with missing values.

Data Analysis

Once the data were grouped into their corresponding date ranges, summary statistics were generated for each set. These included frequency and percentage for categorical data, including gender, race, and ethnicity and median and interquartile range for continuous variables. Continuous variables were compared using the Kruskal-Wallis test and Mann-Whitney test. Categorical variables were compared with chi-square and Fisher exact tests. Multivariable analysis was completed with a logistic regression model to see which variables were associated with positive screen results. We included only variables that showed significant results in the univariable analysis in the multivariable model. Statistical software SAS 9.4 (SAS Institute) was used for all the analyses, and a *P* value < 0.05 was considered statistically significant.

RESULTS

Demographics

A total of 1267 patients were screened during the study period. The median age was 31.5 years (range 17.6 – 85.2). Over half (734; 57.9%) of the patients were White, 371 (29.3%) were Black, 104 (8.2%) were Hispanic, and 162 (12.8%) were "other" races. The majority of patients (58.5%) were married or had a significant other. There were significantly more Hispanic patients screened in 2021 compared to 2020 ($P = 0.046$) (Table 1). There were fewer Hispanic patients in 2019, but the difference was not statistically significant. There was also a significant difference in marital status: more patients were married or had significant others and fewer patients were legally separated, divorced, or widowed in 2021 compared to 2019 and 2020 ($P < 0.0001$) (Table 1). There was no significant difference in the marital status of patients between 2019 and 2020.

Table 2. Intimate Partner Violence (IPV) Positive and Negative Screen Results Compared by Year

	2019 (N = 59)	2020 (N = 418)	2021 (N = 790)	*P* value
IPV screen results				< 0.0001
Positive	6 (10.2)	21 (5.0)	12 (1.5)	
Negative	53 (89.8)	397 (95.0)	778 (98.5)	

Data presented are frequency (%).

IPV Screens

The number of overall screenings increased in 2020 (n = 418) and 2021 (n = 790), with standardized screening significantly higher compared to 2019 (59) when screenings were performed at the clinician's discretion (Table 2). Over the 3-year study period, a total of 39 patients (3.1%) screened positive, defined as answering yes to 1 or more of the 4 HARK questions. There were only a handful of patients who were screened more than once during the study periods, and there was no change in screening results with subsequent screening for any of those patients. For these patients, information from their first IPV screen was used in the analyses.

Results of the IPV screen compared by year showed that positive screens were significantly lower in 2021 compared to 2019 ($P = 0.0008$) and 2020 ($P = 0.0004$) (Table 2). There was no significant difference in IPV screening results between 2019 and 2020. The only significant demographic variable associated with a positive IPV screening result was marital status. The screen-positive group had more single, legally separated, divorced, or widowed patients ($P < 0.0001$) (Table 3). Although screening was completed in less than half of the Black patients compared to White patient, the total number of positive screens was higher among Black patients (Table 3). In a multivariable analysis that included both year and marital status in a logistic regression model, both factors were significant predictors for IPV results ($P = 0.0015$ and $P < 0.0001$ respectively, Table 4).

Table 3. Intimate Partner Violence (IPV) Screen Results Were Compared by Demographic Variables

	IPV Screen Positive (N=39)	IPV Screen Negative (N=1228)	*P* value
Race			0.052
White	16 (41.0)	718 (58.5)	
Black	18 (46.2)	353 (28.7)	
Other	5 (12.8)	157 (12.8)	
Ethnicity			>0.99
Hispanic or Latino	3 (7.7)	101 (8.2)	
Not Hispanic or Latino	36 (92.3)	1125 (91.8)	
Relationship status			<0.0001
Married/significant other	5 (12.8)	736 (60.0)	
Legally separated/ divorced/widowed	5 (12.8)	41 (3.3)	
Single	29 (74.4)	450 (36.7)	
Age	30.73 (26.22 – 39.32)	31.53 (27.30 – 36.14)	

Data presented are frequency (%) and median (interquartile range).

Table 4. Multivariable Analysis of Positive Intimate Partner Violence (IPV) Screen Results

Patient Factor	Odds Ratio (95% CI)	*P* value
Year		
2019	5.66 (1.97 – 16.25)	0.0013
2020	2.96 (1.42 – 6.19)	0.0038
2021	Reference	
Relationship Status		
Single	8.89 (3.41 – 23.21)	<0.0001
Legally separated/divorced/widowed	11.56 (3.14 – 42.55)	0.0002
Married/significant other	Reference	

DISCUSSION

Several findings emerged from this study related to patient screening for IPV. The primary question in our study compared screening practices and positive screen rates with and without a standardized screening protocol. Before standardization, IPV screening was completed when there was suspicion of IPV and at the discretion of the clinician. Our findings support the idea that the use of a standardized screening protocol and an EHR screening tool drastically increases the number of patients screened, as the total number of patients screened increased immediately after implementation of the standardized screening process. And although the positive screen percentage was lower in 2020 than in 2019, a higher total number of positive screens occurred in 2020 (n = 21) versus 2019 (n = 6). Those are the patients who likely would have been missed without this universal screening policy. Given these results, screening based on risk factors only would miss patients who otherwise would not be screened but may still be victims of IPV.

In addition to increasing screening rates in the clinic, this study also showed that there was a significantly lower number of positive IPV screens in patients who were married or had significant others. This is consistent with prior studies that found married women experience less IPV than unmarried women living with significant others.[21,22] Our study also showed that separated and single women were more often victims of IPV.

Furthermore, it is possible that the COVID-19 pandemic had important effects on this study's findings. The increase in positive screens in 2020, compared to both 2019 and 2021, occurred during the time of peak lockdowns and shelter-in-place regulations, which have been suggested to increase rates of IPV (Table 2).

Limitations

A key limitation to this study was that the exact timing of when the standardized protocol using the HARK tool went into effect was unknown. Hence, we were unable to compare screening results before and directly after the intervention. Furthermore, the clinic could not provide data on the total number of new, unique patients within each time frame, and their screening circumstances, such as privacy issues, limited us from calculating the clinic's general screening rates. Also, the standardized IPV screening protocol that was used by Froedtert & Medical College of Wisconsin's OB/GYN clinic and evaluated in this study only included pregnant patients, but the data picked up all patients who were screened, including those who were not pregnant at the time. The screening procedures themselves are limited by the stigmatization of IPV and the method of inquiry. The change from an in-person suspicion-driven inquiry to phone screening upon intake likely added to significant underreporting. Finally, the data analyzed were from a single medical clinic and may not represent an overall trend, but our findings align with previous findings discussed above.

Future Directions

In the future, a study may be conducted to evaluate the results with longitudinal or repeat screenings carried out with a standardized protocol. COVID-19 might have influenced the outcome of the positive screening. The results can be evaluated, and the study can be replicated post-COVID when the impact of the pandemic is less salient. While this is an important first step, the treatment of IPV with the creation of a network of support systems, including health care workers and social workers, is of utmost importance. Going forward, researchers should also study the resources and tools available to those who are victims of IPV, identify which are most effective in preventing further violence or abuse, and ensure that staff and clinicians in health care settings are aware of these resources so that they may provide them to patients who screen positive.

CONCLUSIONS

IPV is a serious health crisis that deserves attention from health care providers. Our findings show promising results – that a standardized screening protocol using 4 brief questions is effective in efficiently screening more patients and identifying cases of abuse

that otherwise may be missed if screening is based only on risk factors. This study demonstrates that the IPV screening protocol at this clinic increased the overall screening in an OB/GYN clinic, which can be replicated in other clinics or health care settings. In addition to recognizing those patients who screened positive for abuse, the data additionally showed the important effect of marital status as well as the COVID-19 pandemic on IPV, which could help focus future studies or interventions. Detecting abuse is not enough; guidance and resources should be provided by well-trained and supported clinicians or IPV advocates to end the abuse and hopefully prevent it in the future.

Funding/Support: The Advancing a Healthier Wisconsin Endowment at the Medical College of Wisconsin (#5510270), the Clinical Translational Science Institute (CTSI) of Southeastern Wisconsin supported the research project.

Financial Disclosures: None declared.

REFERENCES

1. Smith SG, Zhang Z, Basile KC, et al. The National Intimate Partner and Sexual Violence Survey: 2015 data brief-updated release. National Center for Injury Prevention and Control, November 2018. Accessed September 15, 2023. https://www.nsvrc.org/sites/default/files/2021-04/2015data-brief508.pdf

2. Haag HL, Toccalino D, Estrella MJ, Moore A, Colantonio A. The shadow pandemic: a qualitative exploration of the impacts of COVID-19 on service providers and women survivors of intimate partner violence and brain injury. *J Head Trauma Rehabil.* 2022;37(1):43-52. doi:10.1097/HTR.0000000000000751

3. Wyckoff KG, Narasimhan S, Stephenson K, Zeidan AJ, Smith RN, Evans DP. "COVID gave him an opportunity to tighten the reins around my throat": perceptions of COVID-19 movement restrictions among survivors of intimate partner violence. *BMC Public Health.* 2023;23(1):199. doi:10.1186/s12889-023-15137-5

4. Johnson L. Exploring factors associated with pregnant women's experiences of material hardship during COVID-19: a cross-sectional Qualtrics survey in the United States. *BMC Pregnancy Childbirth*. 2021;21(1):755. doi:10.1186/s12884-021-04234-1

5. Intimate partner violence during pregnancy information sheet. World Health Organization. 2011. Accessed September 15, 2023. https://www.who.int/publications/i/item/WHO-RHR-11.35

6. Alhusen JL, Ray E, Sharps P, Bullock L. Intimate partner violence during pregnancy: maternal and neonatal outcomes. *J Womens Health (Larchmt).* 2015;24(1):100-106. doi:10.1089/jwh.2014.4872

7. Kofman YB, Garfin DR. Home is not always a haven: the domestic violence crisis amid the COVID-19 pandemic. *Psychol Trauma*. 2020;12(S1):S199-S201. doi:10.1037/tra0000866

8. Thayer ZM, Gildner TE. COVID-19-related financial stress associated with higher likelihood of depression among pregnant women living in the United States. *Am J Hum Biol.* 2021;33(3):e23508. doi:10.1002/ajhb.23508

9. Deshpande NA, Lewis-O'Connor A. Screening for intimate partner violence during pregnancy. *Rev Obstet Gynecol.* 2013;6(3-4):141-148. doi:10.3909/riog0226

10. Felson RB, Messner SF, Hoskin AW, Deane G. Reasons for reporting and not reporting domestic violence to the police. *Criminology*. 2002;40(3):617-648. doi:10.1111/j.1745-9125.2002.tb00968.x

11. Truman JL, Morgan RE. Nonfatal domestic violence, 2003-2012. US Department of Justice, Bureau of Justice Statistics. April 2014. Accessed September 15, 2023. https://bjs.ojp.gov/content/pub/pdf/ndv0312.pdf

12. Campbell J, Matoff-Stepp S, Velez ML, Cox HH, Laughon K. Pregnancy-associated deaths from homicide, suicide, and drug overdose: review of research and the intersection with intimate partner violence. *J Womens Health (Larchmt).* 2021;30(2):236-244. doi:10.1089/jwh.2020.8875

13. Paulson JL. Intimate partner violence and perinatal post-traumatic stress and depression symptoms: a systematic review of findings in longitudinal studies. *Trauma Violence Abuse.* 2022;23(3):733-747. doi:10.1177/1524838020976098

14. Doi S, Fujiwara T, Isumi A. Development of the intimate partner violence during pregnancy instrument (IPVPI). *Front Public Health*. 2019;7:43. doi:10.3389/fpubh.2019.00043

15. Vest JR, Catlin TK, Chen JJ, Brownson RC. Multistate analysis of factors associated with intimate partner violence. *Am J Prev Med*. 2002;22(3):156-164. doi:10.1016/s0749-3797(01)00431-7

16. Berhanie E, Gebregziabher D, Berihu H, Gerezgiher A, Kidane G. Intimate partner violence during pregnancy and adverse birth outcomes: a case-control study. *Reprod Health.* 2019;16(1):22. doi:10.1186/s12978-019-0670-4

17. Rezey ML. Separated women's risk for intimate partner violence: a multiyear analysis using the National Crime Victimization Survey. *J Interpers Violence.* 2020;35(5-6):1055-1080. doi:10.1177/0886260517692334

18. Sutton D, Dawson M. Differentiating characteristics of intimate partner violence: do relationship status, state, and duration matter? *J Interpers Violence.* 2021;36(9-10):NP5167-NP5191. doi:10.1177/0886260518795501

19. Nelson HD, Bougatsos C, Blazina I. Screening women for intimate partner violence: a systematic review to update the US Preventive Services Task Force recommendation. *Ann Intern Med*. 2012;156(11):796-282. doi:10.7326/0003-4819-156-11-201206050-00447

20. Halpern-Meekin S, Costanzo M, Ehrenthal D, Rhoades G. Intimate partner violence screening in the prenatal period: variation by state, insurance, and patient characteristics. *Matern Child Health J*. 2019;23(6):756-767. doi:10.1007/s10995-018-2692-x

21. Moyer VA; US Preventive Services Task Force. Screening for intimate partner violence and abuse of elderly and vulnerable adults: US preventive services task force recommendation statement. *Ann Intern Med.* 2013;158(6):478-486. doi:10.7326/0003-4819-158-6-201303190-00588

22. O'Doherty L, Hegarty K, Ramsay J, Davidson LL, Feder G, Taft A. Screening women for intimate partner violence in healthcare settings. *Cochrane Database Syst Rev.* 2015;2015(7):CD007007. doi:10.1002/14651858.CD007007.pub3

Sterilization Rates of Pregnancy-Capable People at a Single Institution in Wisconsin Before and After *Dobbs v Jackson Women's Health Organization*

Camille Phillips, BS; Jeannette Larson, MD; Amy Godecker, PhD, MS; Laura Jacques, MD; Laura Hanks, MD

ABSTRACT

Introduction: On June 24, 2022, the United States Supreme Court decided *Dobbs v Jackson Women's Health Organization* (*Dobbs*), overturning *Roe v Wade* and banning abortions in almost all circumstances in Wisconsin. We tested the hypothesis that the rate of interval tubal sterilizations in people capable of pregnancy increased after the *Dobbs* decision.

Methods: We conducted a retrospective cohort study of all pregnancy-capable patients ages 18 to 55 years old who underwent interval surgical sterilization at an academic hospital in Wisconsin from June 24, 2016, through June 23, 2023. We defined the annual sterilization rate by dividing the number of sterilizations by total gynecologic surgeries performed each year. We compared the annual rates of interval surgical sterilization in the 6 years prior to the *Dobbs* decision to the year following the *Dobbs decision*.

Results: There were 1088 interval tubal sterilization procedures for pregnancy-capable people during the study period. The sterilization rate increased from 4.6% to 8.1% ($P < .001$) from the year before the *Dobbs* decision to the year after. In the 6 years prior to *Dobbs*, 23.6% of patients receiving sterilizations were aged 20 – 29, compared to 35% post-*Dobbs* ($P < .001$). Patients who were nulligravid (never been pregnant) increased from 23.0% in the 6 years pre-*Dobbs* to 54.7% post-*Dobbs* ($P < .001$). Similarly, 28.0% of patients pre-*Dobbs* were nulliparous (never had a live birth) versus 60.4% post-*Dobbs* ($P < .001$).

Conclusions: There was an increase in the rate of interval sterilization procedures for pregnancy-capable people – particularly among younger and nulliparous patients – at a single academic institution in Wisconsin in the year following the *Dobbs* decision.

INTRODUCTION

Provision of contraceptive and abortion care throughout the United States has changed dramatically based on individual state legislation since June 24, 2022, when the *Dobbs v Jackson Women's Health Organization*[1] decision overruled prior Supreme Court decisions and removed federal protections for abortion care. In Wisconsin, the *Dobbs* decision reinstated the Criminal Abortion Ban – an 1849 law that states, "Any person, other than the mother, who intentionally destroys the life of an unborn child is guilty of a Class H felony" (Wis. Stat. § 940.04).

However, as of December 5, 2023, a judge in Dane County, where our hospital is located, ruled that the 1849 law did not apply to consensual abortion and, therefore, abortions were found to be legal again in Wisconsin. This date was outside of our data set but worth noting. Following the *Dobbs* decision, there were reports in the news media and preliminary research showing an increased demand for sterilization procedures.[2]

Data from the National Survey of Family Growth (NSFG) in the United States shows recent declines in reliance on tubal sterilization for reproductive-aged women and for women aged 30 and below, at least through 2019.[3,4] More recent national statistics are not available, as the NSFG did not collect data for 2020-2021, and data from January 2022 onward are not yet available for analysis. Our study sought to investigate changes in the rate of permanent sterilization procedures in pregnancy-capable people at a single institution in a state where abortion is no longer accessible. Our hypothesis was that sterilization rates

• • •

Author Affiliations: University of Wisconsin School of Medicine and Public Health (UWSMPH), Madison, Wisconsin (Phillips); Department of Obstetrics and Gynecology, UWSMPH, Madison, Wisconsin (Larson, Jacques, Hanks); Department of Obstetrics and Gynecology, Management and Statistical Core, University of Wisconsin-Madison, Madison, Wisconsin (Godecker).

Corresponding Author: Camille Phillips, email cphillips22@wisc.edu; ORCID ID 0009-0003-0314-7358

Table. Sterilization Patients' Demographic Results by Year

	Year 1[a] n (%)	Year 2[a] n (%)	Year 3[a] n (%)	Year 4[a] n (%)	Year 5[a] n (%)	Year 6[a] n (%)	Year 7[a] n (%)	Total n (%)	*P* value[b]
Total Sterilizations	105	114	123	124	126	162	334	1088	
Age									<0.001
20–24	2 (1.9)	4 (3.5)	2 (1.6)	12 (9.7)	13 (10.3)	13 (8.0)	37 (11.1)	83 (7.6)	
25–29	17 (16.2)	15 (13.2)	24 (19.5)	22 (17.7)	25 (19.8)	29 (17.9)	80 (24.0)	212 (19.5)	
30 – 39	50 (47.6)	63 (55.3)	65 (52.9)	58 (46.8)	54 (42.9)	88 (54.3)	172 (51.5)	550 (50.6)	
40 – 50	36 (34.3)	32 (28.1)	32 (26.0)	32 (25.8)	34 (27.0)	32 (19.8)	45 (13.5)	243 (22.3)	
Total	105 (100)	114 (100)	123 (100)	124 (100)	126 (100)	162 (100)	334 (100)	1088 (100)	
Race/ethnicity									0.306
Asian	1 (1.0)	1 (0.9)	2 (1.6)	6 (4.8)	0 (0)	6 (3.7)	14 (4.2)	30 (2.8)	
Black or African American	1 (1.0)	5 (4.4)	7 (5.7)	9 (7.3)	8 (6.3)	9 (5.6)	16 (4.8)	55 (5.1)	
Hispanic/Latina	9 (8.6)	9 (7.9)	7 (5.7)	11 (8.9)	10 (7.9)	13 (8.0)	20 (6.0)	79 (7.3)	
None of the above	6 (5.7)	2 (1.8)	3 (2.4)	2 (1.6)	2 (1.6)	2 (1.2)	11 (3.3)	28 (2.6)	
White	88 (83.8)	97 (85.1)	104 (84.6)	96 (77.4)	106 (84.1)	132 (81.5)	273 (81.7)	896 (82.4)	
Total	105 (100)	114 (100)	123 (100)	124 (100)	126 (100)	162 (100)	334 (100)	1088 (100)	
Gravida[c]									<0.001
Gravida 0	27 (25.7)	19 (17.1)	21 (17.4)	19 (15.6)	31 (24.8)	54 (33.5)	181 (54.7)	352 (32.7)	
Gravida 1+	78 (74.3)	92 (82.9)	100 (82.6)	103 (84.4)	94 (75.2)	107 (66.5)	150 (45.3)	724 (67.3)	
Total	105 (100)	111 (100)	121 (100)	122 (100)	125 (100)	161 (100)	331 (100)	1076 (100)	
Para[c]									<0.001
Para 0	30 (28.6)	25 (22.5)	28 (23.1)	23 (18.9)	35 (28.0)	67 (41.6)	200 (60.4)	408 (37.9)	
Para 1	18 (17.1)	18 (16.2)	22 (18.2)	16 (13.1)	27 (21.6)	14 (8.7)	39 (11.8)	154 (14.3)	
Para >1	57 (54.3)	68 (61.3)	71 (58.7)	83 (68.0)	63 (50.4)	80 (49.7)	92 (27.8)	514 (47.8)	
Total	105 (100)	111 (100)	121 (100)	122 (100)	125 (100)	161 (100)	331 (100)	1076 (100)	
Medicaid									<0.001
No	86 (81.9)	95 (83.3)	95 (77.2)	87 (70.2)	89 (70.6)	113 (69.8)	197 (59.0)	762 (70.0)	
Yes	19 (18.1)	19 (16.7)	28 (22.8)	37 (29.8)	37 (29.4)	49 (30.3)	137 (41.0)	326 (30.0)	
Total	105 (100)	114 (100)	123 (100)	124 (100)	126 (100)	162 (100)	334 (100)	1088 (100)	

[a]Year 1 = June 24, 2016 – June 23, 2017; Year 2 = June 24, 2017 – June 23, 2018; Year 3 = June 24, 2018 – June 23, 2019; Year 4 = June 24, 2019 – June 23, 2020; Year 5 = June 24, 2020 – June 23, 2021: Year 6 = June 24, 2021 – June 23, 2022; Year 7 = June 24, 2022 – June 23, 2023.

[b]Associated *P* values included, calculated by comparing differences for each category pre-*Dobbs* and post-*Dobbs*.

[c]Para was documented as number of living children. 12 patients were missing gravidity and parity.

in this population would increase following the *Dobbs v Jackson* decision.

METHODS

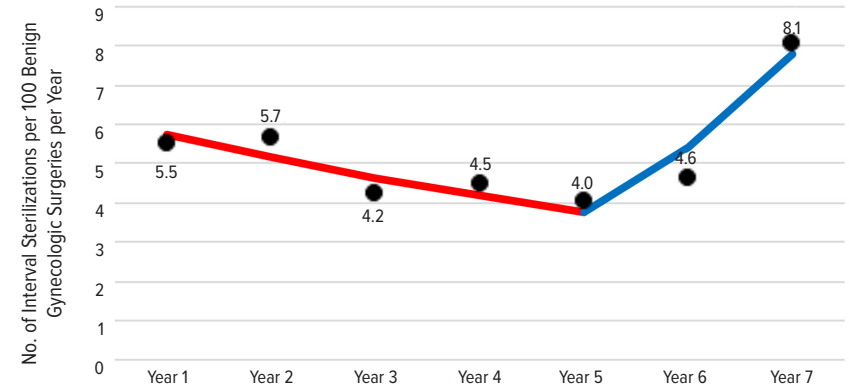
We conducted a retrospective cohort study of all pregnancy-capable patients who received interval sterilizations from June 24, 2016, through June 23, 2023, at Meriter Hospital in Madison, Wisconsin. This study was exempt from Institutional Review Board approval. Patient charts were identified by using Current Procedural Terminology (CPT) codes 58661 (laparoscopy removal of adnexal structures) or 58700 (salpingectomy, complete or partial). Once the patient population was identified, we used Epic's SlicerDicer (Epic Systems Corp) to pull in additional details about the patient or their encounter. We included patients aged 18 to 55 years. We also included all types of interval tubal sterilizations – ie, tubal ligations, tubal fulgurations, and bilateral salpingectomies, excluding procedures done postpartum or during a cesarean delivery. To verify that all correct charts were identified, we reviewed hospital operating room (OR) schedules for each day during our study period. Upon completion of this data acquisition, we verified with our Institutional Review Board that our data acquisition and methodology remained fully compliant and that the study status remained exempt.

We started the data series in 2016 to account for any trends due to tensions on reproductive autonomy during the presidential administration of Donald Trump and for any disruptions to elective surgery frequencies during the COVID-19 pandemic or other temporal trends. Study years run from June 24 of one year to June 23 of the following year, as the *Dobbs* decision was released on June 24, 2022, and abortions in Wisconsin ceased immediately afterward. To control for potential temporal changes in tubal sterilizations related to a changing patient population at our institution, COVID-19 practice patterns, or other factors, we report sterilization rates with a numerator equal to the number of sterilizations in a study year and a denominator of total gynecologic surgeries in that year at the same institution. Gynecologic surgeries include all benign surgeries performed by generalists, urogynecologists, and minimal invasive gynecologic surgeons as

well as abdominal, laparoscopic, and vaginal surgeries. We recorded demographic data including patient age, race, ethnicity, gender, gravity and parity, and payor status as documented in the medical record at the time of the tubal sterilization procedure. In Wisconsin, patients assigned female at birth with Medicaid insurance must sign a sterilization consent form between 30 and 180 days (about 6 months) before interval sterilization. There were no changes to this policy during the study period.

Annual frequencies of tubal sterilizations and total gynecologic surgeries and the calculated rates are reported, as well as the rates, incidence rate difference, incidence rate ratio, and incidence rate ratio confidence interval for the aggregate 6 years pre-*Dobbs* to the single year post-*Dobbs*. Frequencies and percentages are reported for sterilization patient characteristics, and chi-squared or Fisher exact tests were used to test for significant differences in these categorical variables pre-*Dobbs* versus post-*Dobbs*, as appropriate. The Mann-Kendall nonparametric test for trend was used for the trend in numbers of sterilizations over time, and a joinpoint analysis assessed whether there were "joinpoints" or significant changes in the annual percentage change (APC) between timepoints.[5] A 2-sided *P* value of < 0.05 was considered statistically significant. The Joinpoint Regression Program[6] 5.0.2 was used for the joinpoint trend analysis and Stata/SE 18.0[7] was used for all other analyses.

Figure 1. Rate of Interval Sterilizations Observed and Joinpoint Model by Study Year



	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Interval sterilizations (N)	105	114	123	124	126	162	334
Benign gynecologic (N) surgeries	1904	2016	2912	2758	3117	3489	4139
Observed rate	5.5	5.7	4.2	4.5	4.0	4.6	8.1
Joinpoint modeled rate years 1–5 (APC = -10.01	5.7	5.2	4.7	4.3	3.8		
Joinpoint modeled rate years 5–7 (APC = -43.83					3.8	5.4	7.8

● Observed rate — Joinpoint modeled rate 1-5 APC = -10.01[a] — Joinpoint modeled rate 5-7 APC = -43.83[a]

Year 1 = June 24, 2016 – June 23, 2017; Year 2 = June 24, 2017 – June 23, 2018; Year 3 = June 24, 2018 – June 23, 2019; Year 4 = June 24, 2019 – June 23, 2020; Year 5 = June 24, 2020 – June 23, 2021: Year 6 = June 24, 2021 – June 23, 2022; Year 7 = June 24, 2022 – June 23, 2023.

[a]Indicates that the annual percent change (APC) is significantly different from zero at the alpha = 0.05 level. Final selected model: 1 Joinpoint.

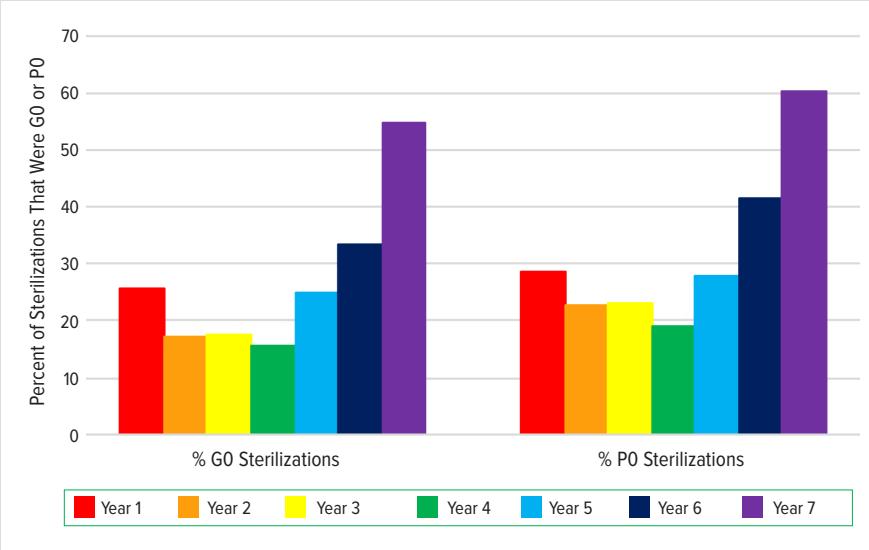
RESULTS

There were 1088 pregnancy-capable patients who underwent interval sterilization from June 24, 2016, through June 23, 2023, and were included in the study cohort. We found a significant trend in increasing annual sterilization frequencies in this population over the 7-year period ($P < 0.001$). The most substantial increase was from the year preceding the *Dobbs* decision to the year after the *Dobbs* decision, from 162 to 334 procedures – a 106.2% increase (Figure 1). Total gynecologic surgeries also increased annually from 2016 to 2023. The rate of sterilization procedures in pregnancy-capable people per 100 gynecologic surgeries in the first study year (June 24, 2016 – June 23, 2017) was 5.51, decreasing to a low of 4.04 in study year 5 (June 24, 2020 – June 23, 2021). The rate increased to 4.64 in the year preceding the *Dobbs* decision and to 8.07 in the post-*Dobbs* year. The joinpoint regression found 1 joinpoint at year 5, with significant APCs of 10.01 in years 1-5 and 43.83 in years 5-7 (Figure 1). The aggregate sterilization rate in this population for years 1-6 (and years 1-5) was 4.66. Comparing this pre-*Dobbs* period to the rate of 8.07 for the post-*Dobbs* year yields an incidence rate difference of 3.41 (95% CI, 2.49-4.34) and an incidence rate ratio of 1.73 (95% CI, 1.52-1.97).

There were significant changes to selected demographics of pregnancy-capable patients receiving sterilization procedures pre-*Dobbs* and post-*Dobbs* (Table). Patients receiving sterilizations were younger after the *Dobbs* decision, with patients receiving sterilizations aged 20 to 29 increasing from 23.6% pre-*Dobbs* to 35.0% post-*Dobbs* ($P < .001$). Additionally, post-*Dobbs* patients were more likely to be nulligravid (G0) and/or nulliparous (P0). Nulligravid patients increased from 23.0% in the 6 years pre-*Dobbs* to 54.7% post-*Dobbs* (Figure 2). Patient-reported gender and race/ethnicity did not change significantly in the years surrounding the *Dobbs* decision. A significantly higher percentage of patients were using Medicaid post-*Dobbs* (41.0%) than pre-*Dobbs* (25.1%). Results

when analyzing individual years were comparable to analysis with the aggregate of 6 years before the *Dobbs* decision.

Figure 2. Percent of Sterilizations That Were Gravida 0 (G0) or Para 0 (P0) Each Year



Year 1 = June 24, 2016 – June 23, 2017; Year 2 = June 24, 2017 – June 23, 2018; Year 3 = June 24, 2018 – June 23, 2019; Year 4 = June 24, 2019 – June 23, 2020; Year 5 = June 24, 2020 – June 23, 2021: Year 6 = June 24, 2021 – June 23, 2022; Year 7 = June 24, 2022 – June 23, 2023.

Twelve patients included in the study analysis were misssing gravidity.

DISCUSSION

Principal Findings

The number and rate of sterilization procedures increased significantly among pregnancy-capable people at a single academic institution in Wisconsin following the Supreme Court decision in *Dobbs v Jackson*. Patients undergoing surgical sterilization in the post-*Dobbs* year were younger, had less gravidity and parity, and were more likely to have Medicaid insurance than in the pre-*Dobbs* years. We believe this change is due, at least in part, to decreased accessibility to abortion care in Wisconsin.

A joinpoint analysis of annual sterilization rates found a joinpoint and significant increase in the APC at the point of the year prior to the *Dobbs* decision (June 24, 2021, to June 23, 2022). This is likely due to the increase in interval procedures following the COVID-19 pandemic, as well as the strong uncertainty of abortion rights during the year the *Dobbs* case was deliberated, with oral arguments December 1, 2021, and a historic Supreme Court opinion leak, which occurred on May 2, 2022.

Results in the Context of What We Know

A similar study conducted at the University of Michigan found tubal sterilization request rates at their institution increased in the months following the *Dobbs* decision. However, there was a decrease back to baseline after 6 months, which may have been due to the demand being met, a decreased sense of urgency after abortion access was temporarily protected, or crisis fatigue.[2]

There are numerous anecdotal reports from physicians caring for these patients that suggest the increase in sterilization procedures is due to a perceived loss of bodily autonomy; however, more qualitative research is needed to solidify this indication.

Clinical Implications

An implication of younger patients seeking tubal sterilizations is that patients under 30 years are more likely to experience sterilization regret and seek information on sterilization reversal.[8] While the American College of Obstetricians and Gynecologists states that age and parity should not be a barrier to tubal sterilization in a well-informed patient,[9] investigating sterilization regret in Wisconsin over the next 5 to 20 years will be important.

We chose to analyze insurance status and found a significant increase in Medicaid insurance among tubal sterilization patients after the *Dobbs* decision; however, Medicaid enrollment increased by 34.8% in Wisconsin from February 2020 to December 2022.[10] It is unclear from our study alone whether the increase in Medicaid status among our participants is from the general increase in enrollment or from an increased interest in sterilizations among the Medicaid patient population.

Research Implications

Looking forward, we hope to compare these data to other states where abortion access is less restricted. We also plan to expand our study into the next post-*Dobbs* year (June 24, 2023 – June 23, 2024). On July 7, 2023, Dane County Judge Diane Schlipper announced a preliminary decision that the 1849 Abortion Ban Law did not, in fact, outlaw abortions, but instead only applied to feticide. Planned Parenthood of Wisconsin deemed this sufficient to restore abortion care at its clinics on September 18, 2023. Most facilities followed suit after consensual abortions were officially deemed legal in Wisconsin on December 5, 2023; however, some institutions in Wisconsin interpreted the final decision more conservatively and have not yet resumed abortion care. We will continue to analyze if tubal sterilization frequency changes in response to the changes in accessibility of abortion care across the state. We also would like to compare these trends to vasectomy rates at the same institution before and after *Dobbs*. We predict that, as already shown in our study, when access to abortion is limited, patients will seek more permanent forms of sterilization.

Strengths and Limitations

Our study had some limitations. The first limitation was its retrospective design and reliance on CPT codes. Second, we performed our study at a single institution in Madison, Wisconsin, and our findings may not be generalizable to the entire state or national context. However, this small cohort may provide some insight into sterilization rates in pregnancy-capable people in a state where abortion restrictions are in place. Third, patients who were postpartum or received their sterilization at the time of a cesarean delivery were not included in the study. This decreases the average gravidity and parity for each year and could introduce bias into our results. However, in the interest of evaluating a similar population over time and exploring the impact of the *Dobbs* decision on this population, we decided to exclude postpartum tubal sterilizations to keep our population more homogenous. We also only reported if patients had Medicaid or not. We did not gather data about specific insurers. Lastly, our study population was predominantly White females and, therefore, may not be generalizable to the national population.

Our study had several strengths. There are few studies that describe changes to reproductive health care in abortion-restricted states in the post-*Dobbs* era, and our study is one of the first in Wisconsin. We analyzed data going back 7 years, allowing us to identify associations and trends over this extended time.

CONCLUSIONS

We found a significant increase in tubal sterilization procedures after the *Dobbs v Jackson Women's Health Organization* decision. This increase was most pronounced in younger patients who were either nulliparous or nulligravid. These findings demonstrate some of the reproductive implications of legally limiting bodily autonomy and highlight the need for larger, more comprehensive studies at the state and national levels.

Funding/Support: Funding was provided by the University of Wisconsin School of Medicine and Public Health Shapiro Summer Research Program. Funding support was provided to Dr Jacques from an anonymous family foundation to support research looking into the impact of state legislation around medication abortion

Financial Disclosures: Dr Jacques reports receiving payment/honoraria for the following: Society for Family Planning Grant reviewer, Bixby Foundation honoraria for facilitating Values Clarification workshops and Alameda Healthcare System honoraria for facilitating Values Clarification workshop.

Acknowledgements: This work was presented previously at the American College of Obstetricians and Gynecologists District VI Annual Meeting in Omaha, Nebraska, on October 1, 2023 (Junior Fellow Prize Paper) and at the 22nd Annual Medical Student Research Forum at the University of Wisconsin School of Medicine and Public Health in Madison, Wisconsin, on November 20, 2023 (Excellence in Student Research Reward).

REFERENCES

1. *Dobbs v Jackson Women's Health Organization*, 597 U.S. 215 (2022)

2. Liang AC, Gliwa C, Loder CM, Dalton VK, Smith RD. Tubal sterilization requests at a single institution following the Supreme Court decision to overturn the constitutional right to abortion. *JAMA*. 2023;330(4):374-375. doi:10.1001/jama.2023.11073

3. Kavanaugh ML, Jerman J. Contraceptive method use in the United States: trends and characteristics between 2008, 2012 and 2014. *Contraception*. 2018;97(1):14-21. doi:10.1016/j.contraception.2017.10.003

4. Daniels K, Abma JC. Current contraceptive status among women aged 15–49: United States, 2015–2017. NCHS Data Brief. 2018;(327):1-9. Accessed October 10, 2023. https://www.cdc.gov/nchs/products/databriefs/db327.htm

5. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000;19(3):335-351. doi:10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z

6. *Joinpoint Regression Program.* Version 5.0.2. Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute; May 2023. Accessed October 10, 2023. https://surveillance.cancer.gov/joinpoint/

7. *Stata 18.* Version 18. StataCorp; 2023. Accessed October 10, 2023. https://www.stata.com/

8. Danvers AA, Evans TA. Risk of sterilization regret and age: an analysis of the National Survey of Family Growth, 2015-2019. *Obstet Gynecol*. 2022;139(3):433-439. doi:10.1097/AOG.0000000000004692

9. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 208: benefits and risks of sterilization. *Obstet Gynecol*. 2019;133(3):e194-e207. doi:10.1097/AOG.0000000000003111

10. Corello B, Moreno S. Analysis of national trends in Medicaid and CHIP enrollment during the COVID-19 pandemic. April 4, 2023. KFF. Accessed October 16, 2023. https://www.kff.org/coronavirus-covid-19/issue-brief/analysis-of-recent-national-trends-in-medicaid-and-chip-enrollment/

Maternal Adverse Childhood Experiences and Perinatal Anxiety, Obsessive Compulsive Disorder, Posttraumatic Stress Disorder, and Substance Use

Kathleen N. Hipke, PhD

ABSTRACT

Introduction: Postpartum mental health conditions including depression are a leading cause of maternal morbidity and mortality. Maternal adverse childhood experiences (ACE) have a dose-response predictive relationship to postpartum depression, highlighting mothers' own early relational trauma as an important risk factor for both mother and infant's postpartum course. Currently, far less is understood about whether maternal ACEs create risk for other postpartum mental health conditions that can negatively impact mother and baby.

Objective: This study sought to understand the relationship between maternal ACEs and the risk for development of perinatal anxiety, obsessive compulsive disorder, posttraumatic stress disorder, and substance abuse disorder via narrative review of published literature.

Methods: PubMed, PsycINFO, and Google Scholar databases were searched with terms: adverse childhood experiences or ACEs; perinatal or prenatal or pregnancy or postpartum; and either anxiety, obsessive compulsive disorder, posttraumatic stress disorder, or substance use disorder.

Results: Maternal ACEs increase risk for anxiety and posttraumatic stress disorder in pregnancy and postpartum. No studies were identified for obsessive compulsive disorder. Maternal ACEs increase the risk for substance use in pregnancy but are understudied postpartum despite risk for maternal overdose and mortality.

Conclusions: ACEs – especially those involving child maltreatment – are predictive of a wide range of perinatal mental health concerns, including anxiety, posttraumatic stress disorder, and substance use. Findings of this study support recommendations for inclusion of ACEs screening with perinatal patient populations as a component of trauma-informed care to contextualize and identify mothers who may have increased postpartum mental health risk and support needs.

• • •

Author Affiliations: Department of Psychiatry, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Hipke).

Corresponding Author: Kathleen N. Hipke, PhD, Department of Psychiatry, University of Wisconsin School of Medicine and Public Health, 6001 Research Park Blvd, Madison, WI 53719; phone 608.263.1751; email khipke@wisc.edu; ORCID ID 0009-0003-2515-0064

INTRODUCTION

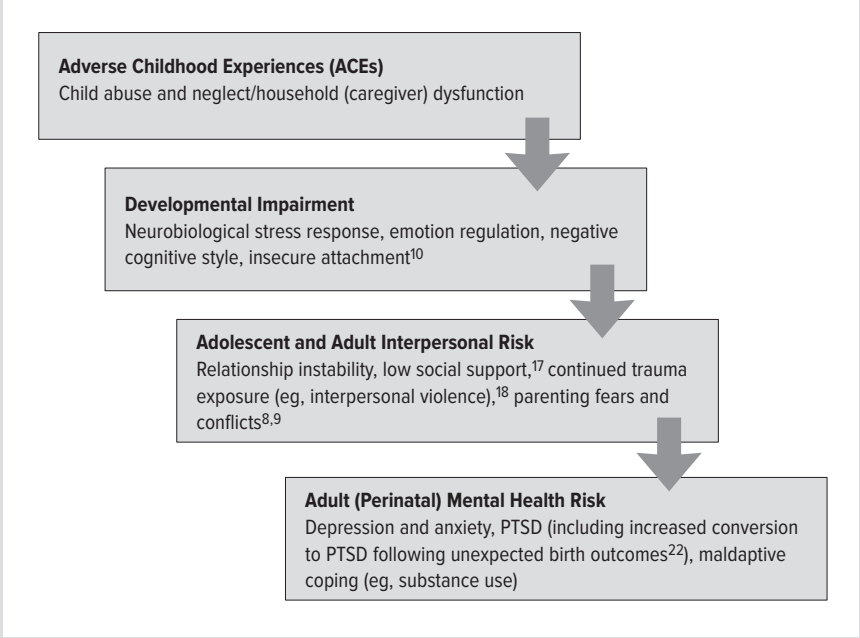
Mental health conditions are a leading contributor to alarming rates of US maternal morbidity and mortality in the postpartum period,[1,2] yet they remain a largely underrecognized and under-addressed postpartum complication. They are also a source of substantial health disparity,[3] with mothers from underrepresented racial backgrounds much more likely to experience postpartum depression relative to their White counterparts.[4] Clinical research has long focused on depression in the postpartum period, but there is growing awareness of the need to also attend to other mental health conditions, including anxiety, obsessive compulsive disorder (OCD), posttraumatic stress disorder (PTSD), and substance use disorders, which can have a debilitating impact on maternal distress and health, the developing maternal-infant relationship, and/or infant developmental trajectory.[5-7]

Postpartum mental health is complex and multidetermined. Understanding the role of mothers' early relational trauma during the transition to parenthood, when painful memories involving a lack of safety in childhood may be activated,[8,9] can provide timely opportunities for clinicians to increase awareness of heightened mental health risk and support needs for new parents.[10] Doing so may be especially important in working with expectant and new parents from historically underrepresented and/or oppressed communities coping with higher levels of stress and trauma exposure over the life course.[11]

Adverse childhood experiences (ACEs), most often measured

in health care environments via the ACE Questionnaire,[12] include adult-reported events that occurred before age 18 years along 2 dimensions: (1) child maltreatment, which includes history of child abuse (physical, emotional, or sexual) and/or neglect, and (2) household dysfunction, which captures negative effects on caregiver availability or stability via events such as substance involvement, mental illness, domestic violence, and incarceration. ACEs represent early relational stress and trauma yet are associated with a range of physical and mental health outcomes in adulthood,[12-14] including adverse birth outcomes such as pregnancy loss, preterm birth, and low birth weight.[15] A recent systematic review and meta-analysis summarized the ACEs literature with respect to postpartum depression.[16] Total maternal ACEs were identified as a significant risk factor for postpartum depression, with child maltreatment items showing the strongest associations (eg, emotional neglect, odds ratio [OR] = 2.95; 95% CI, 2.08-4.20).

Figure. Summary of Pathways Under Study: From Adverse Childhood Experiences (ACE) to Adult Mental Health Disorder



Abbreviation: PTSD, posttraumatic stress disorder

Multiple pathways likely explain the relationship between childhood relational trauma and adult mental health. As illustrated in the Figure, developmental effects of ACEs currently under study include impaired neurobiological stress response processes, emotion regulation deficits, negative cognitive style, and insecure attachment,[10] which in turn create vulnerability for interpersonal relationship challenges, low social support, and exposure to additional stressful and traumatic events into adulthood (eg, interpersonal violence).[17,18] These factors generally are associated with poorer adult mental health, and the perinatal period additionally represents a time of increased mental health vulnerability given increased physical and emotional demands.[19]

This review expands our knowledge base of the predictive value of maternal ACEs to the development of mental health conditions other than depression that significantly impact the experience of mothers and infants in the postpartum period. These include anxiety, OCD, PTSD, and substance use disorder. Because the perinatal literature is skewed toward prenatal health and risks over study of the postpartum period, studies conducted during pregnancy also are included, considering the risk symptoms in pregnancy may confer to the postpartum trajectory[20] yet be reported separately.

METHODS

PubMed, PsycINFO, and Google Scholar were each searched as follows: [Adverse Childhood Experiences or ACEs] AND [perinatal or prenatal or pregnancy or postpartum] AND [Anxiety]. The search was repeated replacing the last field with: [obsessive compulsive disorder or OCD], then [post-traumatic stress disorder or PTSD]; and finally [substance use or substance abuse or substance abuse disorder or SUDS]. No cutoff year was specified as it was anticipated that studies including these perinatal mental health conditions would be relatively contemporary. Published peer-reviewed articles in English were retained that reported relations between maternal ACEs and anxiety, OCD, PTSD, or substance use symptoms or diagnosis and included the following: a sample of majority adult birthing people assessed during the prenatal or postpartum year (up to 12 months); a measure of adverse childhood experiences (eg, ACE Questionnaire,[11] Childhood Trauma Questionnaire[21]); and a measure of anxiety, OCD, PTSD, or substance use/abuse symptoms or diagnosis and that did not exclude participants for current psychiatric diagnosis or treatment. Each identified article (and supplementary tables when applicable) was reviewed to determine appropriateness for inclusion (versus title and abstract alone).

RESULTS

As summarized in Table 1 (Postpartum) and Table 2 (Pregnancy), a total of 50 studies that met review criteria were identified. Consistent with the larger perinatal literature, there were substantially more studies conducted with women in pregnancy versus postpartum – especially for substance use. The majority were published in the past 5 years, although where data collection timing could be ascertained, data were typically collected prior to the

COVID-19 pandemic. Most studies were conducted in the US or with other large samples from Canada and western Europe. Studies from other nations and/or diverse sampling practices within the US are highlighted below.

Table 1. Maternal Adverse Childhood Experiences and Mental Health: Postpartum

Study	Country (Setting)	Sample N (Majority)	ACE Measure	Symptom Measure	Key Findings
Anxiety					
Williams, et al 2023[23]	US (NICU)	119 (Black, low income)	ACE-Q	GAD-2	ACES/anxiety (r = .38[a])
Zak-Hunter, et al, 2023[24,c]	US (outpatient)	123 (racially diverse)	ACE-Q	GAD-7	PPD of anxiety for each ACE .04[b]
Erickson, et al 2021[25]	US (psychiatric)	159 (White, high education)	ACE-Q	GAD-7	ACES/anxiety (r = .17[a]-.21[a])
Bilginer, et al 2020[26]	Turkey (outpatient)	31 (literate)	CTQ	BAI	ACEs/anxiety (r = .35[b])
Letourneau et al, 2019[27,c]	US (community)	907 (White, high income)	ACE-Q	SCL-90	ACEs/anxiety (r = .10[a]- .20[a])
McDonald, et al, 2018[28]	Canada (outpatient)	1994 (White, high education)	ACE-Q	SAI	> State anxiety when 3+ ACEs
Menke, et al, 2019[29]	US (outpatient)	328 (White, high education)	ACE-Q	GAD-7	ME ACEs on anxiety (b = 28[b]) if intact sleep
Oosterman et al, 2019[30,c]	Netherlands (social risk)	193 (White, high education)	ACE-Q	STAI	>Trait anxiety if high ACEs (t = -2.2[b])
Agrati, et al 2018[31,c]	Canada (community)	159 (White)	CTQ	STAI	ACEs/elevated anxiety trajectory
PTSD					
Brenner, et al, 2024[45]	Israel (hospital)	440 (Jewish, high education)	CTQ, CM items	PCL-5	ACEs/PTSD (r = .18[b]-.33[b])
Williams, et al, 2023,[23]	US (NICU)	119 (Black, low income)	ACE-Q	IES-R	ACEs/PTSD (r = .43[b])
Grasso, et al, 2020,[46]	US (outpatient)	114 (Latina, low income)	CTQ	STRESS-A	Threat ACEs/PTSD (r = .29[b])
Menke, et al, 2019[29]	US (outpatient)	328 (White, high education)	ACE-Q	IES-R	ME ACEs/PTSD if sleep poor (b = 9.49[b])
Metzler-Brody, et al, 2018[47]	Denmark (Registry)	129 439 (Dane population)	Public records	ASD diagnosis	3+ ACEs → ASD, (HR = 1.51)
Oh, et al, 2016[48]	US (community)	177 (White, high education)	CTQ	PTCI	ACEs/PTSD (r = .27[a])[d]
Substance Use					
Stewart, et al, 2023[49]	US (PRAMS)	920 (White, SES diverse)	ACE, HD items	Any vs poly use	ACEs → use (APR = 2.1-5.5)
Zak-Hunter, et al, 2023[24,c]	US (outpatient)	23 (racially diverse)	ACE-Q	Project EAT urvey	No ME ACEs on use (b = .03)

[a]$P < .05$, [b]$P < .01$.

[c]Mix of some women in pregnancy with postpartum sample.

[d]Significance above and beyond set of control variables.

r = correlation coefficient.

Abbreviations/Key: NICU, neonatal intensive care unit; ACE-Q, ACEs questionnaire; GAD-2, Generalized Anxiety Disorder questionnaire, 2 item; GAD-7, GAD questionnaire, 7 item; PPD, predicted probability difference; CTQ, Childhood Trauma Questionnaire; CM, CM, child maltreatment; BAI, Beck Anxiety Inventory; ME, main effect in regression analyses, controlling for other variables; SCL-90, Symptom Checklist 90, anxiety items; STAI, State Trait Anxiety Inventory; PRAQ-R, Pregnancy Related Anxiety Questionnaire, revised; PCL-5, posttraumatic stress disorder checklist for DSM-V; IES-R, Impact of Events Scale revised; ASD, acute stress disorder; HR, hazard ratio; STRESS-A, Structured Trauma Related Experiences and Symptom Screener for Adults; PTCI, Post Traumatic Cognitions Inventory; PRAMS, Pregnancy Risk Assessment Monitoring System; SES, socioeconomic status; APR, adjusted rrevalence ratio.

Anxiety Disorder

Postpartum: All 9 studies (N = 4013) described in Table 1 that assessed maternal ACEs and anxiety in the postpartum period reported significant associations between total number of ACEs and mothers' report of anxiety symptoms.[23-31] Types of symptoms assessed included those of generalized anxiety disorder,[23-25,29] general cognitive and physiological anxiety,[26,27] current anxious mood, and more stable anxious traits.[28,30,31] Where data were reported that allowed for estimation of effect size, the magnitude of correlations ranged from small (r's = .10-.29)[25,27,29] to medium (r's = .35-.38).[23,26] Of note is that the first 2 studies described in Table 1 found the ACEs-anxiety association remained significant after controlling for sociodemographic variables, community violence exposure,[24] co-occurring depression, peripartum trauma, and associated distress.[23] For example, a study that sampled specifically for racial and ethnic diversity reported that per linear regression modeling, the predicted probability difference of moderate or severe parental anxiety increased 4.4 percentage points for an increase in 1 ACE (95% CI, 0.01–0.08; $P < 0.05$).[24]

Postpartum studies are just beginning to explore ACE thresholds, with 2 finding higher (eg, >3) maternal ACEs confers substantially increased risk for the development of anxiety.[28,30] An additional study beyond the parameters of this review that combined ACE profiles across expectant couples also is striking in that they identified a large increase in risk for maternal postpartum anxiety when mothers and their partners both had 4 or more ACEs coming into the transition to parenthood.[32]

Pregnancy: As shown in Table 2, an additional 15 studies representing 13 independent data sets (N = 23 258) were identified that reported on the maternal ACEs-anxiety association in pregnancy. The types of anxiety assessed were broader than postpartum studies and included pregnancy-specific anxiety[33-37] and clinician-determined thresholds for clinical levels of anxiety severity[38] or DSM disorder,[39-41] in addition to more generalized symptom screening.

Significant associations between maternal ACEs and a range of anxiety types, including clinical disorders, were reported in 10 of the 13 datasets.[10,33,34,36-44] Several controlled for other key adult sociodemographic factors, stress, and mental health con-

Table 2. Maternal Adverse Childhood Experiences and Mental Health: Pregnancy

Study	Country	Sample n	ACE Measure	Symptom Measure	Effect Size
Anxiety					
Clark, et al, 2024[33]	US	292	ACE-Q	ASR/STAI/PSAS	NS to small
Watson, et al, 2024[39, a]	US	18 852	BRFSS	EMR diagnosis	Medium to large
Foti et al, 2023[40, a]	US	1084	BRFSS	EMR diagnosis	Medium to large
Young-Wolf, et al, 2019[41, a]	US	358	BRFSS	EMR diagnosis	Medium to large
Barclay, et al, 2023[50]	US	162	RFQ	OASIS	NS
Kaliush, et al, 2023[34]	US	152	TEBL-C	PSAS	Small
Ward, et al, 2023[38]	US	229	ACE-Q	HAM-A	CSA > clinical cutoff
Wohrer, et al, 2023[42]	US	202	ACE-Q	GAD-7	Small[b]
Osofsky, et al, 2021[10]	US	303	ACE-Q	GAD-2	Medium[b] to large
Racine, et al, 2021[43]	Canada	338	ACE-Q	GAD-2	Large 3+ACEs
Samia, et al, 2021[35]	Kenya	215	ACE-IQ	PRA	NS
Kotimaki, et al, 2020[44]	Finland	2763	TADS	STAI	Small[b]
Ozsahin, et al, 2020[36]	Turkey	536	ACS-Q	PRAQ-R2	Medium
Menke, et al, 2019[29]	US	250	ACS-Q	GAD-7	NS
Fredricksen, et al, 2017[37]	Norway	1036	ACE-Q	PRAQ-R	Small
Posttraumatic Stress Disorder					
Clark, et al, 2024[33]	US	292	ACE-Q	PCL-5	Medium
Carney, et al, 2023[51]	US	137	ACE-Q	PCL-5	Small[b]
Mackle, et al, 2023[52]	Australia	262	ACE-Q	PSS-I-5	Medium[b]
Wohrer, et al, 2023[42]	US	202	ACE-Q	PCL-5	Small[b]
Osofsky, et al, 2021[10]	US	303	ACE-Q	PCL-C	Large[b]
Goldstein, et al, 2020[53]	US	225	CTQ-SF	Stress-A	Large for CM ACEs
Atzl, et al, 2019[54]	US	101	ACE-Q	PCL-5	Medium[b]
Menke, et al, 2019[29]	US	250	ACE-Q	IES-R	Medium[b]
Isosävi, et al, 2018[55]	Gaza	511	TPO	HTQ	Small CM ACEs
Substance Use/Abuse					
Clark, et al, 2023[33]	US	292	ACE-Q	SIP-2R	Small to medium
Duka, et al, 2023[56]	US	218	ACE-Q	4 Ps Plus, UA	4+ ACEs large
Foti, et al, 2023[40]	US	1084	BRFSS	Intake, UA	3+ACEs medium
Racine, et al, 2020,[57] 2021[58]	Canada	1994	ACE-Q	Multiple yes/no	Small to medium[b]
Racine, et al, 2021[43]	Canada	338	ACE-Q	Multiple yes/no	Small to large[b]
Currie, et al, 2020,[59] 2021,[60]	Canada	1600, 1663	ACE-Q	Multiple yes/no	Small to large[b]
Testa, et al, 2022,[61] 2023[62]	US	5399	ACE-Q	Multiple yes/no	3+ ACEs medium[b]
Thomas, et al, 2023[63]	US	2483	BRFSS	Cannabis yes/no	3, 4+ ACEs large[b]
Crouch, et al, 2022[64]	US	617	PACE	Cannabis yes/no	3+ ACEs medium
Hemady, et al, 2022[65]	Multi	1189	ACE-IQ	ASSIST	Hi ACEs NS, small[b]
Klasner, et al, 2022[66]	US	256	ACE-17	Cannabis, UA	Medium[b]
Kors, et al, 2022[67]	US	93	MACE	UA	Small for sex abuse
Jasthi, et al, 2022[68]	US	192	ACE-Q	Chart extraction	4+ ACEs small
Osofsky, et al, 2021[10]	US	303	ACE-Q	ASSIST	Medium[b] for CM
Bhengu, et al, 2020[69]	S Africa	223	ACE-IQ	ASSIST	Small to medium[b]
Pear, et al, 2017[70]	US	2999	NLSYCYA	Tobacco yes/no	Small to medium[b]
Chung, et al, 2017[71]	US	1476	ACE-7	Multiple yes/no	3+ ACEs medium[b]
Smith, et al, 2016[72]	US	2303	ETI-SF	Multiple yes/no	Large for smoking
Frankenberg, et al, 2015[73]	US	1987	BRFSS	BRFSS	Medium to large[b]
Choi, et al, 2014[74]	S Africa	66	CTQ	AUDIT	Insufficient data

[a]Kaiser-Permanente data set.

[b]Significance above and beyond set of control variables.

Abbreviations/Key: ASR, Adult Self Report; STAI, State Trait Anxiety Inventory; PSAS, Pregnancy Stress and Anxiety Scale; NS, not significant; BRFSS, Behavioral Risk Factor Surveillance System Survey; EMR, electronic medical record; RFQ, Risky Families Questionnaire; OASIS, Overall Anxiety Severity & Impairment Scale; TEBL-C, Traumatic Experiences Endorsed Prior to Age 18 (adapted from several measures); HAM-A, Hamilton Anxiety Scale; CSA, childhood sexual abuse; GAD-7, Generalized Anxiety Disorder scale, 7 item; GAD-2, GAD scale, 2 item; ACE-IQ, ACE International Questionnaire; PRA, pregnancy-related anxiety; TADS, Trauma & Distress Scale (CM ACEs items only); PRAQ-R2, Pregnancy Related Anxiety Questionnaire, Revised 2; PSS-I-5 = Posttraumatic Stress Disorder (PTSD) Symptom Scale Interview; PCL-5 = PTSD checklist for DSM-V; PCL-C, abbreviated PTSD checklist, civilian version;CTQ-SF, Childhood Trauma Questionnaire, short form; STRESS-A, Structured Trauma Related Experiences and Symptom Screener for Adults; CM, child maltreatment; IES-R, Impact of Events Scale, revised; TPO, 13-item survey from Transcultural Psychological Organization; HTQ, Harvard Trauma Questionnaire; SIP-2R, Short Inventory of Problems, 2 Revised; UA, urine assay; PACE, Positive & Adverse (11 item) Childhood Experiences; ASSIST, Alcohol, Smoking & Substance Involvement Screening Test; MACE, Maltreatment and Abuse Chronology of Exposure; ACE 17, 17-item ACE Questionnaire; NLSYCYA, National Longitudinal Survey of Youth 1979 (3 extracted ACE items); ETI-SF, Early Trauma Inventory Self Report, Short Form; AUDIT, Alcohol Use Disorders Identification Test.

ditions.[10,41,43] Where effect sizes could be estimated, magnitude of associations were most often small (β; s = .09-.11; r's = .10-.29)[33,34,37,42,44] versus medium (adjusted OR = 2.57-4.7l; r's = .36).[10,36,39,40] Two studies reporting large effects specifically examined mothers with higher (3 to 4+) ACEs and other intrapersonal risk factors.[39,43] For example, in an analysis of over 18 000 electronic medical records for women receiving obstetric care in an integrated managed health care system, the relative odds of having a recorded anxiety disorder increased by 3.39 (95% CI, 2.87-4.00) for mothers with 4 or more ACEs relative to those with none. Relative risk was further increased by 5.05 (95% CI, 4.04-6.31) for those mothers who had high (>4) ACEs and were categorized as reporting low intrapersonal resilience.[39] Child maltreatment-specific ACEs also were identified in a racially and socioeconomically diverse sample as having a stronger association to anxiety symptoms than household dysfunction ACEs, controlling for other stress or psychiatric concerns (β = .14, SE = .06, $P < .02$).[10]

Posttraumatic Stress Disorder

Postpartum: All 6 postpartum-identified studies (N=130 167) in Table 1 reported a significant increase in risk for posttraumatic stress symptoms with the presence of maternal ACEs.[23,29,45-48] The magnitude of effect sizes across findings ranged from small (eg, r's = .18-29)[45,46,48] to medium (r's = .33-.43)[23,45] to large (β = 9.49),[29] the latter representing a higher risk subgroup of women also experiencing sleep insufficiency. Of significant note is a population-level cohort study from Denmark with an exceptionally large sample size (n = 129 539) drawn from national registry records to include ICD psychiatric diagnoses made after birth.[47] This study reports a persistent effect of maternal ACEs on risk of postpartum psychiatric episodes with a dose–response effect, including for clinical diagnosis of acute stress reaction, which can develop into PTSD with more time. Of the adverse childhood events available from public records, out-of-home place-

ment – likely a proxy for more severe child maltreatment and/or parent loss – carried the greatest risk for development of postpartum acute stress disorder (hazard ratio [HR] = 2.49; 95% CI, 1.54–4.03).

Pregnancy: All 9 studies (N = 2283) with women in pregnancy summarized in Table 2 also reported significant associations between maternal ACEs and PTSD symptoms.[10,29,33,42,51-55] Twice as many studies (6) reported medium to large effects (r's = .24-.56; β's = .32-.38)[10,29,33,51,52,54] versus 3 reporting small effect sizes (r's = .16-.24; β's = .14-.19)[42,51,55] and often above and beyond sociodemographic factors and current supports and stressors, including interpersonal violence and predelivery perinatal trauma.[10,29,52,54]

Stronger associations were again found when examining the predictive role of child maltreatment ACEs,[10,53,55] and large effects when considering the contribution of both child maltreatment ACEs and adult interpersonal violence together,[53] highlighting the importance of considering relational trauma across the lifespan. Stronger associations also were found for child maltreatment ACEs that occurred in early versus middle childhood or adolescence,[54] consistent with broader literature suggesting that early childhood represents a critical period for social emotional development.

Obsessive Compulsive Disorder

No studies were identified that examined ACEs-OCD links in the perinatal period. While OCD is believed to have strong neurobiological etiology, early environmental factors have been identified as important to disease severity.[75] Indeed, in the general adult mental health literature, ACEs predict increases in obsessive-compulsive symptom severity and impairment, with the strongest relationships for ACEs again specific to child maltreatment.[76,77]

It is conceivable that for the perinatal population, where intrusive thoughts and images related to harm befalling one's baby are common,[78] maternal ACEs involving a loss of felt safety and/or protection may be particularly salient to postpartum obsessive compulsive symptom content or expression. An Israeli validation study of the Maternal Disintegrative Response Scale (MDRS) for women with histories of early relational trauma and insecure attachment supports this notion.[79] Women in that study who endorsed any ACEs (>0) rated higher on the Intrusive Thoughts subscale (eg, item:"When I'm holding the baby, the uncontrollable thought that I'm going to drop him/her flits through my mind").

Substance Abuse

Postpartum: As shown in Table 1, only 2 studies (N = 2043) examining maternal ACEs and substance use postpartum were identified. One found no significant association between ACEs and tobacco, alcohol, or other drug use frequency in a racially diverse US sample, controlling for current stressors such as financial instability and community violence.[24] The other focused its analysis on Centers for Disease Control and Prevention (CDC)-led Pregnancy Risk Assessment Monitoring Systems (PRAMS) data from 7 US states with high opioid use.[49] Maternal ACEs were related to postpartum substance use and polysubstance use, with those reporting 2 to 4 ACEs being 2 to greater than 5 times as likely to use as those reporting no ACEs (adjusted prevalence ratio [APR] = 2.1, 95% CI, 1.5-2.7; APR = 5.5, 95% CI, 2.6- 11.4, respectively).

Pregnancy: Findings across 23 studies representing 19 independent datasets (N=25 668) summarized in Table 2 consistently reported significant associations between maternal ACEs and tobacco,[10,58,68-72] alcohol,[10,33,58,59,69,71,73,74] cannabis,[63,64,66] and other drug use[10,57,60,62,65,67,71] during pregnancy. Effect sizes ranged from small to large, at times by substance within the same dataset, and often controlling for a range of sociodemographic and other mental health symptoms and stress variables. A threshold of 3 to 4 or more maternal ACEs often was associated with larger effects.[10,40,56,62-64,68,71] While limited to only 3 studies, associations were smaller but significant in non-Western countries.[65,69,74] For example, data from the Evidence for Better Lives Study (EBLS), which includes longitudinal data from 8 low- to middle-income cities in underrepresented regions of the world, classified women into groups based on maltreatment severity. Mothers in the most severely maltreated group as children reported the most prenatal drug use.[65]

DISCUSSION

Maternal ACEs and Postpartum Mental Health

Mothers' self-report of adverse experiences during their own childhood have been identified previously as a risk factor for postpartum depression.[13] This review extends consideration to other mental health conditions important in the postpartum period for women and their infants. A small body of research has begun to emerge, especially over the past 5 years (albeit primarily reporting on pre-COVID-19 data), which identifies maternal ACEs as a risk factor for the development of postpartum anxiety and PTSD. The magnitude of associations suggest that the risk conferred from ACEs is generally stronger for symptoms of postpartum PTSD, which makes sense given evidence that trauma begets trauma. ACEs have been found to increase risk for adult interpersonal violence,[18] experiencing various peripartum medical events as traumatic,[23] and conversion to postpartum PTSD following unexpected birth outcomes (See Figure).[22] While the number of studies is small, data are emerging that, like with postpartum depression, ACEs specific to child maltreatment or experienced at higher levels (3 to 4+ ACEs) have the most predictive value with respect to risk for symptoms of postpartum anxiety and PTSD.

No studies have yet considered maternal ACEs in relation to OCD and very few for substance use in the postpartum year. The latter is an especially important focus for future study given the burgeoning opioid crisis in the United States. ACEs for perinatal mothers in treatment related to methamphetamine and/or opioid abuse are much higher than the general adult population (4 to 5

ACEs on average vs 1 ACE),[80,81] and overdose is now a leading cause of pregnancy-related death.[1,2] There are many more studies on substance use in pregnancy, including the role of maternal ACEs as a significant risk factor, which is understandable given the heightened concern for intrauterine transmission of licit and illicit substances to the developing fetus. However, recent data from the Wisconsin Maternal Morbidity and Mortality Board found that 50% of fatal overdose events occur in the second half of the postpartum year (6-12 months),[82] a time of sharp reduction in access and/or contact with clinicians (especially without Medicaid expansion to 12 months postpartum in Wisconsin).[83] Understanding risks and needs related to continued or increased substance use after pregnancy, when parental concern for transmission to fetal development is reduced, is an essential priority.[84]

ACEs and Prenatal Mental Health

Studies of maternal ACEs and mental health conditions of interest also were reviewed during pregnancy, as more exist and may inform our emerging understanding of the maternal ACEs/postpartum mental health continuum. Pregnancy studies paralleled the postpartum findings above, showing ACEs increases risk for symptoms of prenatal anxiety and PTSD—especially for women reporting high levels of ACEs (3 to 4+) and for child maltreatment ACEs. In general, pregnancy studies were more likely to include important control variables in their analyses, showing independent effects of maternal ACEs on perinatal mental health and substance abuse symptoms above and beyond the impact of sociodemographic factors or concurrent stress or trauma related to peripartum events or violence. Taken together, maternal ACEs are a consistent risk factor for a range of mental health conditions across the perinatal period.

Limitations

Limitations of this review include the relatively small number of studies that focus specifically on the postpartum versus pregnancy period. As this body of literature grows, summation via more rigorous methods including meta-analysis will be important to identify sources of heterogeneity across studies and confirm magnitude of effects, as well as variations related to types of maternal ACEs or symptom risk. Increased use of diagnostic tools to supplement symptom screeners also will clarify the threshold of maternal ACEs that confer risk for clinical diagnosis and functional impairment across conditions.

Most studies to date have been conducted in the US, Canada, and western European nations. While some have actively worked to sample at a population level or with intentionally diverse communities, data remain biased toward White mothers with higher levels of education and/or economic stability. Diversifying the ACEs-perinatal mental health body of literature is especially important given that membership in underrepresented ethnic and racial groups is more often associated with other key factors that impact mental health access (eg, socioeconomic status, immigration status) or risk (eg, racism),[11,85] creating additional levels of historical and familial vulnerability for expectant or new parents.

Implications for Policy and Practice

Calls for perinatal screening for a broader range of mental health concerns in addition to depression and trauma exposure are increasing.[10,86,87] The American College of Obstetrics and Gynecology (ACOG) offers recommendations and screening guidance that expands beyond depression for other postpartum mood, anxiety, and PTSD symptoms[88] and has advanced a policy priority emphasizing the need for collaborative, patient-centered, and ongoing communication between clinicians and mothers about substance use risk and needs.[89] Further, the ACOG Committee for Healthcare for Underserved Women recommends screening of past and current trauma as a key component of the provision of trauma-informed perinatal care environments.[90]

Trauma-informed perinatal care involves understanding the full range of potential effects that past and/or current trauma may have for women moving through pregnancy, birth, and the postpartum period. This includes recognizing signs of trauma response activation, such as in response to medical visit dynamics (eg, felt powerlessness), procedures, or physical sensations; responding to patients who have experienced trauma effectively to increase trust, collaboration, and maternal confidence; and resisting retraumatization, such as affirming womens' experiences of distress even when perinatal health or outcomes are considered successful.[86] To begin, clinicians must first be aware of patient trauma history.

Screening for early relational trauma using an instrument like the ACE Questionnaire[12] offers a first step toward identification of women who may need additional support to reduce trauma-related risks to their own perinatal experience, emerging parent/infant relationship, and infants' developmental course.[10,86,87] Considering that ACEs can increase feelings of interpersonal distrust and lead to lower levels of adult social support more broadly, compassionate, culturally sensitive ACEs screening conversations between clinicians and patients can serve to build trust and connection, while facilitating shared communication about important mental health risks and support needs in and outside the perinatal care environment.[91] For example, clinicians might wonder with mothers who report high (3 to 4+) ACEs about whether they feel that these difficult experiences from their own childhood are affecting how they think or feel about seeking medical care or becoming a parent themselves. Such conversations can lead to identification of sources of resiliency and fears or concerns, both of which may guide aspects of treatment planning or the identification of helpful resources and referrals.

Barriers to additional screening in health care environments certainly exist, including limits of clinician time.[87] Despite national recommendations above, screening practices for ACEs[92,93] and postpartum mental health symptoms[91] are reported to be low.

However, according to the most recently released (2018-2019) PRAMS data – the ongoing survey of new mothers conducted jointly by the CDC and state health departments – Wisconsin is screening 94% of women for depression either during prenatal or postpartum visits and 72% of women at both.[94] Despite this relative success, the addition of several other recommended perinatal mental health screening tools – for anxiety, PTSD, and substance use – represent a challenge. As summarized in this review, however, because the evidence is growing that ACEs predict a wide range of perinatal mental health conditions, the use of a screening tool to identify women with high (3 to 4+) ACEs during pregnancy may help to prioritize patients for whom increased outreach and mental health screening across the perinatal period – for conditions beyond depression – is most needed.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Declercq E, Zephyrin, lc. maternal mortality in the United States: a primer. Commonwealth Fund. December 16, 2020. Accessed June 25, 2024. https://www.commonwealthfund.org/publications/issue-brief-report/2020/dec/maternal-mortality-united-states-primer

2. Trost SL, Busacker A, Leonard M, et al. Pregnancy-related deaths: data from maternal mortality review committees in 38 U.S. States, 2020. Centers for Disease Control and Prevention. May 28, 2024. Accessed June 2024. https://www.cdc.gov/maternal-mortality/php/data-research/index.html

3. Glazer KB, Howell EA. A way forward in the maternal mortality crisis: addressing maternal health disparities and mental health. *Arch Womens Ment Health.* 2021;24(5):823-830. doi:10.1007/s00737-021-01161-0

4. Haight SC, Daw JR, Martin CL, et al. Racial and ethnic inequities in postpartum depressive symptoms, diagnosis, and care in 7 US jurisdictions. *Health Aff (Millwood).* 2024;43(4):486-495. doi:10.1377/hlthaff.2023.01434

5. Field, T. Postpartum anxiety prevalence, predictors and effects on child development: a review. *J Psychiatry Psychiatr Disord.* 2017;1(2):86-102.

6. Christie H, Hamilton-Giachritsis C, Alves-Costa F, Tomlinson M, Halligan SL. The impact of parental posttraumatic stress disorder on parenting: a systematic review. *Eur J Psychotraumatol.* 2019;10(1):1550345. doi:10.1080/20008198.2018.1550345

7. Wisconsin Department of Health Services. *Wisconsin Maternal Mortality Review Team Recommendations: 2020 Pregnancy Associated Deaths.* Wisconsin Department of Health Services, Bureau of Community Health Promotion; 2024. Accessed July 1, 2024. https://www.dhs.wisconsin.gov/publications/p02108-2020.pdf

8. Lieberman AF, Padrón E, Van Horn P, Harris WW. Angels in the nursery: the intergenerational transmission of benevolent parental influences. *Infant Ment Health J.* 2005;26(6):504-520. doi:10.1002/imhj.20071

9. Scorza P, Monk C. Anticipating the stork: stress and trauma during pregnancy and the importance of prenatal parenting. *Zero Three.* 2019;39(5):5–13.

10. Osofsky JD, Osofsky HJ, Frazer AL, et al. The importance of adverse childhood experiences during the perinatal period. *Am Psychol.* 2021;76(2):350-363. doi:10.1037/amp0000770

11. Kim HG, Kuendig J, Prasad K, Sexter A. Exposure to racism and other adverse childhood experiences among perinatal women with moderate to severe mental illness. *Community Ment Health J.* 2020;56(5):867-874. doi:10.1007/s10597-020-00550-6

12. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) study. *Am J Prev Med.* 1998;14(4):245-258. doi:10.1016/s0749-3797(98)00017-8

13. Daníelsdóttir HB, Aspelund T, Shen Q, et al. Adverse childhood experiences and adult mental health outcomes. *JAMA Psychiatry.* 2024;81(6):586–594. doi:10.1001/jamapsychiatry.2024.0039

14. Zarse EM, Neff MR, Yoder R, Hulvershorn L, Chambers JE, Chambers RA. The adverse childhood experiences questionnaire: two decades of research on childhood trauma as a primary cause of adult mental illness, addiction, and medical diseases. *Cogent Med.* 2019;6(1). doi:10.1080/2331205X.2019.1581447

15. Mersky JP, Lee CP. Adverse childhood experiences and poor birth outcomes in a diverse, low-income sample. *BMC Pregnancy Childbirth*. 2019;19(1):387. doi:10.1186/s12884-019-2560-8

16. Fu C, Li C, Wan X, Yang Y, Zhang S, Hu J. The Relationship between adverse childhood experiences and postpartum depression: a systematic review and meta-analysis. *Trauma Violence Abuse.* 2024;25(4):3066-3081. doi:10.1177/15248380241235639

17. Liu RT. Childhood adversities and depression in adulthood: current findings and future directions. *Clin Psychol (New York).* 2017;24(2):140-153. doi:10.1111/cpsp.12190

18. Ornduff SR, Kelsey RM, O'Leary KD. Childhood physical abuse, personality, and adult relationship violence: a model of vulnerability to victimization. *Am J Orthopsychiatry*. 2001;71(3):322-331. doi:10.1037/0002-9432.71.3.322

19. Munk-Olsen T, Maegbaek ML, Johannsen BM, et al. Perinatal psychiatric episodes: a population-based study on treatment incidence and prevalence. *Transl Psychiatry.* 2016;6(10):e919. doi:10.1038/tp.2016.190

20. Andersson S, Bathula DR, Iliadis SI, Walter M, Skalkidou A. Predicting women with depressive symptoms postpartum with machine learning methods. Sci Rep. 2021;11(1):7877. doi:10.1038/s41598-021-86368-y

21. Bernstein, DP, Fink L. Childhood Trauma Questionnaire: A Retrospective Self-Report Manual. The Psychological Corporation; 1998.

22. Geller PA, Stasko EC. Effect of previous posttraumatic stress in the perinatal period. *J Obstet Gynecol Neonatal Nurs*. 2017;46(6):912-922. doi:10.1016/j.jogn.2017.04.136

23. Williams A, Parlier-Ahmad AB, Thompson E, et al. Peripartum traumas and mental health outcomes in a low-income sample of NICU mothers: a call for family-centered, trauma-informed care. Children (Basel). 2023;10(9):1477. doi:10.3390/children10091477

24. Zak-Hunter L, Carr CP, Tate A, Brustad A, Mulhern K, Berge JM. Associations between adverse childhood experiences and stressful life events and health outcomes in pregnant and breastfeeding women from diverse racial and ethnic groups. *J Womens Health (Larchmt).* 2023;32(6):702-714. doi:10.1089/jwh.2022.0329

25. Erickson NL, Flynn JM, Kim HG. Adverse childhood experiences and current psychosocial stressors: exploring effects on mental health and parenting outcomes from a mother-baby partial hospital program. *Matern Child Health J.* 2022;26(2):289-298. doi:10.1007/s10995-021-03345-7

26. Bilginer C, Bag O, Cekin Yilmaz B. Traumatic Childhood Experiences and Psychiatric Outcomes of Adolescent Mothers in Turkey. *J Child Sex Abus.* 2020;29(5):531-549. doi:10.1080/10538712.2019.1685617

27. Letourneau N, Dewey D, Kaplan BJ, et al. Intergenerational transmission of adverse childhood experiences via maternal depression and anxiety and moderation by child sex. *J Dev Orig Health Dis.* 2019;10(1):88-99. doi:10.1017/S2040174418000648

28. McDonald SW, Madigan S, Racine N, Benzies K, Tomfohr L, Tough S. Maternal adverse childhood experiences, mental health, and child behaviour at age 3: the All Our Families community cohort study. *Prev Med.* 2019;118:286-294. doi:10.1016/j.ypmed.2018.11.013

29. Menke RA, Swanson L, Erickson NL, et al. Childhood adversity and sleep are associated with symptom severity in perinatal women presenting for psychiatric care. *Arch Womens Ment Health.* 2019;22(4):457-465. doi:10.1007/s00737-018-0914-2

30. ~~29.~~ Oosterman M, Schuengel C, Forrer ML, De Moor MHM. The impact of childhood trauma and psychophysiological reactivity on at-risk women's adjustment to parenthood. *Dev Psychopathol.* 2019;31(1):127-141. doi:10.1017/S0954579418001591

31. Agrati D, Browne D, Jonas W, et al. Maternal anxiety from pregnancy to 2 years postpartum: transactional patterns of maternal early adversity and child temperament. *Arch Womens Ment Health*. 2015;18(5):693-705. doi:10.1007/s00737-014-0491-y

32. Andersson SO, Annerbäck EM, Söndergaard HP, Hallqvist J, Kristiansson P. Adverse childhood experiences are associated with choice of partner, both partners' relationship and psychosocial health as reported one year after birth of a common child. A cross-sectional study. *PLoS One*. 2021;16(1):e0244696. doi:10.1371/journal.pone.024469

33. Clark HM, Hankin BL, Narayan AJ, Davis EP. Risk and resilience factors for psychopathology during pregnancy: an application of the Hierarchical Taxonomy of Psychopathology (HiTOP). *Dev Psychopathol*. 2024;36(2):545-561. doi:10.1017/

S0954579422001390

34. Kaliush PR, Kerig PK, Raby KL, et al. Examining implications of the developmental timing of maternal trauma for prenatal and newborn outcomes. *Infant Behav Dev.* 2023;72:101861. doi:10.1016/j.infbeh.2023.101861

35. Samia P, Premji S, Tavangar F, et al. Adverse childhood experiences and changing levels of psychosocial distress scores across pregnancy in Kenyan women. *Int J Envion Res Public Health.* 2020;17(10):3401. doi:10.3390/ijerph17103401

36. Özşahin Z. The effects of adverse childhood experiences on pregnancy-related anxiety and acceptance of motherhood role. Afr Health Sci. 2020;20(3):1217-1228. doi:10.4314/ahs.v20i3.25

37. Fredriksen E, von Soest T, Smith L, Moe V. Patterns of pregnancy and postpartum depressive symptoms: latent class trajectories and predictors. *J Abnorm Psychol.* 2017;126(2):173-183. doi:10.1037/abn0000246

38. Ward LG, Bublitz M, Sokol N, Brown S, Stroud LR. Experiences of maltreatment in childhood are associated with increasing anxiety and lower body acceptance over pregnancy. *J Psychosom Res*. 2023;172:111414. doi:10.1016/j.jpsychores.2023.111414

39. Watson CR, Eaton A, Campbell CI, et al. Association of adverse childhood experiences and resilience with depression and anxiety during pregnancy. *Obstet Gynecol.* 2024;143(5):707-710. doi:10.1097/AOG.0000000000005545

40. Foti TR, Watson C, Adams SR, et al. Associations between adverse childhood experiences (ACEs) and prenatal mental health and substance use. *Int J Environ Res Public Health*. 2023;20(13):6289. doi:10.3390/ijerph20136289

41. Young-Wolff KC, Alabaster A, McCaw B, et al. Adverse childhood experiences and mental and behavioral health conditions during pregnancy: the role of resilience. *J Womens Health (Larchmt)*. 2019;28(4):452-461. doi:10.1089/jwh.2018.7108

42. Wohrer F, Ngo H, DiDomenico J, Ma X, Roberts MH, Bakhireva LN. Potentially modifiable risk and protective factors affecting mental and emotional wellness in pregnancy. *Front Hum Neurosci*. 2024;18:1323297. doi:10.3389/fnhum.2024.1323297

43. Racine N, Byles H, Killam T, Ereyi-Osas W, Madigan S. Asking about childhood adversity in the prenatal care setting: cross-sectional associations with maternal health and mental health outcomes. *Matern Child Health J.* 2021;26(5):994-1004. doi:10.1007/s10995-021-03301-5

44. Kotimäki S, Härkönen J, Karlsson L, Karlsson H, Scheinin NM. Educational differences in prenatal anxiety and depressive symptoms and the role of childhood circumstances. *SSM Popul Health*. 2020;12:100690. doi:10.1016/j.ssmph.2020.100690

45. Brenner I, Ginzburg K, Golan A, et al. Peripartum dissociation, sense of control, postpartum posttraumatic stress disorder and emotional adjustment to motherhood in adult survivors of childhood maltreatment. *Arch Womens Ment Health.* 2024;27(1):127-136. doi:10.1007/s00737-023-01379-0

46. Grasso DJ, Drury S, Briggs-Gowan M, et al. Adverse childhood experiences, posttraumatic stress, and FKBP5 methylation patterns in postpartum women and their newborn infants. *Psychoneuroendocrinology*. 2020;114:104604. doi:10.1016/j.psyneuen.2020.104604

47. Meltzer-Brody S, Larsen JT, Petersen L, et al. Adverse life events increase risk for postpartum psychiatric episodes: a population-based epidemiologic study. *Depress Anxiety*. 2018;35(2):160-167. doi:10.1002/da.22697

48. Oh W, Muzik M, McGinnis EW, Hamilton L, Menke RA, Rosenblum KL. Comorbid trajectories of postpartum depression and PTSD among mothers with childhood trauma history: course, predictors, processes and child adjustment. *J Affect Disord.* 2016;200:133-141. doi:10.1016/j.jad.2016.04.037

49. Stewart A, Ko J, Salvesen von Essen B, et al. Association of mental health conditions, recent stressful life events, and adverse childhood experiences with postpartum substance use - seven states, 2019-2020. *MMWR Morb Mortal Wkly Rep.* 2023;72(16):416-420. doi:10.15585/mmwr.mm7216a1

50. Barclay ME, Rinne GR, Somers JA, Lee SS, Coussons-Read M, Dunkel Schetter C. Maternal early life adversity and infant stress regulation: intergenerational associations and mediation by maternal prenatal mental health. *Res Child Adolesc Psychopathol.* 2023;51(12):1839-1855. doi:10.1007/s10802-022-01006-z

51. Carney JR, Miller-Graff LE, Napier TR, Howell KH. Elucidating the relations between adverse childhood experiences, age of exposure to adversity, and adult posttraumatic stress symptom severity in pregnant women. *Child Abuse Negl.* 2023;136:105995. doi:10.1016/j.chiabu.2022.105995

52. Mackle T, Colodro-Conde L, de Dassel T, et al. "Echoes of a dark past" is a history of maternal childhood maltreatment a perinatal risk factor for pregnancy and postpartum trauma experiences? A longitudinal study. *BMC Pregnancy Childbirth.* 2023;23(1):397. doi:10.1186/s12884-023-05714-2

53. Goldstein BL, Briggs-Gowan M, Grasso DJ. The effects of intimate partner violence and a history of childhood abuse on mental health and stress during pregnancy. *J Fam Violence*. 2021;36(3):337-346. doi:10.1007/s10896-020-00149-1

54. Atzl VM, Narayan AJ, Rivera LM, Lieberman AF. Adverse childhood experiences and prenatal mental health: type of ACEs and age of maltreatment onset. *J Fam Psychol*. 2019;33(3):304-314. doi:10.1037/fam0000510

55. Isosävi S, Diab SY, Kangaslampi S, et al. Maternal trauma affects prenatal mental health and infant stress regulation among Palestinian dyadS. *Infant Ment Health J.* 2017;38(5):617-633. doi:10.1002/imhj.21658

56. Duka S, Rahman S, Hansen SE, Esernio-Jenssen D. the effect of maternal adverse childhood experiences (ACEs) on substance use during pregnancy. *Matern Child Health* J. 2023;27(Suppl 1):153-165. doi:10.1007/s10995-023-03768-4

57. Racine N, McDonald S, Chaput K, Tough S, Madigan S. Maternal substance use in pregnancy: differential prediction by childhood adversity subtypes. *Prev Med.* 2020;141:106303. doi:10.1016/j.ypmed.2020.106303

58. Racine N, McDonald S, Chaput K, Tough S, Madigan S. Pathways from maternal adverse childhood experiences to substance use in pregnancy: findings from the All Our Families cohort. *J Womens Health (Larchmt)*. 2021;30(12):1795-1803. doi:10.1089/jwh.2020.8632

59. Currie CL, Sanders JL, Swanepoel LM, Davies CM. Maternal adverse childhood experiences are associated with binge drinking during pregnancy in a dose-dependent pattern: findings from the All Our Families cohort. *Child Abuse Negl.* 2020;101:104348. doi:10.1016/j.chiabu.2019.104348 -1652. doi:10.1007/s10461-019-02661-y

60. Currie CL, Tough SC. Adverse childhood experiences are associated with illicit drug use among pregnant women with middle to high socioeconomic status: findings from the All Our Families cohort. *BMC Pregnancy Childbirth*. 2021;21(1):133. doi:10.1186/s12884-021-03591-1

61. Testa A, Jackson DB, Boccio C, Ganson KT, Nagata JM. Adverse childhood experiences and marijuana use during pregnancy: findings from the North Dakota and South Dakota PRAMS, 2017-2019. *Drug Alcohol Depend.* 2022;230:109197. doi:10.1016/j.drugalcdep.2021.109197

62. Testa A, Jacobs B, Zhang L, Jackson DB, Ganson KT, Nagata JM. Adverse childhood experiences and prescription opioid use during pregnancy: an analysis of the North and South Dakota PRAMS, 2019-2020. *BMC Pregnancy Childbirth.* 2023;23(1):602. doi:10.1186/s12884-023-05925-7

63. Thomas SA, Clements-Nolle KD, Wagner KD, Omaye S, Lu M, Yang W. Adverse childhood experiences, antenatal stressful life events, and marijuana use during pregnancy: a population-based study. *Prev Med.* 2023;174:107656. doi:10.1016/j.ypmed.2023.107656

64. Crouch D, Chambers C, Bertrand K, Bandoli G. The association between adverse and positive childhood experiences and marijuana use during lactation. *Breastfeed Med.* 2023;18(3):212-218. doi:10.1089/bfm.2022.0243

65. Hemady CL, Speyer LG, Murray AL, et al. Patterns of adverse childhood experiences and associations with prenatal substance use and poor infant outcomes in a multi-country cohort of mothers: a latent class analysis. *BMC Pregnancy Childbirth.* 2022;22(1):505. doi:10.1186/s12884-022-04839-0

66. Klasner C, Brown J, Gopalakrishnan M, Metwally DE, Besse M, Mark K. Effect of maternal adverse childhood experiences (ACE) and cannabis use on pregnancy outcomes. *Arch Womens Ment Health.* 2022;25(6):1097-1104. doi:10.1007/s00737-022-01269-x

67. Kors S, Kurdziel-Adams G, Towers C, Fortner K, Macfie J. Sexual abuse as a risk factor for opioid misuse in pregnancy. *J Child Sex Abus*. 2022;31(5):538-549. doi:10.1080/10538712.2022.2056104

68. Jasthi DL, Nagle-Yang S, Frank S, Masotya M, Huth-Bocks A. Associations between adverse childhood experiences and prenatal mental health and substance use among urban, low-income women. *Community Ment Health J.* 2022;58(3):595-605. doi:10.1007/s10597-021-00862-1

69. Bhengu BS, Tomita A, Mashaphu S, Paruk S. The role of adverse childhood experiences on perinatal substance use behaviour in KwaZulu-Natal Province, South Africa. *AIDS Behav.* 2020;24(6):1643-1652. doi:10.1007/s10461-019-02661-y

70. Pear VA, Petito LC, Abrams B. The role of maternal adverse childhood experiences and race in intergenerational high-risk smoking behaviors. *Nicotine Tob Res.* 2017;19(5):623-630. doi:10.1093/ntr/ntw295

71. Chung EK, Nurmohamed L, Mathew L, Elo IT, Coyne JC, Culhane JF. Risky health behaviors among mothers-to-be: the impact of adverse childhood experiences. *Acad Pediatr.* 2010;10(4):245-251. doi:10.1016/j.acap.2010.04.003

72. Smith MV, Gotman N, Yonkers KA. Early childhood adversity and pregnancy outcomes. *Matern Child Health J.* 2016;20(4):790-798. doi:10.1007/s10995-015-1909-5

73. Frankenberger DJ, Clements-Nolle K, Yang W. The association between adverse childhood experiences and alcohol use during pregnancy in a representative sample of adult women. *Womens Health Issues.* 2015;25(6):688-695. doi:10.1016/j.whi.2015.06.007

74. Choi KW, Abler LA, Watt MH, et al. Drinking before and after pregnancy recognition among South African women: the moderating role of traumatic experiences. *BMC Pregnancy Childbirth*. 2014;14:97. doi:10.1186/1471-2393-14-97

75. Boger S, Ehring T, Berberich G, Werner GG. Impact of childhood maltreatment on obsessive-compulsive disorder symptom severity and treatment outcome. *Eur J Psychotraumatol.* 2020;11(1):1753942. doi:10.1080/20008198.2020.1753942

76. Gu W, Zhao Q, Yuan C, Yi Z, Zhao M, Wang Z. Impact of adverse childhood experiences on the symptom severity of different mental disorders: a cross-diagnostic study. *Gen Psychiatry.* 2022;35(2):e100741. doi:10.1136/gpsych-2021-100741

77. Hodny F, Ociskova M, Prasko J, et al. Early life experiences and adult attachment in obsessive-compulsive disorder. Part 1: relationships between demographic, clinical, and psychological factors in pharmacoresistant OCD. *Neuro Endocrinol Lett.* 2022;43(6):333-344.

78. Hudak R, Wisner KL. Diagnosis and treatment of postpartum obsessions and compulsions that involve infant harm. *Am J Psychiatry*. 2012;169(4):360-3. doi:10.1176/appi.ajp.2011.11050667

79. Chasson M, Taubman-Ben-Ari O. The Maternal Disintegrative Responses Scale (MDRS) and its associations with attachment orientation and childhood trauma. *Child Abuse Negl.* 2022;131:105693. doi:10.1016/j.chiabu.2022.105693

80. Beltrán-Arzate K, Hodson K, Tes HK, et al. Contextual risk and psychosocial profiles of opioid-using mothers: a mixed-methods study. *Womens Health (Lond).* 2021;17:17455065211060624. doi:10.1177/17455065211060624

81. Gannon M, Short V, Becker M, et al. Doula engagement and maternal opioid use disorder (OUD): experiences of women in OUD recovery during the perinatal period. *Midwifery*. 2022;106:103243. doi:10.1016/j.midw.2021.103243

82. *Wisconsin Maternal Mortality Review: Pregnancy-associated overdose deaths (2016-2019).* Wisconsin Department of Health Services and University of Wisconsin Prevention Research Center; 2021. Accessed June 2024. https://prc.wisc.edu/wp-content/uploads/sites/1127/2021/09/MMR-RMOR-Repor.pdf

83. Medicaid postpartum coverage extension tracker. KFF. December 2, 2024. Accessed Accessed June 2024. https://www.kff.org/medicaid/issue-brief/medicaid-postpartum-coverage-extension-tracker/

84. Wisconsin Department of Health Services. Wisconsin Maternal Mortality Review Team recommendations: 2020 pregnancy-associated deaths. June 2024. Accessed June 2024. https://www.dhs.wisconsin.gov/publications/p02108-2020.pdf

85. Mersky J, Plummer Lee C, Janczewski C. Adverse adult experiences and health outcomes: Racial and ethnic differences in a low-income sample. *Stress Health.* 2023;39(3):627-637. doi:10.1002/smi.3212

86. Kuzma EK, Pardee M, Morgan A. Implementing patient-centered trauma-informed care for the perinatal nurse. *J Perinat Neonatal Nurs.* 2020;34(4):E23-E31. doi:10.1097/JPN.0000000000000520

87. Tran N, Callaway L, Shen S, et al. Screening for adverse childhood experiences in antenatal care settings: a scoping review. *Aust N Z J Obstet Gynaecol.* 2022;62(5):626-634. doi:10.1111/ajo.13585

88. Screening and diagnosis of mental health conditions during pregnancy and postpartum: ACOG Clinical Practice Guideline No. 4. *Obstet Gynecol.* 2023;141(6):1232-1261. doi:10.1097/AOG.0000000000005200

89. Policy priorities: substance use disorder in pregnancy. American College of Obstetricians and Gynecologists. Accessed June 2024. https://www.acog.org/advocacy/policy-priorities/substance-use-disorder-in-pregnancy

90. Caring for patients who have experienced trauma: ACOG Committee Opinion Summary, Number 825. *Obstet Gynecol.* 2021;137(4):757-758. doi:10.1097/AOG.0000000000004328

91. Burkhard, J & Reynolds, B. U.S. maternal depression screening rates released for the first time through HEDIS. Policy Center for Maternal Mental Health. November 14, 2022. Accessed June 2024 https://www.2020mom.org/blog/2022/11/14/us-maternal-depression-screening-rates-released-for-the-first-time-through-hedis

92. Farrow VA, Bosch J, Crawford JN, Snead C, Schulkin J. Screening for history of childhood abuse: beliefs, practice patterns, and barriers among obstetrician-gynecologists. *Womens Health Issues.* 2018;28(6):559-568. doi:10.1016/j.whi.2018.09.001

93. Maunder RG, Hunter JJ, Tannenbaum DW, Le TL, Lay C. Physicians' knowledge and practices regarding screening adult patients for adverse childhood experiences: a survey. *BMC Health Serv Res.* 2020;20(1):314. doi:10.1186/s12913-020-05124-6

94. Wisconsin Department of Health Services. Wisconsin PRAMS 2018-2019 surveillance report. March 2022. Accessed June 2024. https://www.dhs.wisconsin.gov/publications/p02500-2019.pdf

Trends in Teenage Birth Rates in Wisconsin, 2011-2022: Continued Declines and Persistent Disparities

Josh Hoffner, DO, MPH; Ayanna Vasquez, MD, MS; Patrick Remington, MD, MPH

ABSTRACT

Background: Teenage pregnancy remains an important public health problem despite recent declines in teen births.

Methods: Teen (ages 15-19) birth rates (per 1000 females) in Wisconsin from 2011 through 2022 were compared by race/ethnicity and county using Wisconsin Interactive Statistics on Health data.

Results: Teen birth rates declined by 50% from 23.3 per 1000 teens in 2011-2013 to 11.5 per 1000 teens in 2020-2022, with the greatest decline among American Indian/Alaska Native teens (64%) and least among Black teens (40%), resulting in persistent 3-fold to 6-fold disparities between racial/ethnic groups. Teen birth rates by county had a 20-fold difference between Ozaukee (2.7 per 1000) and Menominee counties (54.5 per 1000).

Discussion: The remarkable decline in teen births suggests public health and health care interventions are working, but targeted effort is needed to reduce the growing disparities.

BACKGROUND

Although overall teen birth rates are decreasing in the United States, it continues to be an important public health problem with significant economic, health-related, and social consequences.[1] Teen birth rates vary by geographic region in the US and range from a low of 4.6 teen births per 1000 in New Hampshire and high of 26.4 in Mississippi.[2] Research has demonstrated that social determinants of health at the family and community levels may contribute to high teen birth rates.[3] These differences may be due to variations in the demographic characteristics of communities as well as socioecological factors, such as the availability of health care resources and public health and cultural norms.

Early identification of teens at risk for becoming pregnant is key.[1] Public health programs designed to prevent teen pregnancy have demonstrated mixed findings for preventing teen pregnancies and births, but federally funded programs with more comprehensive sex education have resulted in overall decreases in the rate of teen births at the county level.[4] Common education provided in comprehensive sex education programs includes information on sex, contraception, and reproductive health, and these are more comprehensive compared to abstinence-only programs.[4]

The purpose of this paper is to review trends in teen births in Wisconsin from 2011 through 2022, updating an analysis published in this journal in 2013.[5]

METHODS

Data Source

Data on teen (ages 15-19) birth rates per 1000 females in Wisconsin from 2011 through 2022 were obtained from the Wisconsin Interactive Statistics on Health (WISH) available at https://www.dhs.wisconsin.gov/wish/index.htm.

Data Analysis

Teen birth rates were calculated by dividing the number of births by the population of female teenagers overall, by year, race, ethnicity, and county of residence. Race/ethnicity groups identified in this paper are based on WISH reporting standards, and all race groups are non-Hispanic.

• • •

Author Affiliations: Preventive Medicine Residency Program, Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Hoffner, Vasquez, Remington).

Corresponding Author: Josh Hoffner, DO, MPH, University of Wisconsin School of Medicine and Public Health, Department of Population Health Sciences, 610 Walnut St, Madison, WI 53726; email Josh.hoffner@lmunet.edu; ORCID ID 0009-0006-9246-4428

For reliable trend analysis, 3-year average rates were calculated for 2011-2013 and 2020-2022. Rate ratios (RR) were calculated by dividing the rate of births among White female teens (the lowest rates in 2011-2013) by the rates in other race/ethnicity groups. Percent change was calculated by dividing the difference in rates by the rate at the baseline time period. Rates by Wisconsin counties were calculated and compared for the 12-year period 2011-2022.

The following was used to calculate the 95% Confidence Limits (CL): 95% CL = 1.96*rate/(square root of n), where n = number of births.[5] The number of excessive teen births was calculated by multiplying the teen birth rate in 2011 (25.2 births/1000) by the population in each year (2012-2022) to get the "expected" number of teen births if the 2011 rate had not changed. The number of "observed" births during this 11-year period was then subtracted from this total to determine the number of teen births that were avoided.

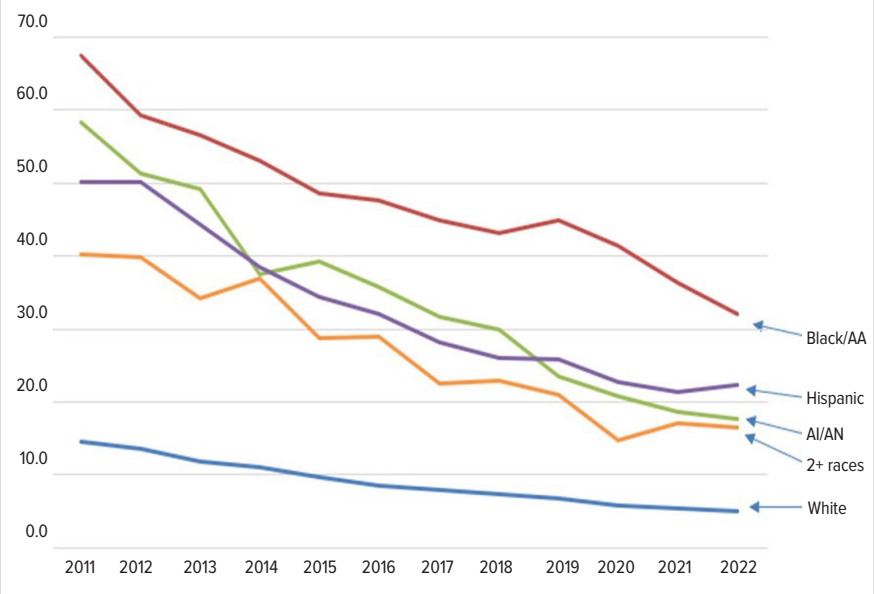
This study performed a secondary analysis of existing data from WISH, which did not require institutional review board review since it did not fall within the regulatory definition of research involving human subjects.

Table. Trends in Teen (ages 15-19) Birth Rates (per 1000 females) from 2011-2013 to 2020-2022, by Maternal Race and Ethnicity, Wisconsin.

Race/Ethnicity	Rate in 2011–13 (95% CI)	RR[a] 2011–13	Rate in 2020–22 (95% CI[a])	RR[a] 2020–22	% Change (2011–13 to 2020-22)
White[c]	13.3 (13.3–13.4)	1.0[b]	5.4 (5.4–5.5)	1.0[b]	–59%
American Indian/Alaska Native[c]	52.9 (50.7–55.1)	4.0	19.0 (18.1–19.9)	3.5	–64%
Black[c]	61.1 (60.2–62.0)	4.6	36.6 (36.0–37.1)	6.7	–40%
Hispanic	48.2 (47.5–48.9)	3.6	22.1 (21.8–22.4)	4.1	–54%
Two or more races[c]	38.1 (36.9–39.3)	2.9	16.1 (15.6–16.6)	3.0	–58%
All[d]	23.4 (23.2–23.4)		11.5 (11.5–11.6)		–50%

[a]Relative risk.
[b]Referent group.
[c]Non-Hispanic.
[d]Includes all races.

Figure 1. Trends in Teen (ages 15-19) Birth Rates (per 1000 females) by Race and Ethnicity in Wisconsin, 2011-2022.



Abbreviations: AA, African American; AI/AN, American Indian, Alaska Native.

RESULTS

There were 34 714 births to mothers 15 to 19 years of age in Wisconsin during 2011-2022, which corresponds to an annual rate of 17.1 teen births per 1000 females ages 15 to 19 years. The rate steadily declined from 23.4 per 1000 teens in 2011-2013 to 11.7 per 1000 teens in 2020-2022—a relative decline of 50% or about 4.5% per year (Table). If the teen birth rate had not declined from 2011, there would have been 16 719 additional teen births during these 11 years than were actually observed.

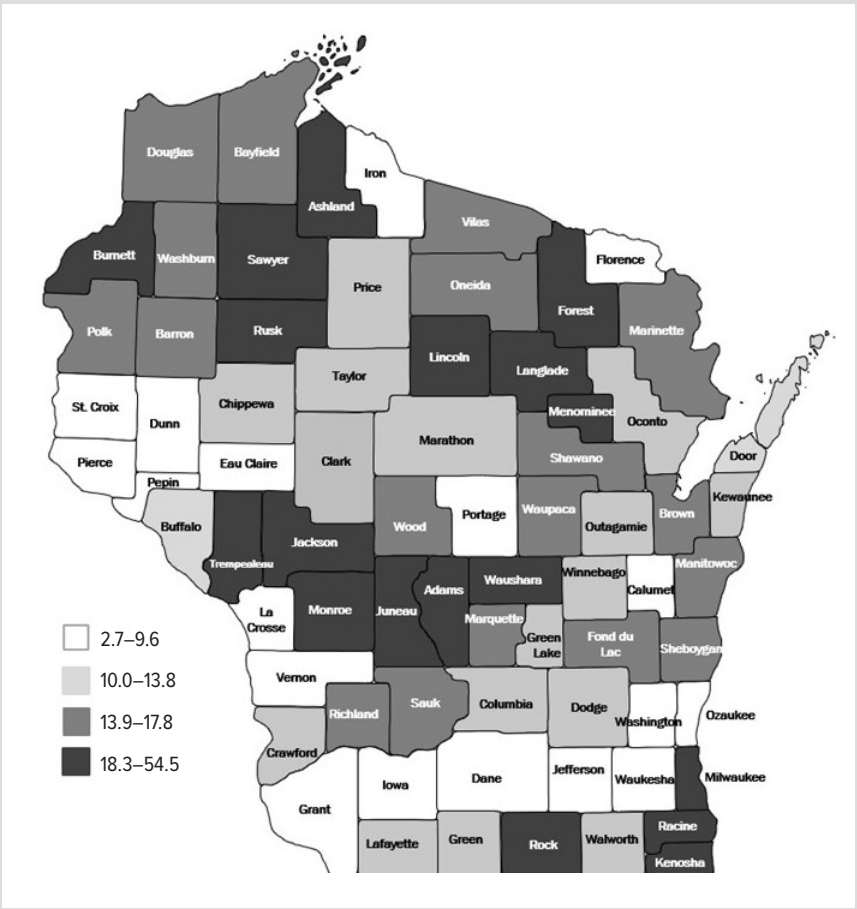
All racial/ethnic populations revealed declines in teen births; however, degrees of decline varied by race/ethnicity (Figure 1). During the 12-year period, teen birth rates were highest for American Indian/Alaska Native, Black, and Hispanic teens. The American Indian/Alaska Native female teenagers' birth rate was 34.3 per 1000 per year. For Black teens, the birth rate was 48.3 per 1000 per year. The Hispanic teen birth rate was 31.7 per 1000 per year. For the population that identified with 2 or more races, the rate was 25.8 per 1000 per year. These rates are 3 to 5 times the White population rate of 9.1 per 1000 per year.

In examining percent differences of 3-year rate ratios of teen birth rates (2011-2013 vs 2020-2022) by race, it was found that over time American Indian/Alaska Native teens had a 64% decline, Black teens had a 40% decline, Hispanic teens had a 54% decline, White teens had a 59% decline, and those identifying with 2 or more races had a 58% decline. Nevertheless, when comparing 3-year periods to the reference group (White), Wisconsin's Black teenage females had the greatest relative risk of giving birth during the 2011-2013 period and the 2020-2022 period (RR = 4.6 and 6.7, respectively) when compared to the White population. Hispanic teen females also had a high relative risk of giving birth during the 2 periods (RR = 3.6 and 4.1,

respectively) when compared to the reference group. American Indian/Alaskan Native was the only group that revealed a decrease in teen birth relative risk (RR = 4.0 and 3.5, respectively) (Table). All overall and race/ethnic-specific trends were statistically significant, using $\alpha = 0.05$ as the cutoff.

Teen birth rates varied even greater by county, with over a 20-fold difference between the county with the lowest rate (Ozaukee County at 2.7/1000) and the county with the highest rate (Menominee County at 54.5/1000) (Figure 2).

Figure 2. Variation in Teen (Ages 15-19) Birth Rates (per 1000 females) in Wisconsin, 2011-2022, by County



Counties are grouped by quartile (n = 18 counties in each group).

DISCUSSION

This study found that Wisconsin birth rates among females ages 15-19 years old decreased by half from 2011-2022. Declines were seen in all racial/ethnic groups. However, American Indian/Native American, Black, and Hispanic teens did not experience as large a reduction in teen birth rates as their White counterparts.

Compared to national data from Osterman et al, Wisconsin birth rate trends in this paper aligned with national patterns.[6] Their study reported that since 2007, US birth rates for mothers 15 to 19 years old dropped 67%.[6] Though, when comparing 2020 to 2021 birth rates, Osterman et al revealed smaller differences between ethnic groups than this study demonstrated. For example, national birth rates for mothers 15 to 19 years old fell 7% for White, 8% for Black, 8% for Hispanic, and 9% for Asian teens.[6] In contrast, when comparing Wisconsin 2020 to 2021 birth rates, there were larger declines and unequal degrees of declines: 10% for American Indian, 12.5% for Black, and 5% for White teens.[6]

Wisconsin birth rates started declining as early as 2001, with an overall 20% reduction in birth rates during 2001-2010 for female Wisconsinites 15 to 19 years old.[5] This study also revealed that Menominee and Milwaukee counties had the 2 highest rates of live births to young mothers, which persists in the current study's results.[5] Ozaukee, Pierce, and Waukesha continued to have the lowest birth rates for females within the 15- to 19-year-old age group.[5] During 2001-2011, Menominee County had a 15-fold greater birth rate than Ozaukee County;[5] however, during 2011-2022, Menominee County's teen birth rate was 20-fold greater. This disparity increased due to Ozaukee's sharper birth decline during 2011-2022 compared with Menominee County (34% vs 7%).

Strengths of this study include the ability to analyze 12 years of birth rate data, which allows for a comprehensive understanding of statewide, countywide, and racial/ethnic trends for this population. This study also compared Wisconsin 2011-2022 teen birth rate trends to 2001-2010 trends.

Limitations of this study include that the WISH dataset only recorded live births; therefore, all pregnancies (eg, miscarriages, abortions, stillbirths) were not included. Another limitation is that birth rates were based on maternal characteristics, such as age and racial/ethnic identity. Maternal characteristics might not extrapolate to the identity or experiences of the father. Additionally, this study did not comment on whether live births are a result of unplanned versus planned or unintended versus intended pregnancies. This study also did not demonstrate data on teen sexual activity or access to contraceptives or other pregnancy prevention services. In addition, the teen birth estimates for some smaller counties may be unreliable due to the small number of teen births. Lastly, this study is limited to reflecting on the causes of birth rate declines or its subsequent impact on teen mothers or society. Nevertheless, the literature suggests that increases in contraceptive use, changes in teenage sexual activity

norms, socioeconomic status, sexual assault, school attendance, and educational attainment are all factors that impact teen birth rates.[2,7-9]

In Wisconsin, teen birth rates have declined significantly over the past 20 years. However, there is room for improvement. A review of the literature suggested that implementation of effective pregnancy prevention policies, methods, and strategies for all teens, such as removing barriers to effective birth control (eg, long-acting contraceptives), improving socioeconomic status, educational attainment, eliminating sexual violence, and school attendance may be utilized to reduce teen pregnancy rates.[2,7,8] In addition, encouraging norms that reduce sexual activity for all teens, such as delaying first sexual encounters and decreasing the number of sexual partners among adolescents may be considered.[9] Counties and populations with the highest rates should be prioritized when executing and supporting these pregnancy prevention methods, strategies, and norms.

Acknowledgments: The authors wish to thank the Wisconsin Department of Health Services for allowing public access to these data through WISH.

Funding/Support: Support for this work was provided to the Preventive Medicine Residency Program by the Wisconsin Partnership Program, Health Resources and Services Administration, William S. Middleton Memorial Veterans Hospital, and the University of Wisconsin School of Medicine and Public Health.

Financial Disclosures: None declared.

REFERENCES

1. Wisconsin Department of Health Services. *Adolescent Health Issue Brief: Young motherhood in Wisconsin.* Wisconsin Department of Health Services; 2020. Accessed July 28, 2024. https://www.dhs.wisconsin.gov/publications/p02247.pdf

2. Teen Birth Rates by State. National Center for Health Statistics. Accessed July 30, 2024. https://www.cdc.gov/nchs/pressroom/sosmap/teen-births/teenbirths.htm.

3. Penman-Aguilar A, Carter M, Christine Snead M, Kourtis AP. Socioeconomic disadvantage as a social determinant of teen childbearing in the U.S. *Public Health Rep.* 2013;128(Suppl 1):5-22. doi:10.1177/00333549131282S102.

4. Mark NDE, Wu LL. More comprehensive sex education reduced teen births: Quasi-experimental evidence. *Proc Natl Acad Sci U S A*. 2022;119(8):e2113144119. doi:10.1073/pnas.2113144119

5. Layde M, Remington PL. Geographic and racial variation in teen pregnancy rates in Wisconsin. *WMJ*. 2013;112(4):169-172. PMID 2473440.

6. Osterman MJK, Hamilton BE, Martin JA, Driscoll AK, Valenzuela CP. Births: final data for 2020. *Natl Vital Stat Rep.* 2022;70(17):1-50. doi:10.15620/CDC:112078

7. Banvard-Fox C, Linger M, Paulson DJ, Cottrell L, Davidov DM. Sexual assault in adolescents. *Prim Care.* 2020;47(2):331-349. doi:10.1016/J.POP.2020.02.010

8. Mason-Jones AJ, Sinclair D, Mathews C, Kagee A, Hillman A, Lombard C. School-based interventions for preventing HIV, sexually transmitted infections, and pregnancy in adolescents. *Cochrane Database Syst Rev*. 2016;11(11):CD006417. doi:10.1002/14651858.CD006417.pub3

9. Scott RH, Wellings K, Lindberg L. Adolescent sexual activity, contraceptive use, and pregnancy in Britain and the U.S.: A multidecade comparison. *J Adolesc Health.* 2020;66(5):582-588. doi:10.1016/j.jadohealth.2019.11.310.

Permanent Contraception and the Federal Consent Process: Barriers to Access

Callie M. Cox Bauer, DO; Paige Anschutz, BA; Layan Safi, BA; Emily Malloy, PhD, CNM

Since the US Supreme Court overturned *Roe v Wade*, legislative efforts to limit reproductive rights both nationally and in Wisconsin have increased. In response, a significant number of women have sought permanent contraception via sterilization. With increased demand, it is apparent that inequity in access to reproductive care exists and is worsened by the federal sterilization requirements.[1] In this commentary, we discuss key aspects of the policy that promote inequity for patients who seek the procedure.

Permanent contraception has a dark past in the United States. The first eugenics-based law allowing forced sterilization for institutionalized people was passed in Indiana in 1907, followed by the passage of laws in 29 additional states over the next 30 years, including Wisconsin in 1913. Approximately 60 000 institutionalized, poor, and/or minority people were forcibly sterilized in the United States before World War II. This continued throughout the 1950s, with over 200 procedures per year in the Midwest. In 1976, the Department of Health, Education, and Welfare enacted a policy mandating an informed consent process for permanent contraception and a 72-hour waiting period; this was increased to 30 days in 1978. The waiting period was meant to act as protection against government-sanctioned and funded forced sterilization. Despite these protections, government-sanctioned sterilizations continue today, and 31 states including Washington, DC have active laws that allow forced sterilization.[2]

One study suggested that annual unfulfilled requests for permanent contraception methods exceeded 62 000 procedures per year. This results in an estimated cost of $215 million annually attributed to 19 000 unintended births and 10 000 abortions.

Current Requirements

The current Medicaid requirements for permanent contraception in Wisconsin include the following: the person is at least 21 years of age and mentally competent; they have been provided counseling by a clinician using a medical interpreter if the patient's primary spoken language is different than the consenting clinician or the language of the consent form; and the hand-written signature of the patient, clinician, and medical interpreter are included on the Medicaid Sterilization Consent form. The consent must be completed at least 30 days before the estimated date of delivery for those seeking postpartum permanent contraception or the procedure date. The consent form is active for 180 days. A 72-hour exception to the 30-day waiting period exists on the federal level for "emergency abdominal surgery" or "preterm delivery." In these exceptional cases, the Medicaid Sterilization Consent form must have been completed and signed at least 72 hours prior to the emergency surgery or preterm delivery and at least 30 days prior to the estimated date of delivery.[3] The above requirements are applicable only to those with Medicaid insurance. The consent form in is available in 2 languages: English and Spanish.

Barriers to Permanent Contraception

Readability, Health Literacy, and Form Completion

A study of the understandability of the Medicaid Sterilization Consent found that it is written at a 9th grade reading level, higher than that of many Americans.[4,5] Average Americans are considered to have a 7th to 8th grade reading level. The American Medical Association (AMA)

Author Affiliations: Aurora Health Care, Department of Obstetrics and Gynecology, Aurora Sinai Medical Center, Milwaukee, Wisconsin (Bauer, Malloy); Chicago Medical School at Rosalind Franklin University of Medicine and Science (Anschutz, Safi).

Corresponding Author: Callie M. Cox Bauer, DO, Advocate Aurora UW Medical Group, Department of Obstetrics and Gynecology, Aurora Sinai Medical Center, Milwaukee, WI 53233; phone 414.219.5800; email callie.coxbauer@aah.org; ORCID ID 0000-0002-9302-0881

recommends that patient information be written at a 6th grade level, making the Medicaid Sterilization Consent form difficult for those with low health literacy who likely experience disproportionate barriers to health care access.

Arbitrary Timelines

The 30-day waiting period for people insured with Medicaid causes harm and furthers inequity. No waiting period exists for those with privately funded health insurance. The mandatory 30-day waiting period imposes a paternalistic, arbitrary timeline, as there is no evidence to support the 30-day timeframe to optimize decision-making and minimize regret. Regret is disproportionally emphasized, another paternalistic feature enforced by the waiting period. Regret is experienced by approximately 2% to 3% of women following permanent sterilization.[6] In fact, many people seeking permanent contraception already have reflected and have made the decision prior to approaching their clinician or completing the consent process, and the mandatory waiting period may cause undue anxiety and self-doubt.[6,7] Despite increases in use of telemedicine and delays of elective procedures during the COVID-19 pandemic, timeline requirements for the Medicaid Sterilization Consent form have not been updated.

Obtaining and Documenting Informed Consent for People Who Do Not Speak English

Patients who do not speak English face additional barriers, such as lack of access to forms in their preferred language and limited availability of in-person interpreter services. The requirement of a physical "wet" signature on the Medicaid Sterilization Consent form also creates a significant barrier. After COVID-19, the use of Video Interpreter Systems with remote interpreters expanded and is common in many clinical settings. Many interpreters are not at a central location and work remotely, which makes sending documents for signature challenging. This often requires additional time and staff. Incorrectly completed forms result in nonpayment for the procedure, disincentivizing clinicians and systems from offering it, and further limiting access. Clinicians and health systems may limit procedures to those languages for which interpreter services are easily available or may delay care to allow time to find interpretive services. Two-thirds of denials result from issues on Medicaid sterilization consent forms.[8] The most frequent are lack of a complete form, issues with signature date/times, and, in 66% of cases, form expiration.[9]

Medicaid Insurance Coverage

Women with Medicaid insurance are less likely than those with private insurance to obtain permanent contraception.[10] According to a recent study, only 50% to 60% of individuals with Medicaid insurance received a desired postpartum permanent contraception procedure before hospital discharge, compared to 60% to 80% of those with private insurance across races.[11] Women of color are more likely than non-Hispanic White and Asian women to have Medicaid and are more likely to have negative outcomes related to unmet contraception requests, including short-interval pregnancy.[10,12] Due to structural racism and barriers to health care, Black women experience greater adverse pregnancy outcomes, including preeclampsia, placental abruption, fetal growth restriction, and stillbirth compared to White women on Medicaid.[10] Obstacles cited for the lack of permanent contraception fulfillment include the 30-day waiting period and incomplete paperwork for Medicaid patients.[13] Studies suggest that women with unfulfilled postpartum contraception might have a pregnancy rate twice that of women without a permanent contraception request.[14] These unintended pregnancies may cause worsened outcomes for those already facing systemic racism and reproductive stratification.

Lack of contraceptive autonomy for women on Medicaid may be an indicator of systemic discrimination. Physicians, including obstetrician-gynecologists (OB-GYN) noted that low-income patients faced increased barriers to receiving their desired form of contraception due to difficulty of the consent forms enforced by Medicaid.[15] Bryne et al showed that when Medicaid consent processes were not a factor in permanent contraception procedures, almost 90% of requested procedures were carried out.[16]

Finally, a significant contributing barrier to immediate postpartum permanent contraception is the short duration of postpartum maternal Medicaid coverage. Despite the 180-day timeline of the Medicaid Sterilization Consent form, current Medicaid maternal coverage in Wisconsin extends only 60 days postpartum. If a person presents to their 4- to 6-week routine postpartum visit with a request for permanent contraception, their Medicaid coverage will expire. Even if the Medicaid Sterilization Consent form is signed immediately after giving birth, the uterus takes 6 to 8 weeks to return to pregravid size, which is a requirement of laparoscopic surgery. As of May 2024, Medicaid expansion to increase postpartum maternal coverage from 60 days to 1 year has passed and been enacted in 47 states. Wisconsin is 1 of only 3 states yet to enact the 12-month expansion; the bill (SB110) was passed by the Wisconsin state senate in September 2023, but it "failed to concur in pursuant to Senate Joint Resolution 1" in April 2024 and no action has been taken since.[17]

Economic Cost

Unintended pregnancy comes with significant economic cost. Literature suggests that unintended pregnancies may cost American taxpayers millions of dollars in direct costs. One study suggested that annual unfulfilled requests for permanent contraception methods exceeded 62 000 procedures per year. This results in an estimated cost of $215 million annually attributed to 19 000 unintended births and 10 000 abortions.[18]

Recommendations

We urge physicians, nurses, health care professionals, health systems, and policymakers to listen to patients who have experienced barriers to access.[14] The 30-day waiting period should be abolished and 180-day form expiration be extended, leaving room for health care decisions to be made in a shared decision-making model between patients and physicians. We encourage equity in care provision for those on Medicaid and private insurance. To do this, we recommend consent forms be written at a 6th grade reading level in multiple different languages. We recommend that all states pass legislation to extend postpartum Medicaid coverage. Finally, we encourage federal Medicaid policymakers to allow for electronic signatures for all parties – especially remote medical interpreters. Together we must advocate for change to increase equity and decrease barriers to health care.

continued on page 470

Abortion Access and Birth-related Outcomes and Inequities: A Call to Dismantle Abortion Restrictions in Wisconsin to Improve Health and Well-being

Jenny Higgins, PhD; Jane W. Seymour, PhD; Tiffany Green, PhD

We applaud this *WMJ* issue's focus on maternal and child health, which we will refer to as reproductive and birth outcomes to include birthing people who do not identify as mothers. (This group includes cisgender women, transgender men, and gender-expansive individuals.) As this issue underscores, Wisconsin faces a reproductive and birth equity crisis—one that disproportionately harms Black, Brown, and Indigenous Wisconsinites, as well as those living in rural areas and/or on low incomes. Eliminating these inequities requires a multilevel approach, from strengthening obstetrical referral systems, to addressing the criminalization of substance use disorder, to dismantling racism within health care systems and society at large.

In this commentary, we wish to foreground another important but often overlooked domain necessary for reproductive and birth equity: abortion access.

From a human rights perspective, abortion access is worth preserving regardless of its effect on reproductive and birth outcomes. However, the science is conclusive that restricting abortion access is associated with myriad health and social consequences, including increases in infant mortality[1]—as well as (but not limited to) increased chronic health problems, such as hypertension; increased anxiety and depression; reduced ability to achieve educational, career, and other life aspirations; and negative developmental and economic impacts on children.[2] In other words, Wisconsin medical and public health professionals have many reasons to protect abortion access.

> Abortion restrictions cause the greatest harm to those already subject to systemic racism and economic injustice, widening existing health, economic, and social inequities—including the ability to have healthy pregnancies, births, and babies.

But in the spirit of this special issue, we focus here on one reason: birth equity. We make three larger points about the intersections between Wisconsinites' ability to obtain abortion care and their ability to have safe and healthy pregnancies, births, and reproductive lives.

First, abortion restrictions force people to remain pregnant and deliver against their wishes, increasing their morbidity and mortality risks. While death from pregnancy is a rare event (22.3 deaths per 100 000 live births in 2022[3]), a person who carries a pregnancy to term and gives birth is 14 times as likely to die compared to a person who has a standard-of-care abortion.[4] Unsurprisingly, states that restrict abortion have significantly higher pregnancy-related mortality rates compared to states that either protect or are neutral toward abortion access.[5]

While many strategies can help decrease the risks of pregnancy and birth, some risks will persist due to the biology of these processes. Wisconsinites should have the ability to choose whether to take on these risks. However, Wisconsin abortion clinic closures between 2009 and 2017 led to increased birth rates in counties with the greatest increases in driving distance to abortion care, indicating restrictions' harms to reproductive autonomy.[6] Further, while Wisconsin has chosen not to use state Medicaid funds to cover the vast majority of abortions,[7] evidence indicates that states that do so experience decreases in pregnancy-related morbidity.[5] Thus, we expect that Wisconsin's limits on abortion access – includ-

• • •

Author Affiliations: Collaborative for Reproductive Equity, Department of Obstetrics and Gynecology, University of Wisconsin School of Medicine and Public Health (UW SMPH), Madison, Wisconsin (Higgins, Seymour); Departments of Obstetrics and Gynecology and Population Health, UW SMPH, Madison, Wisconsin (Green).

Corresponding Author: Jane W. Seymour, PhD, Research Scientist, Collaborative for Reproductive Equity, Department of Obstetrics and Gynecology, University of Wisconsin School of Medicine and Public Health, 1300 University Avenue, 4245 Medical Sciences Center, Madison, WI 53706; phone 608.262.7738; email jwseymour@wisc.edu; ORCID ID 0000-0002-8410-7483

ing the outright suspension of all abortion care between June 2022 and September 2023 due to the US Supreme Court's decision in *Dobbs v Jackson Women's Health Organization*,[8] which overturned *Roe v Wade*[9] and federal protections for abortion – may have resulted in increased numbers of people being forced to carry pregnancies to term and adverse pregnancy-related outcomes.[10] It will be critical to document these potential consequences when vital statistics and hospital data become available.

Second, lack of abortion access increases mental health stressors and struggles, also increasing pregnancy-related morbidity and mortality. The Centers for Disease Control and Prevention estimates that upwards of 1 in 4 pregnancy-related deaths stem from mental health conditions such as depression and substance use disorder.[11] In Wisconsin, more than half (52%) of pregnancy-related deaths in 2016 and 2017 were due to mental health conditions.[12] Research is clear that people who are unable to access wanted abortion care are more likely to experience intimate partner violence and declines in mental health, both in the short term and long term.[13] Pregnant people who do not have reproductive autonomy and cannot choose abortion are therefore at elevated risk for a major but preventable cause of pregnancy-related morbidity and mortality.

Third, abortion restrictions disproportionately affect the communities that experience the worst birth outcomes, which amplifies existing inequities. Both abortion access and complication-free births are most out of reach for individuals and communities facing social oppression, systemic racism, and socioeconomic scarcity: people of color, rural residents, and/or people living on low incomes. For example, most African American, American Indian and Alaskan Native people live in states with abortion bans or restrictions,[14] and for many Americans, including many Wisconsinites, the cost of abortion care is catastrophic.[15] Abortion restrictions can push the cost of abortion care further out of reach when they result in additional costs, such as more time away from work, childcare or eldercare coverage, transportation to services, and/or lodging close to care. Additionally, compared with their White counterparts, people who face systemic racism are more likely to experience poorer reproductive and birth outcomes, including lack of high-quality prenatal care,[16] infants born prematurely and at greater risk of dying before age 1,[17] and pregnancy-related mortality.[3] In other words, abortion restrictions cause the greatest harm to those already subject to systemic racism and economic injustice, widening existing health, economic, and social inequities – including the ability to have healthy pregnancies, births, and babies.

At the time of this writing, abortion care services are currently available in Wisconsin after the *Dobbs*-related suspension of services for over a year. However, a plethora of restrictions still make abortion difficult if not impossible for many Wisconsinites to access.[18] Clinics are few and located in large cities far from rural communities, Medicaid and other payor prohibitions are fierce, telemedicine provision of abortion care is banned, and antiscience regulations such as a two-visit requirement pose unnecessary barriers. These constraints threaten Wisconsinites' health and well-being, as well as their reproductive autonomy. Given the incredibly restrictive environment, as well as the longstanding birth inequities in Wisconsin, we urge readers to work to dismantle the abortion restrictions that stand in the way of reproductive health and well-being for all.

Funding/Support: This work was supported by an anonymous family foundation. The funder had no role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Financial Disclosures: None declared.

REFERENCES

1. Gemmill A, Margerison CE, Stuart EA, Bell SO. Infant deaths after Texas' 2021 ban on abortion in early pregnancy. *JAMA Pediatr.* 2024;178(8):784-791. doi:10.1001/jamapediatrics.2024.0885

2. New CORE brief documents impacts of abortion restrictions on individuals, families, and communities. Collaborative for Reproductive Equity. July 10, 2023. Accessed June 24, 2024. https://core.wisc.edu/2023/07/10/new-core-brief-documents-impacts-of-abortion-restrictions-on-individuals-families-and-communities/

3. Hoyert DL. *Maternal Mortality Rates in the United States, 2022.* National Center for Health Statistics. Centers for Disease Control and Prevention. Published May 2, 2024. Accessed June 24, 2024. https://www.cdc.gov/nchs/data/hestat/maternal-mortality/2022/maternal-mortality-rates-2022.pdf

4. Raymond EG, Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. *Obstet Gynecol.* 2012;119(2 Part 1):215-219. doi:10.1097/AOG.0b013e31823fe923

5. Addante AN, Eisenberg DL, Valentine MC, Leonard J, Maddox KEJ, Hoofnagle MH. The association between state-level abortion restrictions and maternal mortality in the United States, 1995-2017. *Contraception*. 2021;104(5):496-501. doi:10.1016/j.contraception.2021.03.018

6. Venator J, Fletcher J. Undue burden beyond Texas: an analysis of abortion clinic closures, births, and abortions in Wisconsin. *J Policy Anal Manage*. 2021;40(3):774-813. doi:10.1002/pam.22263

7. ForwardHealth: Limited Abortion Coverage. Wisconsin Department of Health Services. Revised January 11, 2023. Accessed January 9, 2025. https://www.dhs.wisconsin.gov/forwardhealth/customerhelp/abortion.htm

8. *Dobbs v Jackson Women's Health Organization*, 597 US 215 (2022).

9. *Roe v Wade*, 410 US 113 (1973).

10. Dench D, Pineda-Torres M, Myers C. The effects of post-Dobbs abortion bans on fertility. *J Public Econ.* 2024;234:105124. doi:10.1016/j.jpubeco.2024.105124

11. Four in 5 pregnancy-related deaths in the U.S. are preventable. News release. CDC Newsroom; September 19, 2022. Accessed June 24, 2024. https://www.cdc.gov/media/releases/2022/p0919-pregnancy-related-deaths.html

12. Wisconsin maternal mortality review: Pregnancy-associated overdose deaths (2016-2019). University of Wisconsin–Madison Prevention Research Center and Wisconsin Department of Health Services; 2021. Accessed July 1, 2024. https://prc.wisc.edu/wp-content/uploads/sites/1127/2021/09/MMR-RMOR-Repor.pdf

13. The mental health impact of receiving vs. being denied a wanted abortion. Mental Health Issue Brief. Advancing New Standards in Reproductive Health; July 2018. Accessed July 2, 2024. https://www.ansirh.org/sites/default/files/publications/files/mental_health_issue_brief_7-24-2018.pdf.

14. Goutos D, Cesare N, Vu C, et al. Race and ethnicity of reproductive-age females affected by US state abortion bans. *JAMA*. 2024;331(20):1765-1767. doi:10.1001/jama.2024.6023

15. Zuniga C, Thompson TA, Blanchard K. Abortion as a catastrophic health expenditure in the United States. *Womens Health Issues.* 2020;30(6):416-425. doi:10.1016/j.whi.2020.07.001

16. Green TL. Unpacking racial/ethnic disparities in prenatal care use: the role of individual-, household-, and area-level characteristics. *J Womens Health (Larchmt).* 2018;27(9):1124-1134. doi:10.1089/jwh.2017.6807

17. Green T, Hamilton TG. Maternal educational attainment and infant mortality in the United States: Does the gradient vary by race/ethnicity and nativity? *Demogr Res.* 2019;41:713-752. doi:10.4054/DemRes.2019.41.25

18. CORE Brief: Wisconsin state laws impacting abortion access. Collaborative for Reproductive Equity; January 2024. Accessed February 13, 2024. https://core.wisc.edu/documents/wisconsin-state-laws-impacting-abortion-access-as-of-january-2024/

Addressing Wisconsin's Rural Maternal Morbidity and Mortality—How General Surgery Can Help

Katherine Bakke, MD, MPH; Ciara Michel, MPH

Maternal morbidity and mortality in the United States is a critical public health issue, particularly in rural areas, which have significantly higher rates compared to urban areas.[1] Reasons for this disparity are multifactorial; however, lack of access to maternal health care, hospital disruptions and closures, inequitable resource distribution, and workforce shortages are major contributors.[1] In many respects, rural Wisconsinites have better maternity care access compared to other rural residents in neighboring states, as demonstrated in the Table.

Table. Maternity Care Access, Wisconsin and Neighboring States

	Maternity Care Desert[a] (% Counties)[2]	% Babies Born in Rural Counties[2]	Cesarean Delivery Rate per Year[7]	Average Miles to Birthing Hospital by Rurality[2]	OB/GYNs per 10 000 Births in Rural Counties[2]	Maternity Care Providers in Rural Counties[2]
National	35.1	13.5[8]	32.1	26.2	58.2	–
Wisconsin	15.3	4	27.5	18.1	44.0	0.9
Iowa	33.3	22.3	29.6	13.0	36.6	9
Illinois	34.3	3.8	31.0	17.9	71.8	1.8
Minnesota	15.9	8.2	30.0	19.6	45.2	3.7

[a]Maternity care deserts are defined as any county without a hospital or birth center offering obstetric care and without any obstetric providers.

When defining "maternity care provider," March of Dimes does not include general surgeons as part of the obstetric workforce, instead counting only obstetric/gynecologic (OB/GYN) physicians, midwives, and family medicine physicians.[2] While general surgeons typically only participate in operative obstetric care, like cesarean deliveries, the availability of a clinician who can perform a cesarean delivery is essential for safe, high-quality, and lifesaving obstetric care. Indeed, cesarean delivery availability is associated with increased local deliveries and decreased preterm births.[3] Often in rural hospitals, the only provider available to perform a cesarean delivery is a general surgeon.

According to the Wisconsin Office of Rural Health (WORH) 2024 report "Obstetric Delivery Services and Workforce in Rural Wisconsin Hospitals," 100% of rural Wisconsin hospitals with labor and delivery units provide cesarean deliveries.[4] However, from 2009 through 2018, 11 rural Wisconsin hospitals closed their labor and delivery units, primarily due to clinician shortages.[5] OB/GYN physicians perform cesarean deliveries at 45% of rural Wisconsin hospitals.[4] In 34% of hospitals, a combination of OB/GYNs, family medicine physicians, and/or general surgeons split this responsibility; in 3% of hospitals, it is the responsibility of general surgeons alone.[4] Interestingly, the 2018 WORH report stated that general surgeons alone performed cesarean deliveries in 9% of rural hospitals.[5] One hypothesis for this 6% decrease is that older surgeons with operative obstetric skills are retiring, and younger surgeons replacing them do not have the same skills.

Advanced obstetrics fellowships (such as those at Gundersen Health System and the University of Wisconsin) exist for family medicine physicians, yet no equivalent training is available to general surgeons. Furthermore, general surgery residents are no longer required by the American College of Graduate Medical Education to complete an OB/GYN rotation, which has implications for residents preparing for rural practice.[6] While the general surgeon's role in obstetric care is small, it requires an understanding of operative obstetrics and the unique management of resuscitation in pregnant patients. An operative obstetric training course for general surgeons is one way to expand the availability of rural obstetric care in Wisconsin, the Midwest, and, potentially, the United States.

As the director of the Regional General Surgery Outreach Program at the University of Wisconsin, Dr Bakke has been in conversa-

Author Affiliations: Division of Acute Care and Regional General Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health (UW SMPH), Madison, Wisconsin (Bakke); UW SMPH, Madison, Wisconsin (Michel).

Corresponding Author: Katherine Bakke, MD, MPH; 600 Highland Ave, Madison, WI 53792-7375; phone 608.262.6246; email bakke@surgery.wisc.edu; ORCID ID 0009-0001-9457-3664

tion with rural general surgeons throughout Wisconsin about obstetric care. Most surgeons state that they, intending to practice in a rural community, took it upon themselves during residency to foster relationships with OB/GYNs and trained for extra hours to learn how to perform cesarean deliveries. Others state that a senior OB/GYN or general surgeon supervised them in cesarean deliveries at their start of practice until they were competent to perform the procedure independently. These conversations also revealed there are essentially no formal operative obstetrics training opportunities available to surgeons in the US. The only course available, which one rural Wisconsin surgeon attended, is a 2-day global health training at Stanford University that teaches basic operative obstetrics along with orthopedics, plastic surgery, and burn care.[9]

Most surgeons said that learning the steps of a cesarean delivery is not difficult; rather, learning how to anticipate and troubleshoot problems is the foremost challenge of operative obstetrics. The amount of bleeding, twin deliveries, fetal or maternal distress, repeat cesarean deliveries, patient obesity, prolonged labor, and breech presentations were cited as clinical challenges they have learned to manage – often emergently with little or no assistance. The risk of litigation looms in these surgeons' minds as to whether they should provide a surgery they are not expected to master by the American Board of Surgery. Yet, their commitment to their patients is strong, with most rural surgeons offering their surgical skills to provide an essential component of care to their community.

The Canadian Association of General Surgeons (CAGS) recognized that rural surgeons in Canada often are responsible for operative obstetrics and created a training program to increase the number of general surgeons able to perform cesarean deliveries.[10] CAGS members can enroll in the "Operative Delivery and Maternal Care for General Surgeons Program," a 10-week online course with a 1-day simulation skills course at the CAGS annual conference and hands-on training at host hospitals where surgeons perform a minimum of 25 cesarean deliveries, 5 dilation and curettage procedures, and 5 tubal ligations.[10] The program results in a "Certificate of Recognition in Operative Delivery and Maternal Care for General Surgeons" for surgeons to demonstrate competency in operative obstetrics to gain hospital privileges.[10]

As evidenced by numerous discussions on the American College of Surgeons "rural surgery" community forum, there is both interest and need for such a program in the US. To be successful, an operative obstetrics training course would require similar rigor as the CAGS program, collaboration between rural and urban hospitals, recognition by the American College of Surgeons and the American College of Obstetricians and Gynecologists, and have the support of both trainee and host hospital leadership.

Existing didactic curricula for operative obstetrics in OB/GYN training programs could be refined for general surgeons, and academic centers with simulation centers could offer operative obstetrics simulation courses. The more challenging piece is how to provide hands-on patient experience in operative obstetrics to general surgeons. In Wisconsin, many rural hospitals are part of a larger health system network, and many have established relationships with academic centers. Leveraging these relationships could allow the creation of "mini fellowships" for general surgeons seeking hands-on patient experience and exposure to operative obstetrics in a proctored setting.

One concern is how such a training course may "take away" cases from trainees in the existing obstetrics programs. This concern is valid but not insurmountable. Data suggest that new learners should perform between 10 and 40 cesarean deliveries before becoming safe for independent practice.[11] These studies were performed with resident physicians; it can be assumed that practicing general surgeons knowledgeable in instrument exchange, tissue handling, and pelvic anatomy would have a shorter learning curve. With Meriter Hospital in Madison, Wisconsin, performing over 1000 cesarean deliveries per year, as one example, there are plenty of educational opportunities for learners at all stages of their careers.[12]

There are logistic and financial issues that must be addressed for an operative obstetrics training program to succeed. To encourage surgeon enrollment, hospitals could reimburse for registration, travel, and lodging via continuing medical education (CME) funds. Certainly, CME credit would be provided to the surgeon for course completion. Host hospitals would need to streamline rapid credentialing of visiting surgeons and have medical staff willing to teach. Rural hospitals would need to hire a locum tenens surgeon to take call while a staff surgeon is training; however, training could be split over several weekends (as opposed to a month-long intensive) to allow rural general surgeons to return to their practice during the week. The cost of providing the training and the administrative overhead at the host hospital also would need to be addressed.

> To expand obstetric services in rural Wisconsin and across the Midwest, collaborative postgraduate training in operative obstetrics for general surgeons should be a priority of the State, its academic medical centers, and its large network of hospital systems.

Overcoming such challenges would be well worth the benefit. According to WORH, "hospital OB units with fewer than four providers covering surgical obstetric services (cesarean deliveries) can be considered 'at risk' of closure due to the non-sustainable nature of coverage."[5] Indeed, one of the most frequently requested services requested from the UW Health Regional Services Program is cesarean delivery coverage, according to Allison Henke, vice president of UW Health Regional Services (personal conversation, June 24, 2024). This suggests there is already a strained rural obstetric workforce in Wisconsin. Increasing operative obstetrics training for general surgeons is not just a maternal morbidity and mortality issue, but also an issue of physician well-being and workforce retention.

In Wisconsin, the number of rural hospitals offering obstetric services is higher than the national average, but some of these units undoubtedly will be at risk of closure in the future. As seen throughout the US, closure of rural labor and delivery units worsens maternal morbidity and mortality for already vulnerable rural populations. General surgeons play a vital role in keeping the doors of labor and delivery units open. Projections predict shortages for both OB/GYN and family medicine physicians, with declines in OB/GYN physicians practicing in rural areas and family medicine physicians practicing obstetrics.[13] The demand for general surgeons who provide operative obstetric care can only be expected to increase in the future. To expand obstetric services in rural Wisconsin and across the Midwest, collaborative postgraduate training in operative obstetrics for general surgeons should be a priority of the State, its academic medical centers, and its large network of hospital systems. Doing so could position Wisconsin as a leader in maternal health care and contribute to efforts urgently needed to reduce the morbidity and mortality facing rural mothers.

Funding/Support: None declared.
Financial Disclosures: None declared.

REFERENCES

1. Kozhimannil KB, Interrante JD, Henning-Smith C, Admon LK. Rural-urban differences in severe maternal morbidity and mortality in the US, 2007-15. *Health Aff (Millwood).* 2019;38(12):2077-2085. doi:10.1377/hlthaff.2019.00805

2. Stoneburner A, Lucas R, Fontenot J, Brigance C, Jones E, DeMaria AL. Nowhere to go: maternity care deserts across the US: 2024 report. March of Dimes. 2024. Accessed October 7, 2024. https://www.marchofdimes.org/peristats/assets/s3/reports/2024-Maternity-Care-Report.pdf

3. Lynch N, Thommasen H, Anderson N, Grzybowski S. Does having cesarean section capability make a difference to a small rural maternity service? *Can Fam Physician*. 2005;51(9):1238-1239.

4. Ledger J, Olson M, Black P. Obstetric delivery services and workforce in rural Wisconsin hospitals. Wisconsin Office of Rural Health. August 2024. Accessed October 7, 2024. https://worh.org/wp-content/uploads/2024/08/2024-OB-Report_13Aug2024.pdf

5. Wisconsin Office of Rural Health. Delivery services and workforce in rural Wisconsin hospitals. Revised July 2019. Accessed May 27, 2024. https://worh.org/wp-content/uploads/2019/09/ObstetricServicesReport2018Revised.pdf

6. Doescher MP, Jackson JE, Fordyce MA, Lynge DC. Variability in general surgical procedures in rural and urban US Hospital inpatient settings. WWAMI Rural Health Research Center. Final Report #142. February 2015. Accessed October 10, 2024. https://depts.washington.edu/uwrhrc/uploads/General%20Surgery_%20Final_2015.pdf

7. Cesarean Delivery Rate by State, 2022. National Center for Health Statistics. Accessed October 10, 2024. https://www.cdc.gov/nchs/pressroom/sosmap/cesarean_births/cesareans.htm

8. Harrington KA, Cameron NA, Culler K, Grobman WA, Khan SS. Rural–urban disparities in adverse maternal outcomes in the United States, 2016–2019. *Am J Public Health*. 2023;113(2):224-227. doi:10.2105/AJPH.2022.307134

9. International Humanitarian Surgical Skills Course–2024. Stanford Center for Innovation in Global Health. September 13, 2023. Accessed September 23, 2024. https://globalhealth.stanford.edu/education/international-humanitarian-surgical-skills-course-2024.html/

10. Operative Delivery and Maternal Care for General Surgeons Program. Canadian Association of General Surgeons. Accessed May 27, 2024. https://cags-accg.ca/operative-delivery-and-maternal-care-for-general-surgeons-postgraduate-course/

11. Madsen K, Grønbeck L, Rifbjerg Larsen C, et al. Educational strategies in performing Cesarean section. *Acta Obstet Gynecol Scand.* 2013;92(3):256-263. doi:10.1111/aogs.12055

12. Cesarean birth trends for UnityPoint-Meriter (lower is better). Wisconsin Hospital Association. Accessed May 27, 2024. https://checkpoint.wha.org/TrendReport/TrendReport?measurementID=84&facilityID=061

13. ACOG Committee Opinion No. 586: Health disparities in rural women. *Obstet Gynecol*. 2014;123(2 Pt 1):384-388. doi:10.1097/01.AOG.0000443278.06393.d6

Permanent Contraception and the Federal Consent Process

continued from page 465

Funding/Support: None declared.
Financial Disclosures: None declared.

REFERENCES

1. Xu X, Chen L, Desai VB, Gross CP, et al. Tubal sterilization rates by state abortion laws after the Dobbs decision. *JAMA*. 2024;332(14):1204-1206. doi:10.1001/jama.2024.16862

2. *Forced sterilization laws in each state and territory.* National Women's Law Center; 2022. Accessed September 18, 2024. https://nwlc.org/wp-content/uploads/2022/01/%C6%92.NWLC_SterilizationReport_2022_Appendix.pdf

3. Sterilizations. 42 CFR §441 Subpart F. Accessed September 25, 2024. https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-C/part-441/subpart-F

4. Zite NB, Philipson SJ, Wallace LS. Consent to Sterilization section of the Medicaid-Title XIX form: is it understandable? *Contraception*. 2007;75(4):256-260. doi:10.1016/j.contraception.2006.12.015

5. Safeer RS, Keenan J. Health literacy: the gap between physicians and patients. *Am Fam Physician*. 2005;72(3):463-468.

6. Amalraj J, Arora KS. Ethics of a mandatory waiting period for female sterilization. *Hastings Cent Rep.* 2022;52(4):17-25. doi:10.1002/hast.1405

7. Rowlands S, Thomas K. Mandatory waiting periods before abortion and sterilization: theory and practice. *Int J Womens Health*. 2020;12:577-586. doi:10.2147/IJWH.S257178

8. Bouma-Johnston H, Ponsaran R, Arora KS. Variation by state in Medicaid sterilization policies for physician reimbursement. *Contraception*. 2021;103(4):255-260. doi:10.1016/j.contraception.2020.12.012

9. Russell CB, Evans ML, Qasba N, Frankel A, Arora KS. Medicaid sterilization consent forms: variation in rejection and payment consequences. *Am J Obstet Gynecol*. 2020;223(6):934-936. doi:10.1016/j.ajog.2020.07.034

10. Arora KS, Chua A, Miller E, et al. Medicaid and fulfillment of postpartum permanent contraception requests. *Obstet Gynecol.* 2023;141(5):918-925. doi:10.1097/AOG.0000000000005130

11. Bullington BW, Berg KA, Miller ES, et al. Association among race, ethnicity, insurance type, and postpartum permanent contraception fulfillment. *Obstet Gynecol.* 2023;142(4):920-928. doi:10.1097/AOG.0000000000005328

12. Keisler-Starkey K, Bunch L. *Health Insurance Coverage in the United States: 2021, Current Population Reports*. US Census Bureau, Department of Commerce; 2022: 60-278. Accessed July 9, 2024. https://www.census.gov/content/dam/Census/library/publications/2022/demo/p60-278.pdf

13. Committee on Health Care for Underserved Women. Committee opinion no. 530: access to postpartum sterilization. *Obstet Gynecol*. 2012;120(1):212-215. doi:10.1097/AOG.0b013e318262e354

14. Bullington BW, Arora KS. Fulfillment of desired postpartum permanent contraception: a health disparities issue. *Reprod Sci.* 2022;29(9):2620-2624. doi:10.1007/s43032-022-00912-3

15. Mosley EA, Monaco A, Zite N, et al. U.S. physicians' perspectives on the complexities and challenges of permanent contraception provision. *Contraception*. 2023;121:109948. doi:10.1016/j.contraception.2023.109948

16. Byrne JJ, Smith EM, Saucedo AM, Doody KA, Holcomb D, Spong CY. Accessibility to postpartum tubal ligation after a vaginal delivery: When the Medicaid policy is not a limiting factor. *Contraception*. 2022;109:52-56. doi:10.1016/j.contraception.2021.11.007

17. Wisconsin SB110 (2023-2024). LegiScan. Accessed June 26, 2024. https://legiscan.com/WI/rollcall/SB110/id/1354466

18. Borrero S, Zite N, Potter JE, Trussell J, Smith K. Potential unintended pregnancies averted and cost savings associated with a revised Medicaid sterilization policy. *Contraception*. 2013;88(6):1691-1696. doi:10.1016/j.contraception.2013.08.004

An Internists' Action Plan to Reduce Morbidity and Mortality Under Abortion Restrictions

Jennifer Cichon Mackinnon, MD, MM; Whitney Lynch, MD

Following the US Supreme Court's decision in *Dobbs v Jackson Women's Health Organization*,[1] an acquaintance was 18 weeks pregnant and considered high risk due to comorbid conditions. She expressed to me her fear of potential complications in light of the recent abortion restrictions, and as we discussed the unfortunate gray area created by the overturn of *Roe v Wade*[2] and Planned Parenthood v Casey,[3] I advised her to discuss a theoretical action plan with her obstetrician.

This acquaintance is not alone in her concerns. Dr Lynch and I both have had to discuss this delicate matter with many of our patients. One patient—the mother of other young children—had already begun to research hospital systems that would allow for safe care, including locations out of state. In case of an emergency, she would be required to travel a long distance for life-saving care—a circumstance that for many is not financially feasible. What civilized country places women in such a position of vulnerability?

When the *Dobbs* decision was announced, I was driving from Milwaukee, Wisconsin, to Minneapolis, Minnesota. En route, I approached my state capital, Madison, and felt drawn to stop and speak out in support of not only my patients, but of all women. As I walked toward the capitol building in my white coat, I was approached by various news outlets and was empowered by seeing other women in protest. I explained the consequences of this devastating ruling and the dangerous ramifications that could result: women suffering and even dying. I discussed the impact on families given that women are often positioned as the head of household. I described the importance of access to safe abortions – particularly for women with chronic disease and those on teratogenic medications. Overall, I was saddened for the two people who ultimately should be involved in this conversation – the patient and their clinician. This is not a politician's place.

One patient – the mother of other young children – had already begun to research hospital systems that would allow for safe care, including locations out of state. In case of an emergency, she would be required to travel a long distance for life-saving care.

Later, at the 2023 National American College of Physicians meeting, I attended a powerful talk on the importance of preserving this right, and it reminded me that we need to stay conscious of the potentially harrowing effects of these restrictive laws at the state level. And as an active member of the Reproductive Advocacy Group within the ACP Wisconsin State Chapter, I plan to advocate at our nation's Capital as well. There is much we can do to have influence.

—Jennifer Cichon Mackinnon

Action Steps

Together, we began considering how we as internists could make a direct impact in our day-to-day practice. Here are some immediate action steps we can initiate:

1. Ask about contraception and prescribe it. This is paramount, as unintended pregnancy rates remain high—particularly among those of low socioeconomic status.[4] Family-planning and control of reproductive health is not only key to economic stability but family stability. As internists, we need to champion these conversations and continue to engage in medical education to improve access to care for our patients. Several studies have shown the benefits of preventing unplanned pregnancies through the use of long-acting reversable contraception,[5,6] so this training becomes extremely valuable to our patients. Consider Plan B prescriptions for patients to have on hand in an event of an unplanned

Author Affiliations: Division of General Internal Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin (Mackinnon, Lynch).

Corresponding Author: Jennifer Cichon Mackinnon, MD, MM, Division of General Internal Medicine, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226; email jmackinnon@mcw.edu.

pregnancy and enact your contraception plan before your patient leaves their visit.

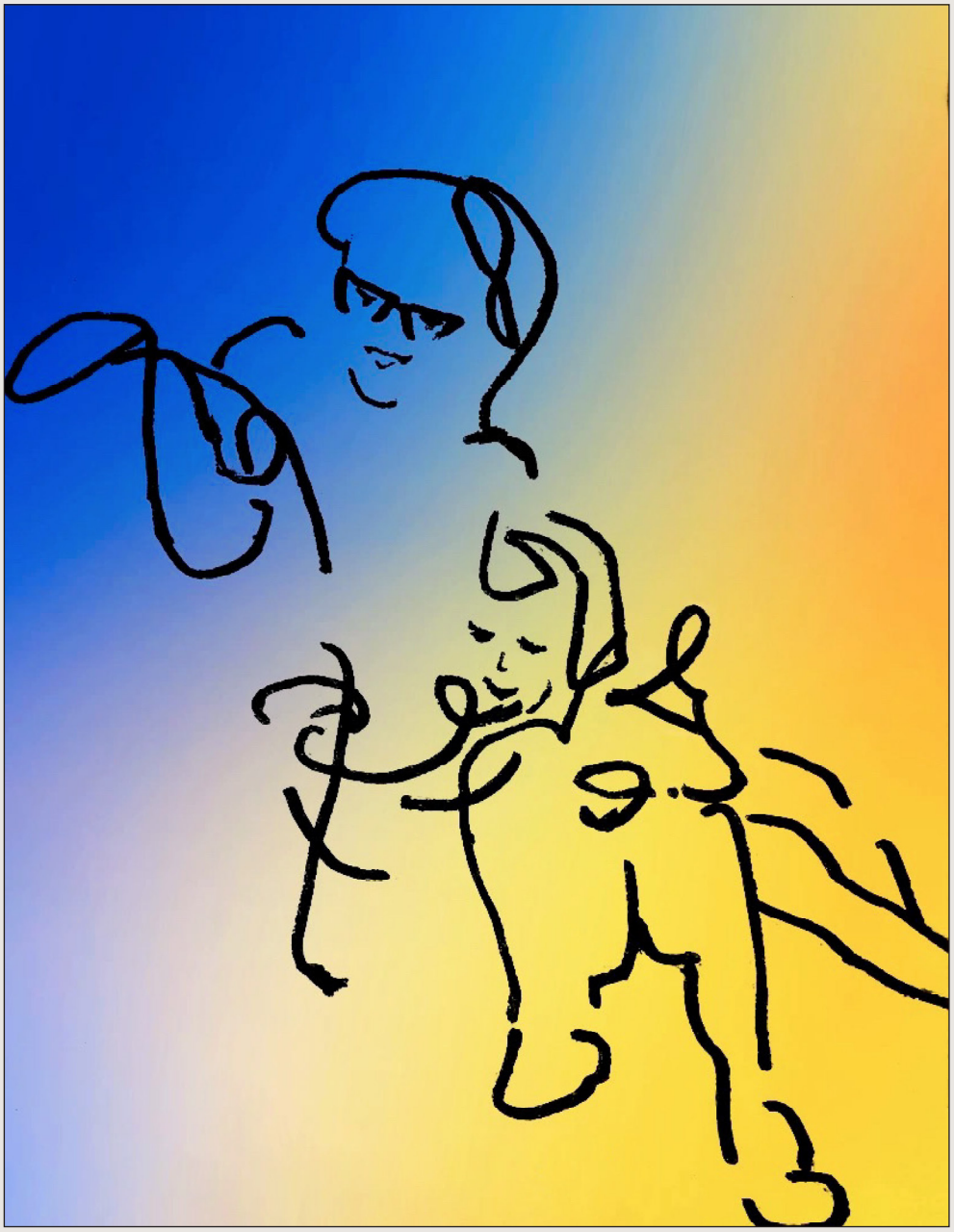
2. Advocate for your patient's health by focusing on excellent chronic disease management, including mental health. Poorly controlled chronic diseases have been linked directly to an increase in maternal morbidity and mortality. One study identified that nearly two thirds of severe maternal morbidity events were deemed preventable with antepartum interventions.[7] These data are supported by statistics from the Centers for Disease Control and Prevention, which launch the "Hear Her Campaign"[8] in 2020 to help prevent pregnancy-related death. As internists, we should feel comfortable and empowered to partner with our obstetric colleagues to help manage these chronic conditions and recognize when our patients require more urgent care. We are critical to eliminating this preventable mortality.
3. Help protect your patient's rights. Abortion is a standard of care that should be safely and readily available in all states. A recent study identified that states that enacted an immediate ban on abortions after the leaked *Dobbs* draft decision in 2022 saw a 42% increase in internet searches of abortion-related terms and a 25% increase in contraception-related terms.[9] By the age of 45, nearly 1 in 4 women will have had an abortion, and early abortion should not be considered a middle ground. Studies have shown upwards of 90% of patients would be affected by an early abortion ban, which would disproportionally affect patients who are Black and of lower socioeconomic status.[10,11] Our patients' rights are endangered, and it is our job to help safeguard them and stand against this injustice. Please call, write, or email your state representatives, senators, and governor and explain as a physician why this right is essential.

We hope you will consider taking these action steps and share their importance with colleagues and learners. In our microcosms, we can create meaningful change and help save lives—the very epitome of why we chose this career.

Funding/Support: None declared.
Financial Disclosures: None declared.

REFERENCES

1. *Dobbs v Jackson Women's Health Organization*, 597 US 215 (2022).
2. *Roe v Wade*, 410 US 113 (1973).
3. *Planned Parenthood v Casey,* 505 US 833 (1992).
4. Finer LB, Zona MR. Declines in unintended pregnancy in the United States, 2008-2011. *N Engl J Med.* 2016;374(9):843-852. doi:10.1056/NEJMsa1506575
5. Birgisson NE, Zhao Q, Secura GM, et al. Preventing unintended pregnancy: the contraceptive CHOICE project in review. *J Womens Health*. 2015;24(5):349-353. doi:10.1089/jwh.2015.5191
6. Luca DL, Stevens J, Rotz D, Goesling B, Lutz R. Evaluating teen options for preventing pregnancy: impacts and mechanisms. *J Health Econ.* 2021;77:102459. doi:10.1016/j.jhealeco.2021.102459
7. Wolfson C, Qian J, Chin P, et al. Findings from severe maternal morbidity surveillance and review in Maryland. *JAMA Netw Open.* 2022;5(11):e2244077. doi:10.1001/jamanetworkopen.2022.44077
8. Hear Her Campaign. Centers for Disease Control and Prevention. Accessed December 1, 2024. https://www.cdc.gov/hearher/index.html
9. Gupta S, Perry B, Simon K. Trends in abortion- and contraception-related internet searches after the US Supreme Court overturned constitutional abortion rights: How much do state laws matter? *JAMA Health Forum.* 2023;4(4):e230518. doi:10.1001/jamahealthforum.2023.0518
10. Redd SK, Mosley EA, Narasimhan S, et al. Estimation of multiyear consequences for abortion access in Georgia under a law limiting abortion to early pregnancy. *JAMA Netw Open.* 2023;6(3):e231598. doi: 10.1001/jamanetworkopen.2023.1598
11. Turner AN, Brenner-Levoy J, Rivlin K, et al. Who loses access to legal abortion with a 6-week ban? *Am J Obstet Gynecol.* 2022;227(5):777-780. doi:10.1016/j.ajog.2022.06.032



The Complementarity of Motherhood

Dian Yao

Digitized Ink Drawing

Artist Statement:

This artwork captures my baby boy's beach fun day near Lake Superior! Our connection is like blue and orange—beautifully complementary. He transformed from a sand-avoider to a sand-savant in no time, and witnessing his growth made me beam with pride. It reminded me of the precious nature of motherhood—creating opportunities for our children to explore the world with us, fostering their confidence, and building cherished connections.

Association of an Enhanced Recovery After Cesarean Surgery Protocol With Postpartum Opioid Utilization: Analysis of a Quality Improvement Project

Kathleen M. Antony, MD, MSCI; India Anderson-Carter, MD; Aimee Teo Broman, MA; Sarah E. Gnadt, Pharm D, BCPS; Delores Krickl, BSN; Shefaali Sharma, MD; Luther L. Gaston, MD; Emily M. Buttigieg, MD; Benjamin B. Whiddon, MD, PhD

ABSTRACT

Introduction: Research has shown that 1 of every 50 to 300 patients can develop chronic opioid use following treatment of acute pain, including after cesarean birth. Our hospital identified that our post-cesarean patients utilized high doses of systemic opioids. This study sought to determine whether implementation of a standardized enhanced recovery after cesarean surgery (ERAS) protocol decreased opioid utilization following cesarean birth.

Methods: An evidence-based ERAS protocol was created and implemented. This protocol included intrathecal morphine and a standardized approach to all phases of perioperative care for both scheduled and unscheduled cesarean deliveries. A before-and-after analysis compared oral morphine milligram equivalents (MME) for 9 months prior to and 9 months after implementation. People with chronic opioid use for any indication or postoperative intubation were excluded. The primary outcome was the cumulative MME utilization in the first 48 hours postoperatively. MME utilization and pain scores at other time points were compared.

Results: Patients who underwent cesarean birth prior to implementation of the ERAS protocol (pre-ERAS) (n = 973) and after implementation (post-ERAS) (n = 1025) were included. The median cumulative opioid dose in the first 48 hours post-cesarean was 122 MME (interquartile range [IQR] 80-164) pre-ERAS compared to 8 MME (IQR 0-48) post-ERAS ($P < 0.001$). The median cumulative MME was higher in the pre-ERAS period compared to the post-ERAS period for all time points assessed. The prevalence of pain scores >7 in the first 24 hours was decreased in the post-ERAS period as was the percentage of patients requiring any opioids.

Conclusions: An ERAS protocol for cesarean birth including intrathecal morphine was associated with a 93.8% reduction in cumulative opioid dose by MME and should be considered by all hospitals that offer obstetric services.

• • •

Author Affiliations: Department of Obstetrics and Gynecology, University of Wisconsin School of Medicine and Public Health (UW SMPH), Madison, Wisconsin (Antony, Anderson-Carter, Gaston, Buttigieg); Department of Biostatics and Medical Informatics, UW SMPH, Madison, Wisconsin (Broman); Department of Pharmacy, UnityPoint Health-Meriter, Madison, Wisconsin (Gnadt); Department of Obstetrics and Gynecology, UnityPoint Health-Meriter, Madison, Wisconsin (Krickl); Associated Physicians: Obstetrics and Gynecology, Madison, Wisconsin (Sharma); Madison Anesthesiology Consultants, LLC, UnityPoint Health- Meriter, Madison, Wisconsin (Whiddon).

Corresponding Author: Kathleen M. Antony, MD, MSCI, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, University of Wisconsin School of Medicine and Public Health, 202 S Park St, Madison, WI 53715; phone 608.417.6099; email kantony@wisc.edu; ORCID ID 0000-0003-3537-8030

INTRODUCTION

Over 30% of births in the United States occur via cesarean delivery. One of every 50 to 300 patients can develop chronic opioid use following treatment of acute pain, including after cesarean.[1] Accordingly, multimodal approaches endorsed by the enhanced recovery after surgery "ERAS" Society and the Society of Obstetric Anesthesia and Perinatology emphasize nonopioid analgesia.[2-6] ERAS refers to a patient-centered, evidence-based, multimodal, and multidisciplinary approach to postoperative recovery with a goal of reducing pain and facilitating recovery.

Our hospital identified that our post-cesarean patients utilized high doses of systemic opioids.[7] Our prior strategy to reduce opioid utilization with scheduled acetaminophen and nonsteroidal anti-inflammatory drugs (NSAID) reduced opioid utilization by approximately 20%, but opioid utilization remained high.[8] We next implemented a post-cesarean ERAS protocol. The analysis presented here evaluated the association of this protocol with post-cesarean opioid utilization. Our hypothesis was that post-cesarean opioid utilization in the first 48 hours (calculated as morphine milligram equivalents [MME]) would decrease following implementation of the ERAS protocol.

MATERIALS AND METHODS

This project was reviewed by the Institutional Review Board at the University of Wisconsin-Madison and UnityPoint Health-Meriter and was deemed to meet requirements for a quality improvement project. UnityPoint Health-Meriter is the setting of the University of Wisconsin's obstetrical service. This quality improvement project is reported in accordance with the SQUIRE 2.0 and RECOvER checklists.[9,10] Here we report analysis of opioid utilization before and after implementation of this post-cesarean ERAS protocol at a single hospital.

A multidisciplinary committee convened in January 2020 to design an evidence-based enhanced recovery after cesarean surgery (ERAS) protocol. The committee consisted of representatives from every phase of prenatal, intrapartum, and postpartum care and included the disciplines indicated in Supplemental Table 1. Together, this group reviewed existing cesarean ERAS protocols and reviewed evidence for additional components considered.[2,3,6,11,12] The protocol had an implementation date of June 29, 2021. However, 1 portion of the protocol – intrathecal morphine – was implemented early on March 2, 2021, for the following reasons: (1) the need for intrathecal morphine was great given the previously identified high post-cesarean opioid utilization, (2) it was feasible to implement this while the remaining educational portions of the project and order sets were being created, and (3) this medication initially was planned for implementation much earlier than the full protocol but was delayed due to external circumstances. Prior to March 2, 2021, intrathecal morphine was not available for use, was not stocked in the pharmacy, and was not part of the intrapartum or postpartum regimen. We previously had a standardized post-cesarean analgesia protocol comprised of scheduled acetaminophen and NSAIDs.[8] Prior to 2021, intrathecal morphine was not used due to early concerns related to respiratory compromise.[13] However, we found that our approach of using systemic opioids rather than intrathecal morphine resulted in a 112-fold higher rate of moderate to severe respiratory events than would be expected with intrathecal morphine.[7,14] Accordingly, we pivoted to implement intrathecal morphine.

Table 1. Characteristics of Patients Pre- and Post-implementation of an Enhanced Recovery After Cesarean Surgery Protocol (ERAS Protocol)

Characteristic	Pre-ERAS (n = 973)	Post-ERAS (n = 1025)	*P* value
Demographic Characteristics			
Maternal age, mean ± 4 SD	31.8 ± 4.9	32.0 ± 5.2	0.390
Married,[a] n (%)	744 (76.5)	774 (75.5)	0.818
Insurance, n (%)			0.9171
Private	768 (78.9)	817 (79.7)	
Medicaid or other public insurance	201 (20.7)	204 (19.9)	
Self-pay, no insurance, other	4 (0.4)	4 (0.4)	
Race, n (%)			0.3954
Asian or Indian	76 (8)	72 (7.2)	
Black	83 (8.7)	84 (8.5)	
Other or not specified[c]	7 (0.7)	15 (1.5)	
White	784 (82.5)	823 (82.8)	
Latinx ethnicity, n (%)[d]	82 (8.4)	114 (11.1)	0.051
Maternal BMI (prepregnancy), mean ± SD	28.7 ± 7.4	29.0 ± 7.9	0.369
Maternal BMI (at delivery), mean ± SD	34.1 ± 7.1	34.4 ± 7.6	0.596
Gravidity,[b] n (%)			0.904
1	362 (37.2)	368 (35.9)	
2	283 (29.1)	300 (29.3)	
3	148 (15.2)	156 (15.2)	
4+	179 (18.4)	200 (19.5)	
Maternal History			
Any diabetes, n (%)	187 (19.2)	191 (18.6)	0.782
Obstetric Characteristics			
Multiple gestation, current pregnancy, n (%)	56 (5.8)	56 (5.5)	0.852
Gestational age at delivery, mean ± SD	38.2 ± 2.4	38.1 ± 2.5	0.340
Infant birthweight (grams), mean ± SD	3241 ± 716	3198 ± 742	0.184
Surgical and Postpartum Characteristics			
Primary versus repeat cesarean birth			0.925
Primary, n (%)	583 (59.9)	611 (59.6)	
Repeat, n (%)	390 (40.1)	414 (40.4)	
Unplanned cesarean birth, n (%)	322 (33.1)	405 (39.5)	**0.003**
Anesthesia modality			
General anesthesia, n (%)	44 (4.5)	45 (4.4)	0.973
Epidural anesthesia, n (%)	367 (37.7)	402 (39.2)	0.520
Spinal anesthesia, n (%)	565 (58.1)	591 (57.7)	0.868

Abbreviation: BMI, body mass index.
Bold font indicates statistical significance.
[a]Marital status was unknown for 1 person in the pre-ERAS and 1 person in the post-ERAS group.
[b]Gravidity data unknown for 1 person in the pre-ERAS and 1 person in the post-ERAS group.
[c]Other racial categories here included American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, and those who chose to not self-identify. Due to low numbers, these designations were grouped to preserve anonymity.
[d]Unknown for 30 people in the pre-ERAS and 21 people in the post-ERAS group.

The ERAS protocol for the prehospital and preoperative period is shown in Supplemental Table 2, with new items indicated by ‡. Among other components of this protocol, at a preoperative visit, patients undergoing planned cesarean births receive multimedia education via in-person counseling, brochures, and a standardized video.[2] The video is available via the hospital website in English and Spanish, as well as YouTube and loaded on tablet devices in clinics and at the hospital (Links: https://

www.unitypoint.org/madison/cesareanbirth.aspx or https://www.youtube.com/watch?v=x1UJysNQKkA). Patients undergoing unplanned cesarean birth are counseled about what to expect by the clinicians and, when time permits, a visual flip-chart aid with diagrams is used to standardize this conversation. Patients undergoing unplanned cesarean delivery also may watch the pre-cesarean educational video if time permits. The contents of the video include how to prepare for a cesarean birth, what to expect, and how postoperative pain will be managed.

The perioperative and intraoperative protocol is shown in Supplemental Table 3.[4,6,11,15] Starting March 2, 2021, intrathecal morphine was added to the spinal and epidural anesthesia regimen. Dosing is indicated in Supplemental Table 3. Patients who underwent general anesthesia without neuraxial analgesia did not receive neuraxial morphine.

Intraoperative considerations included recommendations to avoid a bladder flap, with instructions that foregoing a bladder flap reduces time to delivery, surgical site infection, time to void, urinary retention, and adherence of the bladder to the uterus in subsequent pregnancies, but also that provider discretion is reasonable.[6] Promoting early skin-to-skin contact was implemented in a systematic manner as part of the ERAS protocol, with the pediatric team assessing the baby on the operative field during delayed cord clamping and allowing immediate skin-to-skin contact if further assessment on the warmer was not required.[4,6,12]

Table 2. Percentage of Postpartum People Utilizing ≤15 MMEs Within a Given Time Period and With Severe Pain Scores (≥7) Pre- and Post-ERAS Protocol Implementation

Time Period	Pre-ERAS (n = 973)	Post-ERAS (n = 1025)	*P* value
Percentage who utilized zero MMEs	n (%)	n (%)	
0 – < 6 hours	111 (11.4)	687 (67.0)	**< 0.001**
6 – <12 hours	84 (8.6)	777 (75.8)	**< 0.001**
12 – < 24 hours	86 (8.8)	683 (66.6)	**< 0.001**
24 – < 48 hours	133 (13.7)	533 (52.0)	**< 0.001**
48 – < 72 hours	285 (29.3)	644 (62.8)	**< 0.001**
72 hours – hospital discharge	624 (64.1)	851 (83.0)	**< 0.001**
Percentage who utilized ≤15 total MMEs	n (%)	n (%)	
0 – < 6 hours	260 (26.7)	950 (92.7)	**< 0.001**
6 – < 12 hours	175 (18.0)	924 (90.1)	**< 0.001**
12 – < 24 hours	130 (13.4)	787 (76.8)	**< 0.001**
24 – < 48 hours	167 (17.2)	617 (60.2)	**< 0.001**
48 – < 72 hours	357 (36.7)	736 (71.8)	**< 0.001**
72 hours – hospital discharge	690 (70.9)	915 (89.3)	**< 0.001**
Percentage of patients with any pain score ≥ 7[a]	n (%)	n (%)	
0 – < 6 hours	278 (32.0)	141 (21.2)	**< 0.001**
6 – <12 hours	164 (19.2)	48 (8.6)	**< 0.001**
12 – < 24 hours	179 (19.7)	101 (13.8)	**0.002**
24 – < 48 hours	164 (17.6)	182 (21.1)	0.070
48 – < 72 hours	102 (12.7)	96 (14.1)	0.496
72 hours – hospital discharge	53 (12.2)	33 (10.4)	0.516

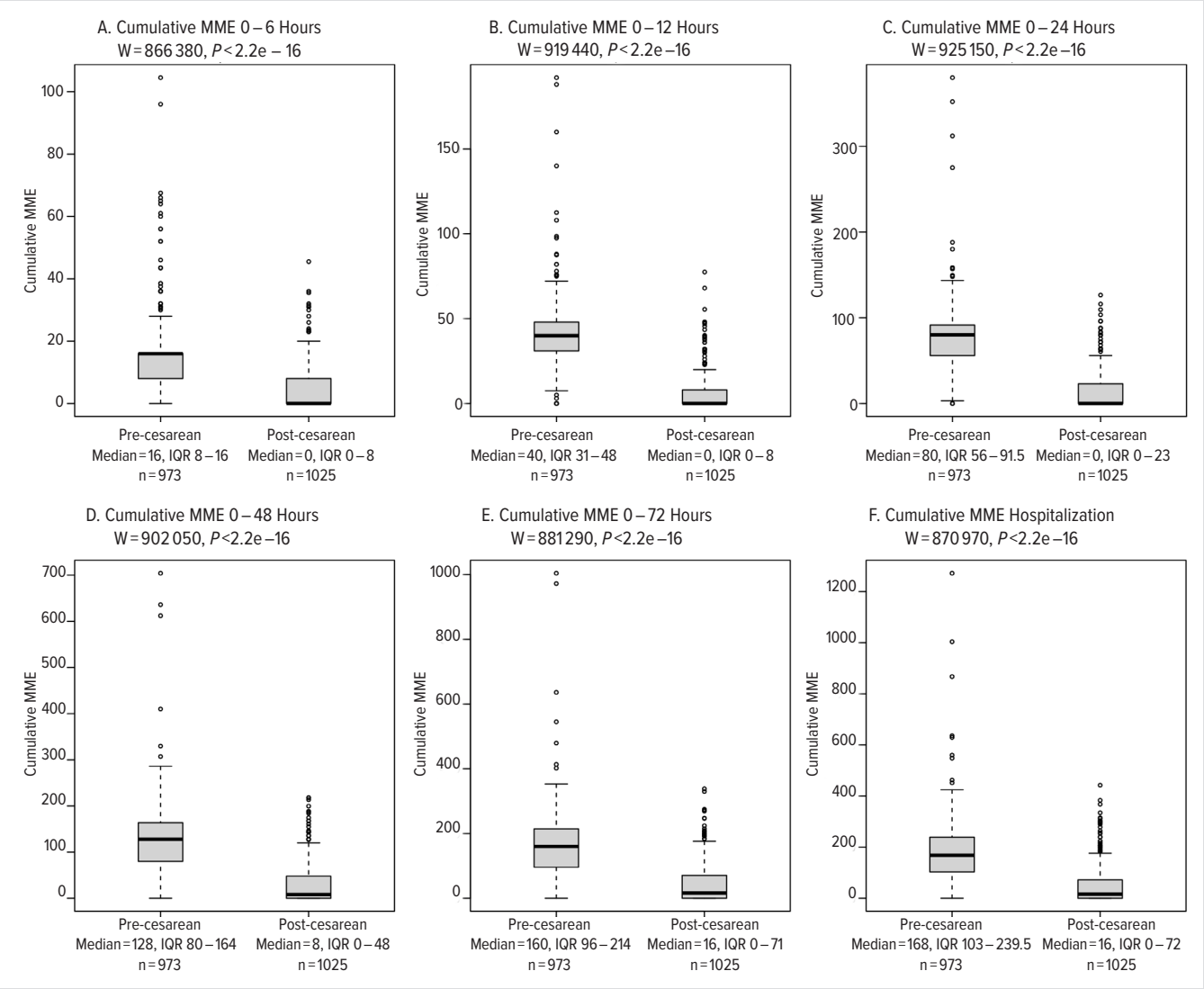
Abbreviations: MME, morphine milligram equivalents; ERAS, enhanced recovery after cesarean surgery.
Bold font indicates statistical significance; *P* values are based upon chi-square or Fisher exact tests.
[a]Denominators only include those with pain scores recorded. For 0 – <6 hours, 869 and 664 people had pain scored recorded for the pre and post-ERAS, respectively; for 6 – <12, 832 and 561; for 12 – <24 hours, 907 and 730; for 24 – <24 hours, 933 and 864; for 48 – <72 hours, 801 and 682; for 72 hours hospital discharge, 434 and 317.

The postpartum ERAS protocol is shown in Supplemental Table 4. Acetaminophen (975 mg orally) and NSAIDs (ketorolac 15 mg intravenously [IV] for the first 24 hours followed by ibuprofen 600 mg orally) are administered every 6 hours simultaneously, which was the case in both the pre-ERAS and post-ERAS period.[8] Opioids – oral or IV – could be administered as needed for breakthrough pain. These typically comprised oral morphine or hydromorphone, but different agents were available or used due to medication shortages or patient factors. New items include earlier removal of the indwelling urinary catheter within 6 rather than 12 hours.[4,16] Early oral nutrition and gum chewing was encouraged.[3,4,11] A postoperative educational video was created with instructions to view the video as early as feasible during the postpartum period. The contents of this video were similar to the preoperative video but with the preparation steps omitted and a few notes about unexpected cesarean births. Finally, routine discharge at post-cesarean day 2 was encouraged.

Education for nurses and all obstetric providers (including resident physicians, certified nurse midwives, family medicine physicians, and obstetricians) was required and made available starting 1 month prior to implementation, allowing time to complete the educational modules. The modules included information on each new portion of the protocol and the rationale for inclusion. The module was followed by a short quiz. Reminder emails were sent to those who did not complete the training modules and the quiz. Reminder fliers were posted on the maternity unit. All modules were to be completed by the implementation date of June 29, 2021, which was the date that use of the order sets was required.

Data were collected for the following date ranges: "pre-ERAS" June 1, 2020-March 1, 2021; "partial" March 3, 2021-June 28, 2021, at which time only the intrathecal morphine portion of the protocol was started; and "post-ERAS" June 29, 2021-March 31, 2022. The primary analysis compared the pre-ERAS to the post-ERAS period. To collect demographic data, we queried the hospital's administrative birth database (PeriData.Net, Ancilla Partners, Inc, Milwaukee, Wisconsin) to generate a list of all cesarean births that occurred during the dates analyzed. Briefly,

Figure 1. Median Cumulative MME Utilization Among the Pre-ERAS and Post-ERAS Groups in (A) the First 6 Hours Post-cesarean, (B) the First 12 Hours Post-cesarean, (C) the First 24 Hours Post-cesarean, (D) the First 48 Hours Post-cesarean, (E) the First 72 Hours Post-cesarean, and (F) From Cesarean Until Discharge From the Hospital



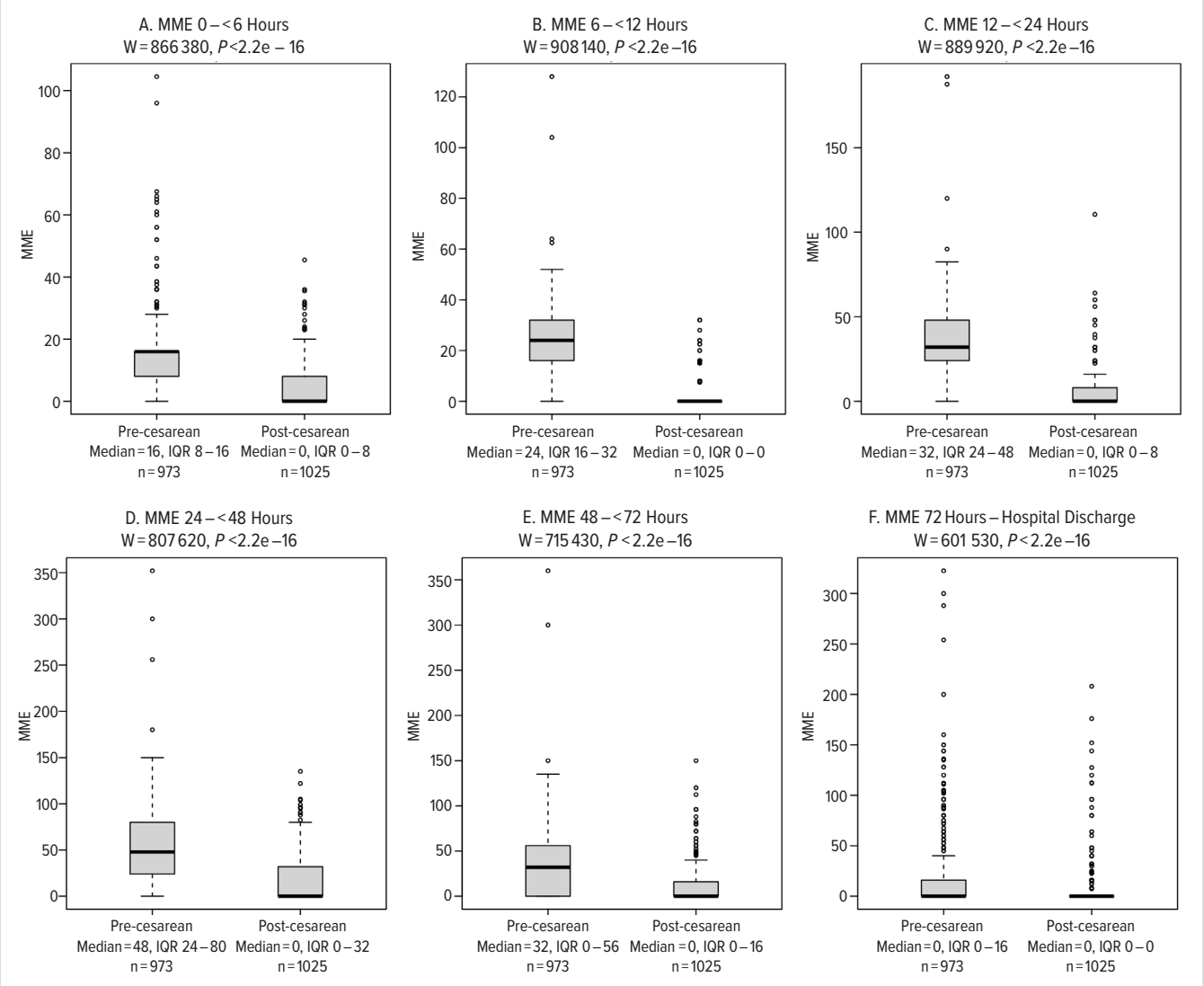
Abbreviations: MME, morphine milligram equivalents; ERAS, enhanced recovery after cesarean surgery.
P values are based on Wilcoxon rank sum tests.

data entry is performed manually via review of information from parents supplemented by review of the hospital's electronic health record.[7,8] All data are audited by perinatal data coordination nursing staff.[7,8] We simultaneously queried the electronic health record system (Epic, Hyperspace 2021, Epic Systems Corporation, Verona, Wisconsin) for recorded pain scores and medication use.

Inclusion criteria for this analysis were cesarean delivery during the indicated time periods. Exclusion criteria included the following: chronic opioid use due to either chronic pain or opioid use disorder due to likely outlier status for post-cesarean opioid utilization and ongoing intubation after completion of cesarean surgery because such patients often receive opioids for purposes unrelated to pain.

The primary outcome was cumulative opioid dose in the first 48 hours postoperatively among the pre-ERAS group versus the post-ERAS group. Doses were converted to MMEs and summed.[17] Secondary outcomes included MME utilization and pain scores at other time intervals. Pain scores from 0 to 10 using the numeric rating scale were collected by nurses at least every 6 hours.[18] Using this pain scale, scores of 0 correspond to no pain, 1 to 3 corresponds to mild pain, 4 to 6 corresponds to moderate pain, and 7 to 10 corresponds to severe pain.[18] Nurses also qualitatively assess the nature of pain and subjectively assess how much pain the patient appears to be experiencing. We assessed the percentage of postpartum people with at least 1 pain score ≥7; the percentage who utilized < 15 MMEs for the whole hospitalization; and the percentage who utilized zero MMEs. A pain score ≥7 was

Figure 2. Median MME Among the Pre-ERAS and Post-ERAS Groups in (A) the First 0 – < 6 Hours Post-cesarean, (B) 6 – < 12 Hours Post-cesarean, (C) 12 – < 24 Hours Post-cesarean, (D) 24 – < 48 Hours Post-cesarean, (E) 48 – < 72 Hours Post-cesarean, and (F) 72 Hours Post-cesarean Until Discharge From the Hospital



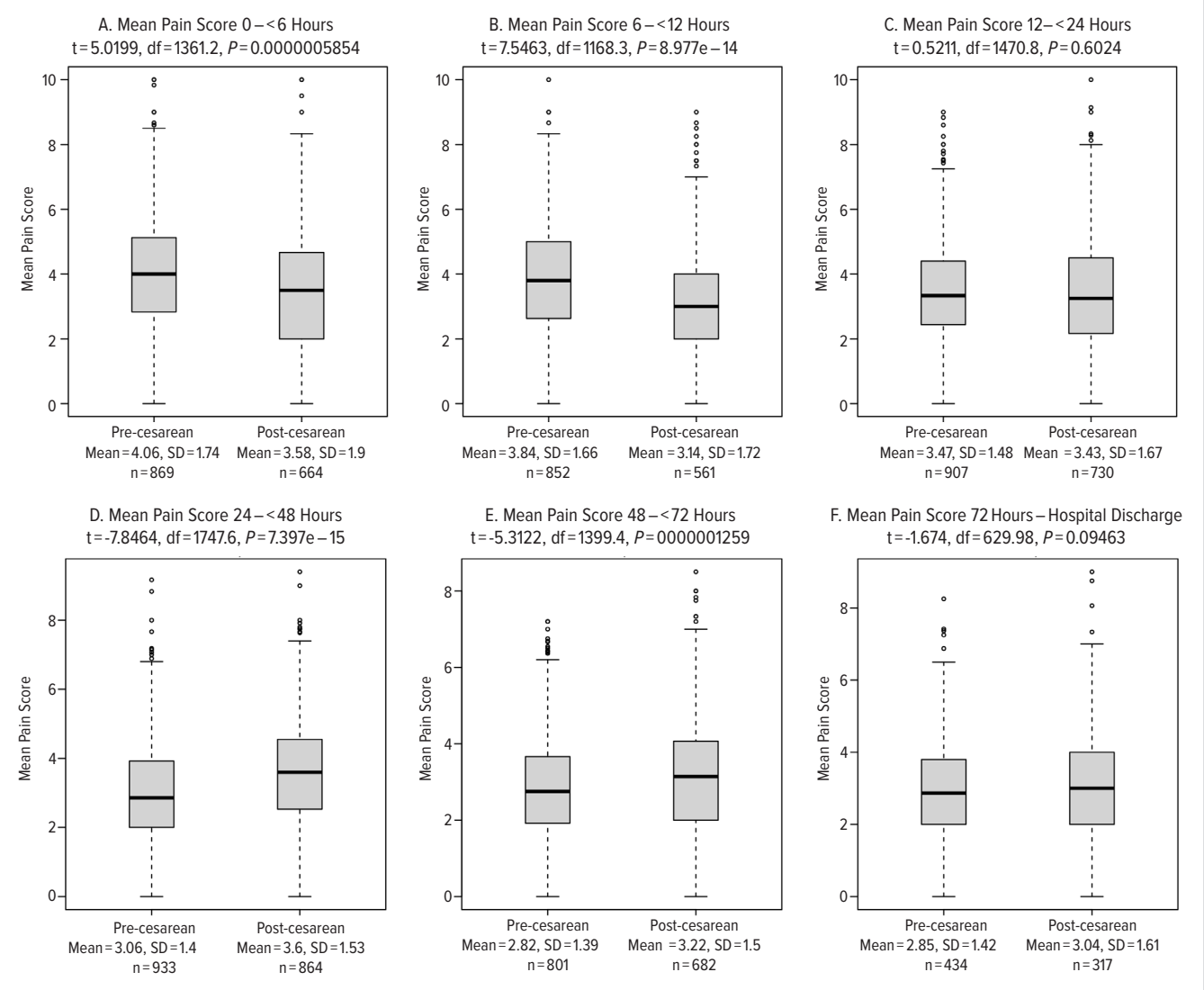
Abbreviations: MME, morphine milligram equivalents; ERAS, enhanced recovery after cesarean surgery.
P values are based on Wilcoxon rank sum tests.

chosen as a cutoff because this signifies severe pain. The threshold of 15 MMEs for the whole hospitalization was evaluated because prior investigators used this as a cut-off at which patients were considered to be "opioid spared." Additional variables collected included body mass index (BMI), age, race/ethnicity, gravidity, parity, and gestational age at delivery. Medical comorbidities and obstetric outcomes were defined as per the American College of Obstetricians and Gynecologists.

To assess compliance with the ERAS protocol, the following items were audited: pre-cesarean glucose beverage consumed (for planned cesarean births only), intrathecal morphine administered, intraoperative temperature obtained, pre-cesarean video viewed, and post-cesarean video viewed.

Based upon our hospital data, in 2019, average cumulative opioid utilization in the first 48 hours post-cesarean birth was 134.9 MME with a standard deviation of 66.2 MME.[8] Given this average baseline data, we anticipated that we would require a sample size of at least 114 to detect a 30% reduction in cumulative opioid dose, accommodating a wide standard deviation, with 80% power and alpha of 0.05. In order to assess our secondary outcomes, we included patient charts for the time period for all who met criteria. Demographic and outcome measures were compared pre-ERAS and post-ERAS using *t* test or Wilcoxon rank sum for normally and non-normally distributed continuous measures, respectively, and chi-square or Fisher exact test for categorical measures. Post hoc analyses of the pre-ERAS, partial-ERAS (intrathecal morphine only), and post-ERAS (full ERAS) groups were performed. A *P* value of < 0.05 was considered statistically significant. R program-

Figure 3. Mean Pain Scores Among the Pre-ERAS and Post-ERAS Groups in the First (A) the First 0 – <6 Hours Post-cesarean, (B) 6 – <12 Hours Post-cesarean, (C) 12 – <24 Hours Post-cesarean, (D) 24 – <48 Hours Post-cesarean, (E) 48 – <72 Hours Post-cesarean, and (F) 72 Hours Post-cesarean Until Discharge From the Hospital



Abbreviations: MME, morphine milligram equivalents; ERAS, enhanced recovery after cesarean surgery.
P values are based on *t* tests.

ming language was used for all statistical analyses (R Core Team, 2020).

RESULTS

From June 1, 2020, through March 31, 2022, 2522 patients were delivered via cesarean. One hundred seven were excluded due to chronic opioid use (n = 98) or post-cesarean intubation (n = 9). From June 1, 2020, to March 1, 2021, 973 were delivered and were included in the "pre-ERAS" group; 1025 were delivered from June 29, 2021, through March 31, 2022, and were included in the "post-ERAS" group; and 417 were delivered during the time from March 2, 2021 through June 28, 2021 and were included in the "partial" group but were excluded from the primary analysis. During the "partial-ERAS" time period, only intrathecal morphine had been implemented. During the "post-ERAS" period the full ERAS protocol had been implemented. Baseline characteristics of the 2 groups were similar except that in the post-ERAS group, more patients experienced unplanned cesarean birth.

The primary outcome of cumulative MME in the first 48 hours after cesarean birth was significantly different between groups with higher MME utilized in the pre-ERAS group compared to the post-ERAS group (median 128 [IQR 80-164] MME vs 8 [IQR 0-48] MME, respectively; Wilcoxon rank test $P < 0.001$) (Figure 1D). Cumulative MME utilization and MME utilization for each time interval was similarly lower in the post-ERAS group (Figures 1 and 2). The percentage of patients who utilized 0 MME and <15 MMEs was significantly lower among the post-ERAS group (Table 2).

Regarding the secondary outcome of pain scores, mean pain scores were lower for the 0 to 6 hours and 6 to 12 hours interval among the post-ERAS group. For the 12- to 24-hour post-cesarean interval and the interval from 72 hours until discharge, there was no statistical difference in pain scores (Figure 3). For the 24- to 48-hour and 48- to 72-hour interval, pain scores were higher in the post-ERAS group. Fewer patients reported pain scores >7 in the post-ERAS group for the first 24 hours post-cesarean (Table 2) but not beyond 24 hours.

Postpartum length of stay was decreased in the post-ERAS group from 3.1 days (SD 0.9) pre-ERAS to 2.9 days (SD 0.9) post-ERAS, (*t* test $P<0.001$).

To determine whether the full ERAS protocol was associated with further MME reduction versus intrathecal morphine alone, the partial-ERAS group was compared to the post-ERAS group. Baseline characteristics between the partial-ERAS and post-ERAS groups were similar with no statistically significant differences in evaluated characteristics (data available upon request). The median opioid utilization at all time periods was similar between groups (Supplemental Figures 1 and 2). Pain score results were similar except that pain scores in the post-ERAS group were slightly higher in the first 0 to 6 hours post-cesarean than in the intrathecal morphine only group, median 3.3 (SD 1.9) versus 3.6 (SD 1.9) for the partial versus post-ERAS groups, respectively (Supplemental Figure 3). The percentage who reported pain scores >7, the percentage who utilized zero MMEs, and the percentage who utilized <15 MMEs were not statistically different between the partial versus post-ERAS groups (Supplemental Table 5). When comparing the pre-ERAS group to the partial-ERAS group, statistically significant differences in both cumulative MME utilization and in the percentage of patients who utilized zero MMEs and <15 MMEs were noted (supplemental Figure 4 and Supplemental Table 6).

Regarding compliance, during the post-ERAS period, the preoperative glucose beverage was administered 608 times for 620 (98.1%) planned cesarean cases. During the partial-ERAS period, 398 of 417 (95.4%) patients undergoing cesarean birth received intrathecal morphine; during the post-ERAS period, 1000 of 1025 (97.5%) patients undergoing cesarean birth received intrathecal morphine. Intraoperative temperature was documented for 1023 (99.8%) cases post-ERAS. The preoperative video was watched an average of 3.9 times daily and the post-cesarean video was watched an average of 4.5 times daily, which exceeds the average number of cesareans births performed daily (3.4). Of video viewings, 11.5% were for the Spanish language version.

DISCUSSION

Following implementation of this post-cesarean ERAS protocol, total opioids utilized in the first 48 hours following cesarean birth decreased by 93.8%. A decrease in opioid utilization was observed at all other time periods. The percentage of patients who utilized zero and <15 MMEs was higher following implementation of this ERAS protocol. MME utilization was statistically significantly lower after implementation of intrathecal morphine alone (partial-ERAS) than during the pre-ERAS period, suggesting that this was the main driver of decreasing opioid dose. Further reductions in opioid utilization after the implementation of the full protocol were limited by low opioid utilization in both the "partial" and post-ERAS time periods.

Our secondary outcome measure of mean pain scores was lower at time periods prior to 12 hours postpartum. The 12- to 24-hour time period is the timeframe where the effects of intrathecal morphine would be expected to wane; thus, this might explain the lack of a difference in pain control in this time period.[19] After 24 hours, pain scores were statistically higher in the post-ERAS group compared to the pre-ERAS group, while MME utilization remained statistically lower. The clinical significance of the difference in pain scores is small, but this suggests that after implementation of the ERAS protocol, pain in the 24- to 48-hour period was less aggressively treated with opioids. Another possible explanation is that patients were more tolerant of mild pain without requesting opioids due to the educational interventions of the ERAS protocol. The absolute differences in pain, while statistically significant, are of unclear clinical significance. We did not capture patient satisfaction scores, but it will be important to consider whether additional efforts are warranted to reduce pain beyond 24 hours post-cesarean. The percentage of subjects with severe pain—scores ≥7—was lower in the first 24 hours post-cesarean in the post-ERAS group, but this was no longer observed after 24 hours.

Prior investigations, quality improvement projects, trials, and meta-analyses have similarly found that implementation of enhanced recovery after cesarean surgery protocols is associated with decreased opioid consumption in the post-cesarean time period,[11,12] decreased pain,[11,12] shorter length of stay,[12] decreased hospital costs,[20] and increased patient satisfaction.[20] Some also notably found no change in opioid utilization,[21] pain scores,[22] or length of stay.[11] Each ERAS protocol differs, which may affect the impact on each of these outcomes. Here, we uniquely evaluated the impact of intrathecal morphine separately from the full ERAS protocol and found that intrathecal morphine is the most impactful component in terms of reducing cumulative MME utilization. These results support wider implementation of ERAS protocols that include intrathecal morphine—especially at institutions with above-average post-cesarean opioid utilization.

We and other institutions have identified racial disparities in treatment of post-cesarean pain.[23,24] One institution has demonstrated that their ERAS protocol reduced racial disparities in postoperative pain scores.[25] Further analysis regarding whether our ERAS protocol reduced disparities is planned.

Our strengths included the following: this project was implemented in the largest delivering hospital in Wisconsin, which allowed for a large sample size. Our multidisciplinary team encompassed all phases of clinical and hospital care that patients

undergoing cesarean births encounter. The staggered implementation of intrathecal morphine and the full protocol allowed us to evaluate whether ERAS was associated with further reduction in MME utilization and pain compared to intrathecal morphine alone. While this was a before-and-after analysis, the obstetrical care teams, anesthesia teams, and patient population before and after the intervention were similar. While not yet published when this protocol and analysis were being planned, we have included many of the standardized outcome measures proposed by the CRADLE (Curating Research Assets and Data Using Lifecycle Education) investigators, including the length of hospital stay, postpartum opioid consumption, and compliance.[26]

Our analysis has limitations. In our analysis comparing the partial protocol to the post-ERAS time period, the median MME utilization for both time periods was low at 8 MME. This low MME and the lower sample size limited our ability to assess further reductions in MME utilization after implementation of the full protocol. This single institution has limited racial/ethnic diversity, which limits generalizability. Mental health diagnoses can impact postoperative pain, but these are not captured in our hospital's administrative database and could not be accounted for.[27] However, such diagnoses are unlikely to differ in this before-and-after population over a short time span. We previously demonstrated that unplanned cesarean birth is associated with higher pain and MME utilization after delivery among people with anxiety.[27] The higher prevalence of unplanned cesarean births in the post-ERAS time period would be expected to potentially limit our findings of less MME utilization in the post-ERAS period. We were not able to assess measures that are less well documented in the medical record, such as time to oral intake or ambulation. We lack patient experience data, which limits our ability to assign clinical significance to the small numeric increase in pain scores.

CONCLUSIONS

ERAS protocols are recommended by many anesthesia and obstetrical societies and a variety of guidelines and reviews are available.[2-6] We provide further evidence that ERAS protocols—particularly one including intrathecal morphine—can reduce MME utilization by 93.8% at a high volume teaching-community hospital with historically high MME utilization after cesarean birth.[7,8] While there was no further reduction in MME utilization with the full ERAS protocol than with intrathecal morphine alone, the median MME during both time periods was low, which limits the ability to measure further reductions. Notably, pain scores increased after 24 hours post-cesarean. Accordingly, ongoing research efforts should focus on pain control after the first 24-hour time period.

Funding/Support: The project was supported by the Meriter Foundation and the Clinical and Translational Science Award program, through the National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS), grant UL1TR002373 (ATB) and the University of Wisconsin Department of Obstetrics and Gynecology (KMA). The content is the sole responsibility of the authors and does not necessarily represent the official views of the NIH. The funding source had no role in the design, collection, analysis, or interpretation of data, writing of the report, or decision to submit the article for publication.

Financial Disclosures: None declared.

Acknowledgements: The authors would like to thank members of the multidisciplinary committee, including Jackie Adams, Michael Nyffeler, Jill Cardwell, Lisa Reinke, Sue Briggs, Julie Schurr, Laura Berghan, Shelly Weisheipl, Gregory Bills, Connie Potts, Carla Griffin, Kathy Frigge, Elizabeth Goetz, Janna Lind, Nicolle Hovland, and Nicole Allman, (employed by the University of Wisconsin-Madison, Madison Anesthesiology Consultants, and UnityPoint Health-Meriter) and the leadership teams at UnityPoint Health-Meriter, the Center for Perinatal Care, and the University of Wisconsin School of Medicine and Public Health Department of Obstetrics and Gynecology. They would like to acknowledge Ruth Hallquist, Janna Lind, and Jonathan Garvey (employed by UnityPoint Health-Meriter) for their support and assistance extracting data from the electronic health record. They would also like to acknowledge Carla Ruhland, Carla Griffin, and Ancilla Partners for their support and assistance with data extraction from PeriData.Net for this project (employed by UnityPoint Health-Meriter). PeriData.Net is a comprehensive birth registry maintained by Ancilla Partners, Inc. This registry provides process and outcome measure results as well as birth-level data on how well a given hospital and its providers are administering quality of care before, during, and after the birthing lifecycle. They would finally like to acknowledge Robert Koehler for assisting with the literature review and article acquisition (employed by UnityPoint Health-Meriter).

Appendices: Supplemental Materials available at www.wmjonline.org.

REFERENCES

1. Landau R, Cavanaugh PF, DiGiorgi M. Persistent opioid use after cesarean delivery in the United States of America: a systematic review. *Int J Obstet Anesth.* 2023;54:103644. doi:10.1016/j.ijoa.2023

2. Wilson RD, Caughey AB, Wood SL, et al. Guidelines for antenatal and preoperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations (part 1). *Am J Obstet Gynecol.* 2018;219(6):523-532. doi:10.1016/j.ajog.2018.09.015

3. Macones GA, Caughey AB, Wood SL, et al. Guidelines for postoperative care in cesarean delivery: Enhanced Recovery After Surgery (ERAS) Society recommendations (part 3). *Am J Obstet Gynecol.* 2019;221(3):247.e1-247.e9. doi:10.1016/j.ajog.2019.04.012

4. Bollag L, Lim G, Sultan P, et al. Society for Obstetric Anesthesia and Perinatology: consensus statement and recommendations for enhanced recovery after cesarean. *Anesth Analg.* 2021;132(5):1362-1377. doi:10.1213/ANE.0000000000005257

5. Pharmacologic stepwise multimodal approach for postpartum pain mangement. ACOG Clinical Consensus No. 1. *Obstet Gynecol*. 2021;138:507-517. doi:10.1097/AOG.0000000000004517

6. Caughey AB, Wood SL, Macones GA, et al. Guidelines for intraoperative care in cesarean delivery: Enhanced Recovery After Surgery Society recommendations (part 2). *Am J Obstet Gynecol*. 2018;219(6):533-544. doi:10.1016/j.ajog.2018.08.006

7. Walker JL, Adams JH, Broman AT, Pryde PG, Antony KM. Postoperative respiratory compromise following cesarean birth: the impact of obesity and systemic opioids. *AJP Rep*. 2022;12(1):e1-e9. doi:10.1055/s-0041-1741539

8. Meyer MF, Broman AT, Gnadt SE, Sharma S, Antony KM. A standardized post-cesarean analgesia regimen reduces postpartum opioid use. *J Matern Fetal Neonatal Med.* 2022;35(25):8267-8274. doi:10.1080/14767058.2021.1970132

9. Elias KM, Stone AB, McGinigle K, et al. The reporting on ERAS compliance, outcomes, and elements research (RECOvER) checklist: a joint statement by the ERAS® and ERAS® USA Societies. *World J Surg.* 2019;43(1):1-8. doi:10.1007/s00268-018-4753-0

10. Davidoff F, Batalden P, Stevens D, Ogrinc G, Mooney S; SQUIRE Development

Group. Publication guidelines for quality improvement in health care: evolution of the SQUIRE project. *Qual Saf Health Care*. 2008;17(suppl 1):i3-i9. doi:10.1136/qshc.2008.029066

11. Hedderson M, Lee D, Hunt E, et al. Enhanced recovery after surgery to change process measures and reduce opioid use after cesarean delivery: a quality improvement initiative. *Obstet Gynecol.* 2019;134(3):511-519. doi:10.1097/AOG.0000000000003406

12. Kleiman AM, Chisholm CA, Dixon AJ, et al. Evaluation of the impact of enhanced recovery after surgery protocol implementation on maternal outcomes following elective cesarean delivery. *Int J Obstet Anesth.* 2020;43:39-46. doi:10.1016/j.ijoa.2019.08.004

13. American Society of Anesthesiologists Task Force on Neuraxial Opioids; Horlocker TT, Burton AW, Connis RT, et al. Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration. *Anesthesiology*. 2009;110(2):218-230. doi:10.1097/ALN.0b013e31818ec946

14. Sharawi N, Carvalho B, Habib AS, Blake L, Mhyre JM, Sultan P. A systematic review evaluating neuraxial morphine and diamorphine-associated respiratory depression after cesarean delivery. *Anesth Analg*. 2018;127(6):1385-1395. doi:10.1213/ANE.0000000000003636

15. Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 199: use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol*. 2018;132(3):e103-e119. doi:10.1097/AOG.0000000000002833

16. Dahlke JD, Mendez-Figueroa H, Maggio L, Sperling JD, Chauhan SP, Rouse DJ. The case for standardizing cesarean delivery technique: seeing the forest for the trees. *Obstet Gynecol.* 2020;136(5):972-980. doi:10.1097/AOG.0000000000004120

17. American Society of Addiction Medicine. Public policy statement on morphine equivalent units/morphine milligram equivalents. 2016. Accessed July 9, 2020. https://www.asam.org/docs/default-source/public-policy-statements/2016-statement-on-morphine-equivalent-units-morphine-milligram-equivalents.pdf?sfvrsn=3bc177c2_6

18. Karcioglu O, Topacoglu H, Dikme O, Dikme O. A systematic review of the pain scales in adults: which to use? *Am J Emerg Med.* 2018;36(4):707-714. doi:10.1016/j.ajem.2018.01.008

19. Mugabure Bujedo B. A clinical approach to neuraxial morphine for the treatment of postoperative pain. *Pain Res Treat.* 2012;2012:612145. doi:10.1155/2012/612145

20. Pan J, Hei Z, Li L, et al. The advantage of implementation of enhanced recovery after surgery (ERAS) in acute pain management during elective cesarean delivery: a prospective randomized controlled trial. *Ther Clin Risk Manag*. 2020;16:369-378. doi:10.2147/TCRM.S244039

21. Tanner LD, Chen HY, Chauhan SP, Sibai BM, Ghebremichael SJ. Enhanced recovery after scheduled cesarean delivery: a prospective pre-post intervention study. *J Matern Fetal Neonatal Med.* 2022;35(25):9170-9177. doi:10.1080/14767058.2021.2020237

22. Shinnick JK, Ruhotina M, Has P, et al. Enhanced recovery after surgery for cesarean delivery decreases length of hospital stay and opioid consumption: a quality improvement initiative. *Am J Perinatol*. 2021;38(S 01):e215-e223. doi:10.1055/s-0040-1709456

23. White RS, Matthews KC, Tangel V, Abramovitz S. Enhanced recovery after surgery (ERAS) programs for cesarean delivery can potentially reduce healthcare and racial disparities. *J Natl Med Assoc*. 2019;111(4):464-465. doi:10.1016/j.jnma.2019.02.001

24. Poehlmann JR, Avery G, Antony KM, Broman AT, Godecker A, Green TL. Racial disparities in post-operative pain experience and treatment following cesarean birth. *J Matern Fetal Neonatal Med*. 2022;35(26):10305-10313. doi:10.1080/14767058.2022.2124368

25. Felder L, Cao CD, Konys C, et al. Enhanced recovery after surgery protocol to improve racial and ethnic disparities in postcesarean pain management. *Am J Perinatol.* 2022;39(13):1375-1382. doi:10.1055/a-1799-5582

26. Sultan P, George R, Weiniger CF, et al. Expert consensus regarding core outcomes for enhanced recovery after cesarean delivery studies: a Delphi study. *Anesthesiology*. 2022;137(2):201-211. doi:10.1097/ALN.0000000000004263

27. Poehlmann JR, Stowe ZN, Godecker A, Xiong PT, Broman AT, Antony KM. The impact of preexisting maternal anxiety on pain and opioid use following cesarean delivery: a retrospective cohort study. *Am J Obstet Gynecol MFM*. 2022;4(3):100576. doi:10.1016/j.ajogmf.2022.100576

Assessing Accuracy of Blood Loss Measurements During Cesarean Birth in a Diverse Patient Population: A Quality Improvement Study

Jessica J. F. Kram, MPH; Yuri Zermeno, MD; James O. Adefisoye, MS; Elizabeth Dickson Michelson, MD; Emily Malloy, PhD, CNM; Nicole Salvo, MD

ABSTRACT

Background: Accurate measurement of blood loss during delivery is important for early hemorrhage detection.

Methods: We compared quantitative blood loss and estimated blood loss to calculated blood loss. We reviewed cesarean deliveries for estimated blood loss and quantitative blood loss, December 1, 2018, to December 1, 2019. A standard formula was used for calculated blood loss.

Results: Overall (n = 483), median values (m; interquartile range [IQR]) for estimated blood loss (600.0 mL; IQR 500.0–800.0) and quantitative blood loss (557.0 mL; IQR 350.0 – 824.0) were significantly lower (both *P* values < 0.001) than calculated blood loss (929.4 mL; IQR 551.5 – 1351.5). Compared to calculated blood loss, both estimated blood loss and quantitative blood loss had low sensitivity, high specificity, and low negative predictive values. Only 10 additional patients were identified as having a postpartum hemorrhage through quantitative blood loss.

Discussion: Quantitative blood loss and estimated blood loss are immediately available in clinical practice, while calculated blood loss is not and requires additional time to obtain. All methods currently available have shortcomings. Continued efforts to create a reliable tool for identifying blood loss are needed.

• • •

Author Affiliations: Academic Affairs, Aurora University of Wisconsin Medical Group, Advocate Health, Aurora Sinai Medical Center, Milwaukee, Wisconsin (Kram, Adefisoye); Center for Urban Population Health, Milwaukee, Wisconsin (Kram); Department of Obstetrics and Gynecology, Advocate Health, Aurora Sinai Medical Center, Milwaukee, Wisconsin (Zermeno, Salvo); Department of Oncology, Advocate Health, Aurora West Allis Medical Center, Milwaukee, Wisconsin (Dickson Michelson); Department of Obstetrics and Gynecology and Midwifery, Aurora University of Wisconsin Medical Group, Advocate Health, Aurora Sinai Medical Center, Milwaukee, Wisconsin (Malloy).

Corresponding Author: Jessica J. F. Kram, MPH; 1020 N 12th St, Suite 4180, Milwaukee, WI 53233; phone 414.219.5594; email jessica.kram@aah.org; ORCID ID 0000-0001-9831-7353

BACKGROUND

Postpartum hemorrhage accounts for approximately 16% of maternal-related deaths in developed countries.[1] Measuring blood loss during and after birth for early detection of hemorrhage to prevent maternal morbidity and mortality is standard of care, and efforts are being made to improve measurement accuracy.[1] Historically, the most common way of measuring blood loss was through visual estimated blood loss. However, estimated blood loss overestimates[2] or underestimates[3,4] blood loss compared to gravimetric and colorimetric methods. More recently, maternal and obstetric committees have recommended quantitative blood loss methods. Some studies have reported quantitative blood loss to be more accurate than visual estimation,[5,6] yet others have found no statistically significant difference between quantitative blood loss and estimated blood loss.[7,8] Additionally, quantitative and estimated blood loss have been found to comparably predict the need for blood transfusion.[8]

In November 2018, our Wisconsin-based hospital started using quantitative blood loss for measuring blood loss in a diverse patient population. The primary objective of this quality improvement study was to compare the accuracy of quantitative and estimated blood loss during cesarean delivery to calculated blood loss, a patient-specific tool to measure blood loss that is not in standard use. Secondarily, we aimed to determine the sensitivity and specificity of estimated and quantitative blood loss compared to calculated blood loss for predicting hemorrhage.

METHODS

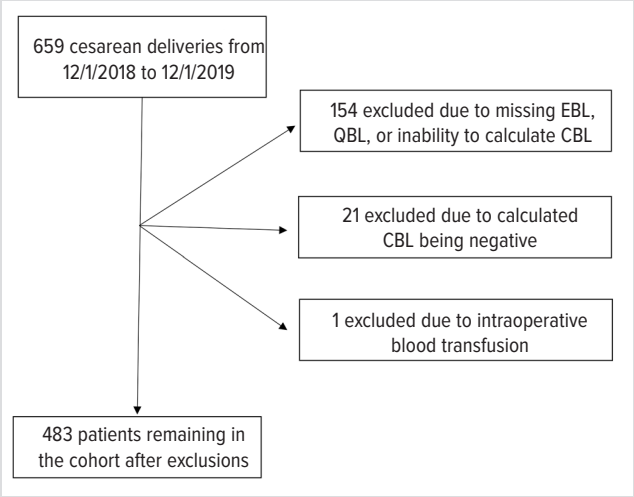
We retrospectively reviewed all pregnant patients who underwent a cesarean delivery at a mid-size, urban academic medical cen-

Table 1. Overall Demographic and Delivery Characteristics and Outcomes (n = 483)

Characteristics and Outcomes	
Age, years, median (IQR)	29.1 (24.5–33.0)
Race/ethnicity, n (%)	
Asian, non-Hispanic	38 (7.9)
Black, non-Hispanic	277 (57.3)
Hispanic	66 (13.7)
Pacific Islander, non-Hispanic	6 (1.2)
White, non-Hispanic	93 (19.3)
Other, non-Hispanic[a]	2 (0.4)
Body mass index, kg/m^2, median (IQR)	34.6 (29.8 – 40.9)
Gestational hypertension, n (%)	184 (38.1)
Multiple gestations this pregnancy, n (%)	22 (4.6)
Administration of uterotonic medications, n (%)	78 (16.1)
Number of uterotonic medications, median (IQR)	1.0 (1.0 – 2.0)
Initiation of massive transfusion, n (%)	1 (0.2)
Transfusion of blood products, n (%)	21 (4.3)
Length of hospital stay, days, median (IQR)	3.4 (2.9 – 4.4)
Post-delivery complications, n (%)	19 (3.9)
Acute kidney injury	3 (15.8)
Chorioamnionitis/endometritis	14 (73.7)
ICU admission for acute respiratory distress syndrome	1 (5.3)
Pulmonary edema	1 (5.3)
Maternal death, n (%)	0 (0.0)
Redosing of prophylactic antibiotics secondary to intraoperative blood loss, n (%)	2 (0.4)
Extended monitoring with higher level nursing care secondary to blood loss, n (%)	24 (5.0)

Abbreviations: IQR, interquartile range; ICU, intensive care unit.
[a]Other race/ethnicity includes 'unknown' and 'mixed race' as defined in our electronic medical record.

Figure 1. Flowchart for Inclusion in Final Cohort



Abbreviations: EBL estimated blood loss; QBL, quantitative blood loss; CBL, calculated blood loss.

ter in Wisconsin from December 1, 2018 to December 1, 2019. The study was determined not human subjects research by our Institutional Review Board.

Patients were included if both quantitative and estimated blood loss values were recorded. Estimated blood loss was obtained from the anesthesia log or the operative note. If estimated blood loss in the operative note did not match the anesthesia log, the study team collected the value documented by the anesthesia team, as their estimate also was based on intraoperative vital sign measurements in addition to real-time communication with the surgery team. If it was not documented in the anesthesia log, the value for estimated blood loss from the operative note was collected. Quantitative blood loss was recorded and collected from nursing flowsheets and was obtained by weighing all blood-soiled lap pads, surgical sponges, and Chux pads and subtracting their dry weight and the volume of any fluid used for irrigation. Additionally, the volume of all suction canisters was included in the calculation. Per institutional practice, only the blood suctioned after delivery of the placenta was included to exclude the volume of amniotic fluid. Hemorrhage was defined as blood loss ≥ 1000 mL.[1] We also documented the number of uterotonics used, if any, in addition to the institutional standard 30 units of oxytocin postdelivery, including additional oxytocin (beyond standard administration), misoprostol, methylergonovine, and/or 15-methyl prostaglandin F2. Postdelivery complications also were documented and defined as infection (chorioamnionitis/endometritis), acute kidney injury, pulmonary edema, acute respiratory distress syndrome, and intensive care unit admission.

To address the primary objective, patients were further excluded from the study if calculated blood loss could not be determined, if the calculation was negative, or if they received an intraoperative blood transfusion, as it would affect accuracy of the calculated blood loss. If a patient received a postoperative blood transfusion after their blood was drawn, they remained in the analysis using the hematocrit obtained prior to transfusion. Admission hemoglobin and hematocrit were used for predelivery values, unless additional hemoglobin and hematocrits were collected prior to delivery, in which case the one drawn closest to the time of delivery was used. Postdelivery hemoglobin and hematocrit were used for postdelivery values and were taken closest to the time of discharge. Use of the hemoglobin and hematocrit closest to time of discharge is considered more reflective of blood loss given the time it takes for the hemoglobin and hematocrit to equilibrate after surgery.[6] Ultimately, to determine calculated blood loss (CBL), the following formula by Stafford et al[4] was used:

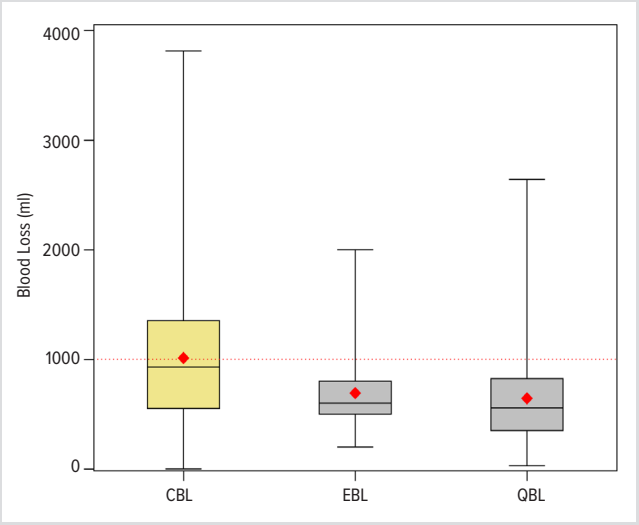
CBL = calculated blood volume x percent of blood volume lost

To determine calculated blood volume (CBV), this formula was used: CBV = 0.75 x ([maternal height (inches) x 50] + [maternal weight (pounds) x 25])

To determine percent of blood volume (%BV) lost, this formula was used: %BV lost = ([predelivery hematocrit – postdelivery hematocrit]/predelivery hematocrit)

Data were collected from the electronic medical record and

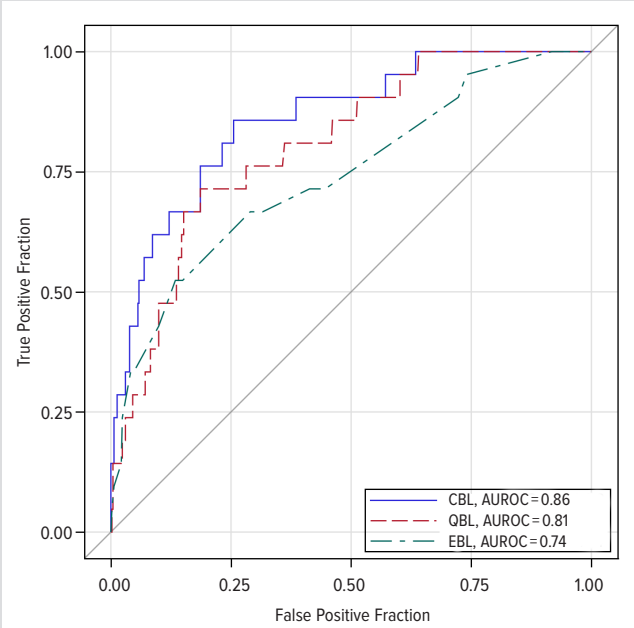
Figure 2. Box-and-Whisker Plots of the Distribution of Blood Loss Values



Abbreviations: EBL estimated blood loss; QBL, quantitative blood loss; CBL, calculated blood loss.

Median is indicated by the solid black line and mean by the red diamond. Dotted red line is set at a blood loss value of 1000 ml where 1000 ml and above indicates a hemorrhage. CBL is color-filled gold as it is considered the gold standard.

Figure 3. Receiver Operating Characteristic Curves of Blood Loss Methods Ability to Predict Blood Transfusion Need



Abbreviations: EBL estimated blood loss; QBL, quantitative blood loss; CBL, calculated blood loss; AUROC, Area Under Receiver Operating Characteristic.

Comparison of EBL, QBL, and CBLs ability to predict need for blood transfusion using estimated AUROC.

recorded in REDCap. Descriptive statistics, including frequency with percentages and median with interquartile range, were computed. Wilcoxon signed-rank test was used to compare quantitative and estimated blood loss to calculated blood loss. Box-and-whisker plots were used to describe the distributions of blood loss values. Sensitivity, specificity, positive predictive value, and negative predictive value of both quantitative and estimated blood loss in detecting postpartum hemorrhage were calculated and compared to calculated blood loss. To predict the need for blood transfusion, logistic regression and receiver operating characteristic (ROC) curves were used, and area under the ROC (AUROC) was estimated for each blood loss method. P values ≤ 0.05 were considered statistically significant. Statistical analyses were carried out using SAS Version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

A total of 659 patients underwent cesarean delivery. Following exclusion criteria, 483 patients were included in the final cohort (Figure 1). Patients predominantly had a singleton gestation (95.4%), identified as Black, non-Hispanic (57.3%), were of median age 29.1 years, and over one-third had gestational hypertension (38.1%; Table 1).

The median values for blood loss (M; interquartile range [IQR]) for estimated blood loss (600.0 mL; IQR 500.0–800.0) and quantitative blood loss (557.0 mL; IQR 350.0–824.0) were significantly lower (P<0.001 for each) than calculated blood loss (929.4 mL; 551.5–1351.5). Overall, calculated blood loss demonstrated a wider distribution of values for blood loss estimates, with a large proportion of values (43.7%, n=211) identified as postpartum hemorrhage (Figure 2). Smaller proportions of the distributions for estimated blood loss (11.4%, n=55) and quantitative blood loss (13.5%, n=65) were identified as postpartum hemorrhage (Figure 2); only 10 additional patients were identified as having a postpartum hemorrhage through use of quantitative blood loss.

When compared to calculated blood loss, estimated blood loss had low sensitivity (19.4%; 95% CI, 14.1–24.8) and high specificity (94.9%; 95% CI, 92.2–97.5). Quantitative blood loss also demonstrated low sensitivity (23.2%; 95% CI, 17.5–28.9) and high specificity (94.1%; 95% CI, 91.3–96.9). The negative predictive values for estimated blood loss (60.3%; 95% CI, 55.6–64.9) and quantitative blood loss (61.2%; 95% CI, 56.6–65.9) were also low. The positive predictive value for estimated blood loss (74.6%; 95% CI, 63.0–86.1) was similar to quantitative blood loss (75.4%; 95% CI, 64.9–85.9).

While quantitative, estimated, and calculated blood loss all predicted the need for blood transfusion (n=21, P<.001), calculated blood loss was most predictive of blood transfusion need (AUROC 0.86; 95% CI, 0.78–0.94), followed by quantitative blood loss (0.81; 95% CI, 0.72–0.89) and estimated blood loss (0.74; 95% CI, 0.62–0.86). There was no significant difference in the predictive ability of need for blood transfusion with calculated blood loss versus quantitative blood loss (difference 0.05; 95% CI -0.04 to 0.14, P=0.265) or quantitative blood loss versus estimated blood loss (0.06; -0.04 to 0.17, P=0.238); however, calculated blood loss versus estimated blood loss differed significantly (0.12; 95% CI, 0.01–0.22, P=0.027), Figure 3.

DISCUSSION

Quantitative blood loss assessment requires additional training of the labor and delivery staff, which can be time consuming and labor intensive. Like Wesley et al and Torres et al,[7,8] our quality improvement study questions the utility of quantitative blood loss compared to estimated blood loss given similar median values for blood loss between methods; further, both were significantly lower than calculated blood loss. Quantitative blood loss was only slightly more sensitive than estimated blood loss in the detection of hemorrhage, and both had similar specificity. Of greatest clinical significance, negative predictive values of both quantitative and estimated blood loss methods were similarly low. Our study demonstrated that for both estimated and quantitative blood loss, nearly 40% of hemorrhages may screen negative, falsely reassuring the medical team. Similarly to Torres et al,[8] our study also demonstrated that quantitative and estimated blood loss comparably predicted the need for blood transfusion. Given the high rate of morbidity and mortality associated with postpartum hemorrhage, a more sensitive method for the assessment of blood loss is needed.

It is important to note that this study used calculated blood loss as the "gold standard" for measuring blood loss; however, there is no gold standard method. For example, in our study patients were excluded if the calculated blood loss was negative, as this is physiologically and intellectually inaccurate. Inaccurate postdelivery hematocrit could be related to fluid shifts as expected postpartum.[9] Additionally, approximately one-third of patients in our study were diagnosed with hypertensive disease of pregnancy, which is known to cause third spacing of fluids due to deceased oncotic pressure and increased vascular permeability.[10] To account for these fluid shifts, the ideal time to measure hematocrit and allow for appropriate equilibration should be further studied for the postpartum period, as significant decreases in hematocrit postdelivery could lead to a wide range of calculated blood loss estimates, which may overestimate blood loss.

While a drop in hematocrit may provide the most accurate assessment of blood loss, it is not always available in real-time at the bedside. Further, hematocrit is not reliable in cases of ongoing blood loss (eg, cesarean birth). Therefore, a feasible and accurate method of measuring blood loss intraoperatively and immediately postoperatively must be established.

This quality improvement study aimed to evaluate a change in blood loss calculation method at a mid-size, urban academic medical center in Wisconsin. A strength of our study was the diverse patient population, including groups that are historically underrepresented in obstetric literature, such as Black and Brown birthing people. Our study was limited by data discrepancies, such as equal estimated and quantitative blood loss values and incomplete documentation of variables of interest within the electronic medical record. Despite these limitations, we were able to evaluate and analyze a fairly large sample to directly compare estimated, quantitative, and calculated blood loss among patients who underwent cesarean delivery. Even so, comparisons between estimated and quantitative blood loss to calculated blood loss are limited, as calculated blood loss accounts for additional blood loss and fluid intake postoperatively, while estimated and quantitative blood loss are used exclusively at the time of delivery.

CONCLUSIONS

This quality improvement study highlights the poor sensitivity of both estimated blood and quantitative blood loss. Given the potentially limited availability of all necessary measuring materials to determine quantitative blood loss, we recommend continued education and training efforts for staff on visual blood loss estimates at the time of delivery in addition to quantitative blood loss. This quality improvement study also calls into question the limitations of calculated blood loss and its use in clinical practice with the calculation of negative calculated blood loss values. Efforts to increase accuracy of blood loss evaluation both during and after cesarean birth are warranted.

Financial Disclosures: None declared.

Funding/Support: None declared.

Previous Presentations: Some of this work was submitted as an abstract for presentation at the 2022 Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists on May 6-8, 2022, in San Diego, California. Some of this work also was presented internally.

REFERENCES

1. Lepine SJ, Geller SE, Pledger M, Lawton B, MacDonald E. Severe maternal morbidity due to obstetric haemorrhage: Potential preventability. *Aust N Z J Obstet Gynaecol.* 2020;60(2):212-217. doi:10.1111/ajo.13040

2. Doctorvaladan SV, Jelks AT, Hsieh EW, Thurer RL, Zakowski MI, Lagrew DC. Accuracy of blood loss measurement during cesarean delivery. *AJP Rep*. 2017;7(2):e93-e100. doi:10.1055/s-0037-1601382

3. Prasertcharoensuk W, Swadpanich U, Lumbiganon P. Accuracy of the blood loss estimation in the third stage of labor. *Int J Gynaecol Obstet*. 2000;71(1):69-70. doi:10.1016/s0020-7292(00)00294-0

4. Stafford I, Dildy GA, Clark SL, Belfort MA. Visually estimated and calculated blood loss in vaginal and cesarean delivery. *Am J Obstet Gynecol.* 2008;199(5):519.e1-7. doi:10.1016/j.ajog.2008.04.049

5. Lertbunnaphong T, Lapthanapat N, Leetheeragul J, Hakularb P, Ownon A. Postpartum blood loss: Visual estimation versus objective quantification with a novel birthing drape. *Singapore Med J.* 2016;57(6):325-328. doi:10.11622/smedj.2016107

6. Ladella S, Nguyen L, O'Byrne H, Cortez C. Quantitative blood loss is a more accurate measure of blood loss compared to estimated blood loss [17N]. *Obstet Gynecol. 2*018; 131(1):156S. doi:10.1097/01.AOG.0000533113.62315.b5

7. Wesley SR, Holmes HJ, Kauffman RP, Gouldy D, Bramnik A. 688 Estimating blood loss: A continuing look. *Am J Obstet Gynecol.* 2021;224(2):S431-S432. doi:10.1016/j.ajog.2020.12.712

8. Torres K, McKenna D, Wiegand S. 882: A comparison of quantified versus estimated blood loss at the time of cesarean delivery. *Am J Obstet Gynecol*. 2020;222(1):S550-S551. doi:10.1016/j.ajog.2019.11.895

9. Chauhan G, Tadi P. Physiology, postpartum changes. Updated November 14, 2022. In: StatPearls [Internet]. StatPearls Publishing; 2024.

10. Natarajan V, Hariharan U, Garg R. Perioperative fluid management in obstetric patients. *Anesthesiol Open J.* 2018;SE(1):S1-S7. doi:10.17140/AOJ-SE-1-101

Lead Exposure Risk and Testing for Pregnant People in Milwaukee

Anne Getzin, MD; Jessica J. F. Kram, MPH; James O. Adefisoye, MS, PhD; Diana Kleber, RN; Lauren Oberbroeckling, DO

ABSTRACT

Background: Despite established lead exposure risks in Milwaukee from leaded water service lines and lead dust exposure with aged housing stock, most pregnant people do not have lead levels tested. We aimed to assess the prevalence of elevated lead levels among pregnant people and assess for differences in maternal and neonatal outcomes by lead detection.

Methods: We conducted a prospective, longitudinal study. English-speaking pregnant people ≥18 years of age receiving prenatal care were consented to receive a point-of-care (POC) lead test from June 2019 through July 2021. POC lead testing was not offered outside of the study. Venous lead labs were ordered to confirm elevated POC results (≥5 mcg/dL).

Results: Overall (n=233), 42.1% had an exposure risk given lead service line to their homes. Nine (3.9%) had an elevated POC lead test; half completed venous lead tests, and none were elevated. Twenty-two (9.4%) had detectable lead (≥3.3 mcg/dL).

Discussion: Venous lead testing should be considered in high-risk areas with standard prenatal labs to facilitate effective lead screening given the study population's risk of lead exposure.

BACKGROUND

Elevated blood lead levels during the prenatal period are associated with adverse neonatal and maternal outcomes. Studies demonstrate that lead exposure during pregnancy affects fetal growth and neurodevelopment,[1,2] as well as gestational hypertension and preterm delivery—even with very low blood lead levels.[3] The Centers for Disease Control and Prevention (CDC) published recommendations in 2010 (reaffirmed by the American College of Obstetricians and Gynecologists in 2018) to screen all pregnant people for risk of lead exposure and to test all with identified risk factors.[4] Risk factors for exposure include lead-contaminated drinking water, household member(s) with an elevated lead level, recent immigration from areas with high ambient lead contamination, and a personal history of previous lead exposure.[4] Risk factors also include housing built before 1978 with renovations or peeling paint, which can lead to lead exposure through dust.[5]

Currently, there is high risk for lead exposure in the city of Milwaukee, Wisconsin, with 74% of homes built before 1960 and an additional 18% built between 1960 and 1979.[6] Additionally, Milwaukee's water system is laden with lead service lines, with efforts to replace 65 000 residential leaded water service lines currently underway.[7] Lead poisoning rates for children in Milwaukee have been and continue to be disproportionately high. In 2016, the rate of elevated blood lead levels (≥5mcg/ dL) in children <6 years old was 10.8% in the city of Milwaukee, compared to a state prevalence of 5.0% and national prevalence of 4.0%.[8] In the most impoverished areas of Milwaukee, the prevalence rate has ranged from 25% to 31%.[9]

Personal history of childhood lead exposure is a risk factor that could contribute to increased prevalence of elevated lead levels during pregnancy in Milwaukee. Lead is deposited in the bones, with 90% of lead burden stored in the bones as adults. During pregnancy, bone lead stores are mobilized into the serum.[4] Studies suggest that serum lead levels may be affected equally by bone stores as by contemporaneous environmental Disease Control and

Author Affiliations: Department of Family Medicine, Aurora University of Wisconsin Medical Group, Advocate Health, Aurora Midtown, Milwaukee, Wisconsin (Getzin); Academic Affairs, Aurora University of Wisconsin Medical Group, Advocate Health, Aurora Sinai Medical Center, Milwaukee, Wisconsin (Kram, Adefisoye); Center for Urban Population Health, Milwaukee, Wisconsin (Kram); Advocate Aurora Research Institute, Milwaukee, Wisconsin (Kleber); Department of Family Medicine, Advocate Health, Aurora St. Luke's Medical Center, Milwaukee, Wisconsin (Oberbroeckling).

Corresponding Author: Anne Getzin, MD, 5818 W Capitol Dr, Milwaukee WI 53216; phone 715.212.2830; email anne.getzin@aah.org; ORCID ID 0009-0007-7482-2727

Prevention (CDC) published recommendations in 2010 (reaffirmed by the American College of Obstetricians and Gynecologists in 2018) to screen all pregnant people for risk of lead exposure and to test all with identified risk factors.[4] Risk factors for exposure include lead-contaminated drinking water, household member(s) with an elevated lead level, recent immigration from areas with high ambient lead contamination, and a personal history of previous lead exposure.[4] Risk factors also include housing built before 1978 with renovations or peeling paint, which can lead to lead exposure through dust.[5]

Currently, there is high risk for lead exposure in the city of Milwaukee, Wisconsin, with 74% of homes built before 1960 and an additional 18% built between 1960 and 1979.[6] Additionally, Milwaukee's water system is laden with lead service lines, with efforts to replace 65 000 residential leaded water service lines currently underway.[7] Lead poisoning rates for children in Milwaukee have been and continue to be disproportionately high. In 2016, the rate of elevated blood lead levels (≥5mcg/ dL) in children <6 years old was 10.8% in the city of Milwaukee, compared to a state prevalence of 5.0% and national prevalence of 4.0%.[8] In the most impoverished areas of Milwaukee, the prevalence rate has ranged from 25% to 31%.[9]

Personal history of childhood lead exposure is a risk factor that could contribute to increased prevalence of elevated lead levels during pregnancy in Milwaukee. Lead is deposited in the bones, with 90% of lead burden stored in the bones as adults. During pregnancy, bone lead stores are mobilized into the serum.[4] Studies suggest that serum lead levels may be affected equally by bone stores as by contemporaneous environmental exposure.[4,10] Given rates of childhood lead poisoning and childhood lead prevalence in Milwaukee, the authors posit that pregnant people raised in high-risk counties in Wisconsin—specifically Milwaukee and Racine counties—may carry a higher risk for elevated bone lead storage.

While childhood rates of elevated lead levels are readily available, data on the prevalence of elevated lead levels in pregnant people are limited. The rate of blood lead level elevation in pregnant people in the National Health and Nutrition Examination Survey (NHANES) was so low that the study could not reliably report prevalence of elevation nationally (0.5% with relative standard errors >50%, total sample n = 732).[11] A recent study examining 40 years of NHANES data (1976-2016) demonstrated dramatic declines of blood lead levels in people of reproductive age, yet identified lead exposure risks continue, and there are increasing reports of subgroups at high risk of lead exposure requiring further study.[12] While the CDC and ACOG recommend to test all those with identified risk factors,[4] adherence to these guidelines may be low within our local health system in

Table 1. Maternal Demographics and Risk Factors at Time of Point-of-Care Lead Test, N = 233

	Total	Lead Detected on POC		*P* value
		Yes (n = 22)	No (n = 211)	
Age (years), Median (IQR)	27.0 (22.0–32.0)	29.0 (26.0–33.0)	26.0 (22.0–32.0)	0.09
Gestational age at time of POC lead test weeks), Median (IQR)[a]	10.5 (8.5–13.2)	10.6 (9.9–17.4)	10.4 (8.3–13.1)	0.02
Race/ethnicity, n (%)				
Black, non-Hispanic	149 (63.9)	12 (54.6)	137 (64.9)	0.33
White, non-Hispanic	55 (23.6)	6 (27.3)	49 (23.2)	0.67
Other[b]	29 (12.4)	4 (18.2)	25 (11.8)	0.39
Area deprivation index at state decile, n (%)				
< 5	33 (14.2)	3 (13.6)	30 (14.2)	1.00
5 – 6	22 (9.4)	2 (9.1)	20 (9.5)	1.00
7 – 8	29 (12.4)	3 (13.6)	26 (12.3)	0.74
9 – 10	144 (61.8)	13 (59.1)	131 (62.1)	0.78
Unknown	5 (2.1)	1 (4.5)	4 (1.9)	0.39
Length of time at current address, n (%)				
< 1 year	100 (42.9)	7 (3.2)	93 (4.2)	0.18
>1 year	131 (56.2)	14 (63.6)	117 (55.5)	0.46
Unknown	2 (0.9)	1 (4.5)	1 (0.5)	0.05
First 6 years of life outside the US, n (%)	10 (4.3)	0 (0.0)	10 (4.7)	0.60
County lived in during first 6 years of life, n (%)				
Milwaukee County	165 (70.8)	14 (63.6)	151 (71.6)	0.44
Racine County	7 (3.0)	0 (0.0)	7 (3.3)	1.00
Neither Milwaukee or Racine counties	58 (24.9)	7 (31.8)	51 (24.2)	0.43
Unknown	3 (1.3)	1 (4.5)	2 (0.9)	0.26
Drinking water, n (%)				
Tap	56 (24.0)	5 (22.7)	51 (24.2)	0.88
Filtered	38 (16.3)	5 (22.7)	33 (15.6)	0.37
Bottled	137 (58.8)	11 (50.0)	126 (59.7)	0.38
Unknown	2 (0.9)	1 (4.5)	1 (0.5)	0.18
Cooking water, n (%)				
Tap	185 (79.4)	15 (68.2)	170 (80.6)	0.17
Filtered	30 (12.9)	5 (22.7)	25 (11.8)	0.18
Bottled	16 (6.9)	1 (4.5)	15 (7.1)	1.00
Unknown	2 (0.9)	1 (4.5)	1 (0.5)	0.18
Anyone with history of elevated lead test in home, n	12	0	12	0.61
Had lead service line to current home, n (%)	98 (42.1)	14 (63.6)	84 (39.8)	0.03

Abbreviations: POC, point-of-care; IQR, interquartile range.

[a]Anembryonic pregnancy with unknown last menstrual period. Yes, lead detected on POC (n = 21).

[b]Other includes Hispanic, Asian, other, multirace, and unknown.

Table 2. Report of Characteristics, Risk Factors, and Outcomes of Pregnant People With an Elevated Point-of-Care Lead Test

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Age (years)	29	27	28	34	36	29	40	34	26
Gestational age at time of POC lead test	9w 6d	Unknown[a]	10w 1d	9w 4d	10w 4d	9w 1d	17w 3d	9w 4d	15w 0d
Race/ethnicity	Black non-Hispanic	Hispanic	Black non-Hispanic	White non-Hispanic	White non-Hispanic	White non-Hispanic	Black non-Hispanic	White non-Hispanic	Black non-Hispanic
Area deprivation index at state decile	9	10	9	7	8	3	10	1	9
POC lead test result	5.7	37.2	6.1	6.3	6.4	7.5	15.4	5.7	9.2
First venous lead test result	–	–	2	–	2	2	–	2	2
Second venous lead test result	–	–	2	–	–	–	–	–	–
Length of time at current address	>1 year	>1 year	3–6 months	>1 year	>1 year	>1 year	3-6 months	>1 year	3–6 months
First 6 years of life outside of the US	No	No	No	No	No	No	No	No	No
County lived in during first 6 years of life	Milwaukee	Milwaukee	Milwaukee	Milwaukee	Not Racine or Milwaukee	Not Racine or Milwaukee	Milwaukee	Not Racine or Milwaukee	Milwaukee
Drinking water	Tap	Bottled	Bottled	Filtered	Filtered	Tap	Filtered	Tap	Tap
Cooking water	Tap	Tap	Filtered	Tap	Filtered	Tap	Filtered	Tap	Tap
Anyone w history of elevated lead test in home	No	No	No	No	–	No	No	No	No
Had lead service line to home	Yes	Yes	No	–	–	No	Yes	–	No
Lost to follow-up	Yes	–	No	No	No	No	Yes	No	Yes
Miscarried	No	Yes	No	No	No	No	–	No	–
Gestational hypertension this pregnancy	No	–	No	No	No	No	–	No	–
Preeclampsia this pregnancy	No	–	Yes	No	No	No	–	No	–
Gestational diabetes this pregnancy	No	–	No	No	No	Yes	–	No	–
Gestational age at time of delivery	–	–	40w 5d	39w 5d	39w 2d	39w 0d	–	39w 2d	–
Birth weight (grams)	–	–	3100	3360	3790	3320	–	3800	–
5-minute Apgar	–	–	9	9	9	9	–	9	–
Neonatal death	–	–	No	No	No	No	–	No	–

Abbreviations: POC, point-of care; NICU, neonatal intensive care unit; w, weeks; d, days.
[a]Anembryonic pregnancy with unknown last menstrual period.

southeastern Wisconsin. From 2014 to 2017, a venous lead test was performed for only 0.12% of pregnancy episodes. Given the paucity of local data, low rates of testing for lead levels during pregnancy, and critically high levels of childhood lead poisoning among the Milwaukee community, our study aimed to assess the prevalence of elevated lead levels among pregnant people in Milwaukee and assess for differences in maternal and neonatal outcomes among those with detectable point-of-care (POC) lead levels.

METHODS

The study was designed as a prospective, longitudinal study in order to assess the prevalence of lead elevation among pregnant people in Milwaukee and to identify differences in risk factors for lead exposure. Additionally, we compared maternal and neonatal outcomes between those with and without elevated lead levels. Our study was approved by our Institutional Review Board and funded departmentally.

Pregnant people ≥18 years of age who voluntarily consented to participate were included if they were English speaking, received prenatal care at 1 of 4 clinics in Milwaukee, and if they had an anticipated delivery in our health care system. Recruitment occurred from June 2019 to July 2021. Pregnant people were recruited and consented during their first prenatal care visit, generally occurring in the first trimester. Following consent, pregnant people completed a POC lead test – a finger stick capillary blood test for lead that is resulted in five minutes – by a medical assistant or study research coordinator. Those with a POC lead test ≥ 5 mcg/dL were considered elevated per CDC guidelines at the time of study onset and were referred for management by their obstetric provider with recommended venous lead lab ordered. The obstetric provider received follow-up recommendations for monitoring the patient's lead levels and resources on best practices for management of elevated lead per CDC guidelines. After the completion of study enrollment, the CDC announced the decision to lower the lab reference value for elevated lead level from 5 mcg/dL to 3.5 mcg/dL in October 2021.[13] In addition to the POC lead test, a brief 8-question questionnaire was administered by the study research coordinator. Additional demographic and pregnancy characteristics were collected from the electronic medical record. Public databases were used to collect information on lead service lines to home and the area deprivation index (state decile 1-10 [low to high]). Data on age of housing stock were difficult to obtain via self-

report (highly mobile population, limited knowledge of construction date) and were deferred in this study. Data were collected and stored in REDCap, a secure electronic data capture application.[14]

Categorical variables were presented as frequency with percentage; continuous variables were presented as median (interquartile) due to non-normality. Chi-square and Fisher exact tests were used to assess associations between lead detection and categorical maternal and neonatal outcomes, while Wilcoxon rank sum test was used for continuous variables. *P* values ≤ 0.05 were considered statistically significant. Statistical analyses were carried out using SAS Version 9.4 (SAS Institute, Cary, North Carolina).

Table 3. Maternal Maternal and Neonatal Outcomes Following Point-of-Care Lead Test, N = 233

	Total	Yes (n = 22)	No (n = 211)	*P* value
Participant status following consent, n (%)				
Delivered	185 (79.4)	17 (77.3)	168 (79.6)	0.78
Miscarried	17 (7.3)	2 (9.1)	15 (7.1)	0.67
Lost to follow-up	31 (13.3)	3 (13.6)	28 (13.3)	1.00
Gestational hypertension this pregnancy, n (%)	23 (12.4)	1 (5.9)	22 (13.1)	0.70
Preeclampsia this pregnancy, n (%)	27 (14.6)	3 (17.6)	24 (14.3)	0.72
Gestational diabetes this pregnancy, n (%)	11 (5.9)	1 (5.9)	10 (6.0)	1.00
Gestational age at time of delivery (weeks), median (IQR)[a]	39.1 (38.0 – 39.9)	39.3 (39.0 – 39.7)	39.0 (37.9 – 39.9)	0.26
Birth weight (grams), median (IQR)[a]	3220 (2890 – 3590)	3320 (3030 – 3670)	3210 (2860 – 3570)	0.30
5-minute APGAR, median (IQR)[b]	9.0 (9.0 – 9.0)	9.0 (9.0 – 9.0)	9.0 (9.0 – 9.0)	0.28
Neonatal intensive care unit admission, n (%)[a]	24 (12.8)	3 (17.6)	21 (12.4)	0.71

Abbreviations: POC, point-of-care; IQR, interquartile range.
[a]Total number of babies delivered, N = 188.
[b]Total number of babies delivered, N=187.

RESULTS

A total of 249 pregnant people were enrolled; 16 were excluded due to POC lead test recall. Overall (n = 233, Table 1), a majority lived in Milwaukee during their first 6 years of life (70.8%), with 2 (<1.0%) identifying a personal history of lead exposure. Nearly half (42.1%, n = 98) had a lead service line to their current home, of which 27.6% used tap water (as opposed to filtered or bottled water) for drinking and 77.6% used tap water for cooking.

POC lead tests were ≥ 5 mcg/dL in 9 (3.9%) pregnant people, but only 5 of the 9 completed additional venous lead tests – none of which had a detectable lead level (Table 2). Overall, 22 (9.4%) pregnant people had lead detectable on POC ≥ 3.3 mcg/dL (POC 3.4 – 4.9 mcg/dL, n = 13; POC ≥ 5 mcg/dL, n = 9). Those with detectable POC lead levels were significantly more likely to have a lead service line to their home (63.6% vs 39.8%; *P* = 0.03). All 17 pregnant people who delivered in our system with detectable POC lead levels had a normal birth weight; 1 delivered preterm. Maternal and neonatal outcomes did not differ between groups (Table 3); there were no neonatal deaths.

DISCUSSION

Our study results highlight concerns for increased risk of lead exposure for pregnant people in Milwaukee through various potential routes. In the context of the lead poisoning crisis that was even worse 20 years ago than today, it is notable that the majority of pregnant people (70.8%) lived in Milwaukee County during their first 6 years of life, when the rates of lead poisoning ranged from 25% to as high as 80%, depending on year and location in the city. While <1.0% of participants self-identified a personal history of lead exposure, these data raise the question if participants could have a personal history of lead exposure and be unaware. Regarding contemporaneous lead exposure, nearly half of the participants had leaded water service lines to their current home address. While not assessed through the study, local city data demonstrate a preponderance of old homes constituting housing stock in Milwaukee. Furthermore, following updated guidance from the CDC identifying lead levels as elevated at and above 3.5 mcg/dl,[13] an additional 13 participants (5.6%) would have indication for venous testing.

Our study is limited by enrollment of English-speaking pregnant people only, which is not necessarily reflective of the diversity of people seen within our hospital. The study is also limited by a prolonged enrollment period due to the onset of the COVID-19 pandemic. Enrollment numbers and further recruitment also were disrupted by a POC lead test recall for lots distributed in December 2020, with no new POC lead tests immediately available following the recall. Pregnant people affected by the POC recall were withdrawn and asked to contact their prenatal provider to discuss their personal risk of an elevated lead level, next steps (which may include repeat venous lead level screening), and any questions they may have. Notably, obtaining indicated venous sample confirmation for elevated lead level on POC testing as indicated posed a challenge, with 4 pregnant people not completing the recommended venous test. While our study is not without limitations, it is strengthened by a fairly large sample size.

Considering the limited literature available on the prevalence of elevated lead levels among pregnant people, the high frequency of risk factors identified in the study population, and challenges to follow-up for venous lead testing for elevated POC, we recommend adding venous lead testing to the routine first trimester prenatal labs. Adding to routine prenatal labs limits addi-

tional finger sticks and provides gold standard lead testing in a community that has been and continues to be adversely affected by the presence of lead exposure. While POC testing allows for immediate office visit results, it may be more cost effective to do venous testing first, as positive POC testing has demonstrated positivity bias[15] and requires confirmatory venous testing with elevated POC results, thus duplicating tests and costs. Currently, there is no cost difference between POC and venous lead testing within our system.

Financial Disclosures: None declared.

Funding/Support: This project was internally funded by the Milwaukee Clinical Faculty Fund.

Previous Presentations: Some of this work was submitted as an abstract for presentation at the 2022 American Public Health Association annual meeting on November 6-9, 2022, in Boston, Massachusetts. Some of this work was also presented internally.

REFERENCES

1. Hong YC, Kulkarni YH, Lim YH, et al. Postnatal growth following prenatal lead exposure and calcium intake. *Pediatrics*. 2014; 134(6):1151-1159. doi:10.1542/peds.2014-1658

2. Liu J, Chen Y, Gao D, Jing J, Hu Q. Prenatal and postnatal lead exposure and cognitive development of infants followed over the first three years of life: a prospective birth study in the Pearl River Delta region, China. *Neurotoxicology.* 2014;44:326-334. doi:10.1016/j.neuro.2014.07.001

3. Perkins M, Wright RO, Amarasiriwardena CJ, Jayawardene I, Rifas-Shiman SL, Oken E. Very low maternal lead level in pregnancy and birth outcomes in an eastern Massachusetts population. *Ann Epidemiol.* 2014;24(12):915-919. doi:10.1016/j.annepidem.2014.09.007

4. Ettinger AS, Wengrovitz AG, eds. *Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women*. Centers for Disease Control and Prevention; November 2010. Accessed October 17, 2024. https://stacks.cdc.gov/view/cdc/147837

5. Childhood lead poisoning prevention: about lead in paint. Centers for Disease Control and Prevention. July 30, 2024. Accessed October 17, 2024. https://www.cdc.gov/lead-prevention/prevention/paint.html

6. City of Milwaukee Department of City Development, Planning Division. 2023 housing affordability report: housing needs and demands. December 2023. Accessed October 17, 2024. https://experience.arcgis.com/experience/c3c8d339565c4ccab821f65433ee132f/page/2_-Housing-Needs%2FDemands/

7. Lead service line replacement program. Milwaukee Water Works. Accessed October 17, 2024. https://city.milwaukee.gov/water/LeadPipes

8. Christensen K, Coons M, Walsh R. *2016 Report on Childhood Lead Poisoning in Wisconsin.* Wisconsin Dept of Health Services. October 2017. Accessed January 6, 2025. https://www.dhs.wisconsin.gov/publications/p01202-16.pdf

9. Environmental Public Health Data Tracker: Childhood Lead Poisoning - Milwaukee - Blood Lead Level ≥ 5ug/dl. Wisconsin Department of Health Services. Accessed January 6, 2025. https://dhsgis.wi.gov/DHS/EPHTracker/#/all/Childhood%20Lead%20Poisoning/leadPoisoningTractIndex/55079/Blood%20lead%20level%20of%20%3E%3D5%C2%B5g%2FdL

10. Miranda ML, Edwards SE, Swamy GK, Paul CJ, Neelon B. Blood lead levels among pregnant women: historical versus contemporaneous exposures. *Int J Environ Res Public Health*. 2010;7(4):1508-1519. doi:10.3390/ijerph7041508

11. Jones L, Parker JD, Mendola P. Blood lead and mercury levels in pregnant women in the United States, 2003-2008. *NCHS Data Brief.* 2010;(52):1-8.

12. Ettinger AS, Egan KB, Homa DM, Brown MJ. Blood lead levels in U.S. women of childbearing age, 1976-2016. *Environ Health Perspect.* 2020;128(1):17012. doi:10.1289/EHP5925

13. Lab advisory: CDC updates blood lead reference value. Centers for Disease Control and Prevention. October 28, 2021. Updated November 8, 2024. Accessed October 17, 2024. https://www.cdc.gov/locs/2021/10-28-2021-lab-advisory-CDC-Updates-Blood-Lead-Reference-Value.html

14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

15. Nakata H, Nakayama SMM, Yabe J, et al. Assessment of LeadCare® II analysis for testing of a wide range of blood lead levels in comparison with ICP-MS analysis. *Chemosphere*. 2021;271:129832. doi:10.1016/j.chemosphere.2021.129832

Gravid Hysterectomy in the Setting of Placenta Increta at 12 Weeks Gestation

Blake Neuburg, MD; Kathryn Dielentheis, MD; Eric Darrah, MD, PhD

ABSTRACT

Introduction: Placenta accreta spectrum is characterized by placental adherence via abnormal trophoblast invasion into uterine myometrium and is associated with significant maternal morbidity and mortality. Given the legal changes to abortion care, discussion of pregnancy termination in the setting of placenta accreta spectrum disorders is worthy of discussion.

Case Presentation: We report the case of a 34-year-old gravida 6 para 2215 who was diagnosed with placenta previa with features consistent with accreta spectrum disease on ultrasound in the late first trimester. Following diagnosis, the patient was counseled on management options and ultimately underwent gravid hysterectomy for definitive treatment in the late first trimester.

Discussion: This case was consistent with placenta accreta spectrum diagnosed in the late first trimester on ultrasound. Following early diagnosis and counseling, definitive management with gravid hysterectomy was undertaken. Pathologic evaluation confirmed placenta increta. Ability to perform gravid hysterectomy was done under the exception to Wisconsin's 1849 ban on termination of pregnancy for necessary termination in the setting of threat to maternal life.

Conclusions: Gestations affected by placenta accreta spectrum result in significant increased risk of maternal morbidity and mortality. Clinicians should be aware of the benefits of early diagnosis and patients counseled on options for definitive management, including termination if desired.

INTRODUCTION

Placenta accreta spectrum (PAS) is a life-threatening condition that is characterized by abnormal placenta adherence and invasion.[1] The prevailing hypothesis for the development of PAS is abnormal trophoblast invasion into the uterine endometrium-myometrial interface.[2] Most commonly, this occurs at the site of an existing uterine scar from prior cesarean section or uterine surgery where the lack of normal decidualization allows for abnormally deep penetration of placental villi into the uterine myometrium. The result is the potential for severe hemorrhage at delivery where estimated average blood loss is reported at 2000-4000 ml, as well as the potential for placental invasion into surrounding pelvic structures beyond the uterus.[3,4] PAS-affected gestations have up to 17-fold higher composite maternal morbidity, measured by hemorrhage, need for embolization, hysterectomy, and intensive care unit admission, whereas mortality rates have been reported up to 7%.[5,6] Unfortunately, the incidence of PAS has increased over the last 4 decades, largely secondary to increasing cesarean delivery rates.[7,8] Pregnancies affected by PAS typically are diagnosed in the second or third trimester. However, increasingly, diagnosis may be made in the late first or early second trimester.[9] The formal recommendation from the American College of Obstetricians and Gynecologists and Society of Maternal Fetal Medicine is that antenatal care for patients diagnosed with PAS is provided at a level III or IV maternal care facility with experience treating PAS.[8]

The authors present the unique case of a multiparous female whose pregnancy was affected by PAS diagnosed in the first trimester. She subsequently underwent gravid hysterectomy in the late first trimester under the condition of threat to maternal life in a state where the provision of abortion care was affected by the 2022 US Supreme Court decision in *Dobbs v Jackson Women's Health Organization*.[10]

CASE PRESENTATION

The patient was a 34-year-old gravida 6 para 2215 Wisconsin

• • •

Author Affiliations: Department of Obstetrics and Gynecology, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Neuburg, Dielentheis); Department of Pathology and Laboratory Medicine, MCW, Milwaukee, Wis (Darrah).

Corresponding Author: Blake Neuburg, MD, Medical College of Wisconsin, Department of Obstetrics and Gynecology, 9200 W Wisconsin Ave, Milwaukee, WI 53226-3522; phone 920.530.6565; email Blake.Neuburg@osumc.edu; ORCID ID 0009-0005-0493-4454

resident with confirmed intrauterine pregnancy who presented initially for abortion care in Illinois. Obstetrical and gynecologic history was significant for 4 term cesarean sections and 1 surgical abortion at approximately 16 weeks. Evaluation in Illinois at approximately 11 weeks gestation revealed concern for placentation overlying the prior cesarean scar and the patient, therefore, deemed not a candidate to proceed with termination in an outpatient setting. Subsequently, she was seen in Wisconsin at 12 weeks 1 day gestation, where ultrasound imaging was consistent with placenta previa and elements consistent with accreta spectrum disease (Figure 1). Attempts to measure myometrial thickness via ultrasound revealed no appreciable tissue between the uterine wall and bladder at the site of prior cesarean sections.

Referral and consultation with maternal fetal medicine and complex family planning were arranged. The patient was offered dilation and curettage with attempt at uterine preservation or gravid hysterectomy. She underwent exploratory laparotomy, significant adhesiolysis, gravid hysterectomy, bilateral salpingectomy, and cystoscopy at 12 weeks and 5 days gestation.

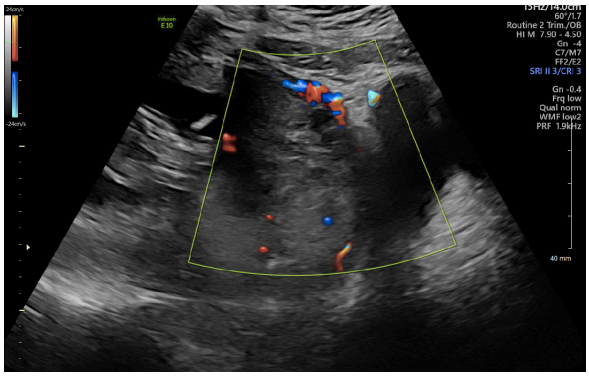
Pathology evaluation revealed placenta previa with increta. Approximately 80% of the placenta was adherent to the myometrium (Figure 2). The depth in placental invasion extended through greater than 90% of the myometrium, to within 0.1 cm from the serosal surface (Figure 3). Gross examination revealed a phenotypically normal appearing 12-week female fetus. The patient had an uncomplicated postoperative course and was discharged postoperative day 3 in good condition. At 2-week follow-up, she was meeting all postoperative milestones.

DISCUSSION

Pregnancies affected by PAS pose significant risks to both the mother and fetus.[4-6] Best clinical outcomes depend on early diagnosis and access to multidisciplinary comprehensive care in timely fashion.[8,9] Clinician awareness of associated risk factors and potential barriers to accessing care are critical for patients as life-threating complications have been reported as early as 7 weeks gestation.[11] Currently, standard surgical technique for delivery and management of PAS in a viable pregnancy is to perform a cesarean hysterectomy with the placenta left in situ following delivery of the fetus to minimize maternal blood loss.[12] The management of previable PAS is dependent on gestational age, disease severity, and patient fertility goals.

This is a unique case of PAS that initially was suspected during early first trimester evaluation for abortion care. The timing of this case occurred after the *Dobbs vs Jackson Women's Health Organization* Supreme Court ruling, where termination is currently unavailable in Wisconsin except in rare circumstances (to save the life of the mother). This case, to our knowledge, is the first reported case of a gravid hysterectomy performed in Wisconsin for the indication of threat to maternal life post *Dobbs* decision and has important precedence implications for women and health care providers that warrant discussion.

Figure 1. Ultrasound at 12 weeks 1 Day Gestation With Placenta Previa With Evidence of Abnormal Placental Adherence to the Anterior Wall



No visible uterine wall in area of prior cesarean section scar with bulging vascular areas (red and blue doppler color) between uterus and bladder.

Figure 2. Gravid Uterus With Placenta Morbidly Adherent to the Myometrium

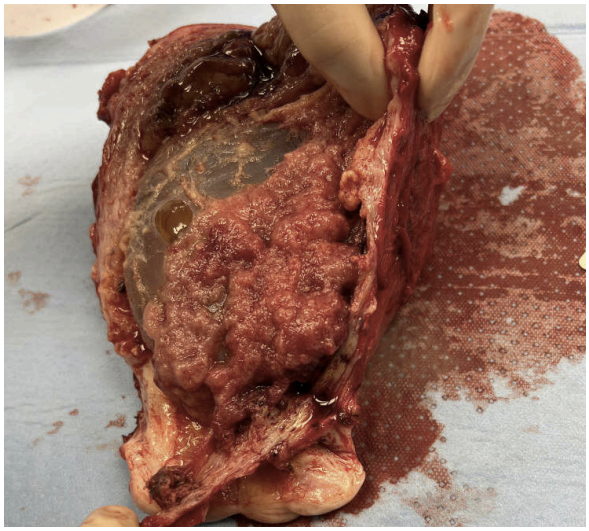
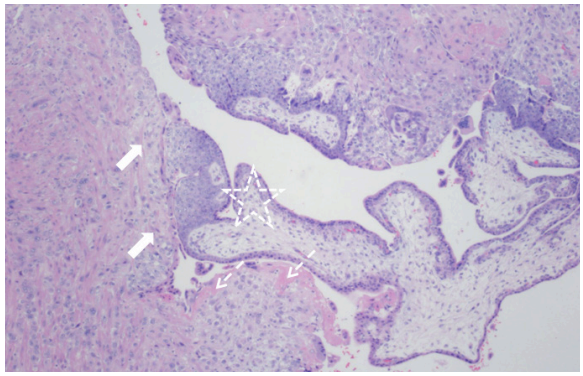


Figure 3. Gravid Uterus and Placenta, Hematoxylin and Rosin Stain, 40x Magnification



Disrupted basal plate architecture. Chorionic villi (star) implanted near myometrial fibers (block arrows) with thin, discontinuous layer of Nitabuch fibrin (dotted arrows) and minimal intervening decidua.

Our patient was confronted with multiple barriers to care that negatively impacted her health. Despite her timely recognition of pregnancy and initial presentation for care, the time from diagnosis to definitive treatment was affected by the need to seek abortion care out of state. There is strong evidence that abortion bans disproportionately affect patients of minority and lower socioeconomic status, potentiating disparities in maternal mortality.[13,14] Insurance coverage across state lines is often minimal, and those with Medicaid often are tasked with paying entirely out-of-pocket.[15-18] In this particular case, the diagnosis of PAS required an inpatient setting for treatment where cost was significantly increased relative to those eligible for outpatient or office-based termination.

Another barrier is the ambiguity of current legislation in Wisconsin surrounding medical indications for abortion.[19] Following the *Dobbs* decision, Wisconsin state criminal abortion statute 940.04 (passed in 1849, one year after Wisconsin statehood) stipulates the penalty for termination of pregnancy in the majority of situations results in a class H felony.[20] A physician may perform abortion "to save the life of the mother;" however, a lack of medical precedent cases or guidance on how imminent the risk of maternal life must be in order justify termination leaves both clinicians and patients exposed.[21] Multiple lawsuits to clarify and challenge the statute are ongoing; however, no immediate clarity exists for Wisconsin clinicians or patients.[22,23] The physicians involved in this patient's care thought this case met criteria for significant risk to maternal life warranting definitive treatment with gravid hysterectomy under Wisconsin statute 940.04.

CONCLUSIONS

Health care providers should be aware of risk factors associated with development of placenta accreta spectrum disease, as early diagnosis and counseling on management options is critical for improved patient outcomes. Some women will elect to carry a pregnancy affected by PAS to viability; however, there is significant maternal and fetal morbidity in doing so. Therefore, women also should be counseled on options including termination. Wisconsin criminal abortion statute 940.04 in its current antiquated form places patients and Wisconsin physicians at risk. Despite this, while awaiting legal clarity, Wisconsin physicians must put patient safety above ambiguity and consider therapeutic abortion whenever and wherever there is a threat to maternal life.

Financial Disclosures: None declared.

Funding/Support: None declared.

REFERENCES

1. Silver RM, Barbour KD. Placenta accreta spectrum: accreta, increta, and percreta. *Obstet Gynecol Clin North Am*. 2015;42(2):381-402. doi:10.1016/J.OGC.2015.01.014

2. Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. *Am J Obstet Gynecol.* 2018;218(1):75-87. doi:10.1016/J.AJOG.2017.05.067

3. Stotler B, Padmanabhan A, Devine P, Wright J, Spitalnik SL, Schwartz J. Transfusion requirements in obstetric patients with placenta accreta. *Transfusion (Paris).* 2011;51(12):2627-2633. doi:10.1111/j.1537-2995.2011.03205.x

4. Hoffman MS, Karlnoski RA, Mangar D, et al. Morbidity associated with nonemergent hysterectomy for placenta accreta. *Am J Obstet Gynecol.* 2010;202(6):628.e1-628.e5. doi:10.1016/J.AJOG.2010.03.021

5. Fonseca A, Ayres de Campos D. Maternal morbidity and mortality due to placenta accreta spectrum disorders. *Best Pract Res Clin Obstet Gynaecol.* 2021;72:84-91. doi:10.1016/J.BPOBGYN.2020.07.011

6. Baldwin HJ, Patterson JA, Nippita TA, et al. Maternal and neonatal outcomes following abnormally invasive placenta: a population-based record linkage study. *Acta Obstet Gynecol Scand*. 2017;96(11):1373-1381. doi:https://doi.org/10.1111/aogs.13201

7. Silver RM, Branch DW. Placenta accreta spectrum. *N Engl J Med*. 2018;378(16):1529-1536. doi:10.1056/NEJMcp1709324

8. Society of Gynecologic Oncology; American College of Obstetricians and Gynecologists and the Society for Maternal–Fetal Medicine, Cahill AG, et al. Placenta Accreta Spectrum. *Am J Obstet Gynecol.* 2018;219(6):B2-B16. doi:10.1016/j.ajog.2018.09.042

9. Doulaveris G, Ryken K, Papathomas D, et al. Early prediction of placenta accreta spectrum in women with prior cesarean delivery using transvaginal ultrasound at 11 to 14 weeks. *Am J Obstet Gynecol MFM*. 2020;2(4):100183. doi:10.1016/j.ajogmf.2020.100183

10. *Dobbs v Jackson Women's Health Organization*, 597 US 215 (2022).

11. De Gennaro E, Orsaria M, Driul L. Placenta accreta in the first trimester: a case report. *Clin Case Rep*. 2021;9(9):e04615. doi:10.1002/ccr3.4615

12. Turan OM, Shannon A, Asoglu MR, Goetzinger KR. A novel approach to reduce blood loss in patients with placenta accreta spectrum disorder. *J Matern Fetal Neonatal Med.* 2021;34(13):2061-2070. doi:10.1080/14767058.2019.1656194

13. Goyal V, Brooks IHML, Powers DA. Differences in abortion rates by race–ethnicity after implementation of a restrictive Texas law. *Contraception*. 2020;102(2):109-114. doi:10.1016/j.contraception.2020.04.008

14. Dehlendorf C, Harris LH, Weitz TA. Disparities in abortion rates: a public health approach. *Am J Public Health*. 2013;103(10):1772-1779. doi:10.2105/AJPH.2013.301339

15. Zuniga C, Bommaraju A, Hasselbacher L, Stulberg D, Thompson TA. Provider and community stakeholder perspectives of expanding Medicaid coverage of abortion in Illinois. *BMC Health Serv Res.* 2022;22(1):413. doi:10.1186/s12913-022-07761-5

16. McNamara B, Joudeh L, Corbetta-Rastelli C, Orlando M, Kerns JL. Traveling to California from out of state to receive abortion services at a hospital-based clinic: A qualitative study of people's experiences. *Sex Reprod Healthc*. 2022;34:100784. doi:10.1016/j.srhc.2022.100784

17. Smith MH, Muzyczka Z, Chakraborty P, et al. Abortion travel within the United States: An observational study of cross-state movement to obtain abortion care in 2017. *Lancet Reg Health Am.* 2022;10:100214. doi:10.1016/j.lana.2022.100214

18. Jones RK, Upadhyay UD, Weitz TA. At what cost? Payment for abortion care by U.S. women. *Womens Health Issues.* 2013;23(3):e173-e178. doi:10.1016/j.whi.2013.03.001

19. Winter J. The Dobbs decision has unleashed legal chaos for doctors and patients. *New Yorker.* July 2, 2022. April 5, 2023. https://www.newyorker.com/news/news-desk/the-dobbs-decision-has-unleashed-legal-chaos-for-doctors-and-patients

20. Wis. Stat. § 940.04.

21. Kremer R. Evers offers clemency for doctors prosecuted for performing abortions in Wisconsin. *Wisconsin Public Radio*. June 25, 2022. Accessed Jan 14, 2023. https://www.wpr.org/justice/evers-offers-clemency-doctors-prosecuted-performing-abortions-wisconsin

22. Gov. Evers, AG Kaul announce direct legal challenge to Wisconsin's 1800s-era criminal abortion ban. News Release. Wisconsin Department of Justice. June 28, 2022. Accessed April 14, 2023. https://www.doj.state.wi.us/news-releases/gov-evers-ag-kaul-announce-direct-legal-challenge-wisconsin%E2%80%99s-1800s-era-criminal

23. McGraw K, Henning A, McCarthy S, Otis A. Developments in constitutional law: abortion. Issue Brief (Wis Legis Counc). July 7, 2022. Accessed April 14, 2023. https://docs.legis.wisconsin.gov/misc/lc/issue_briefs/2022/constitutional_law/ib_abortion_km_ah_sm_ao_2022_07_07

Prophylactic or Poison: The Folic Acid Debate

Cara J. Westmark, PhD

Deborah Blum's 2018 book, *The Poison Squad: One Chemist's Single-Minded Crusade for Food Safety at the Turn of the Twentieth Century,* was the University of Wisconsin-Madison's Go Big Read selection for the 2019-2020 academic year. In the book, Professor Blum describes the state of food adulteration in the United States at the turn of the 20th century, when milk and meat were routinely preserved with formaldehyde, beer and wine preserved with salicylic acid, canned vegetables made greener with copper sulfate, and borax added to rancid butter.[1]

Blum concomitantly tells the story of Harvey Wiley, MD, who was appointed Chief Chemist of the Bureau of Chemistry in the Department of Agriculture in 1883, which later became the Food and Drug Administration (FDA). Dr Wiley conducted the hygienic table trials – better known as the Poison Squad studies – which led to passage of the Pure Food and Drug Act in 1906. He devoted his career to raising public awareness regarding food adulteration, developing standards for food processing, and campaigning for the Pure Food and Drug Act. He vigorously fought the rampant use of potentially harmful food additives, and he promoted accurate labelling of food. While his hygienic table trials tested the effects of food additives on young healthy males, he was most concerned regarding the health effects of food additives on the most vulnerable in the population and the potentially cumulative effects of consuming low doses of food additives.

• • •

Author Affiliations: Department of Neurology, Molecular Environmental Toxicology Center, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Westmark).

Corresponding Author: Cara J. Westmark, Department of Neurology, Molecular Environmental Toxicology Center, Medical Sciences Center, Room 3619, 1300 University Ave, Madison, WI 53706; phone 608.262.9730; email westmark@wisc.edu; ORCID ID 0000-0003-3919-3279

What would Dr Wiley think about national food fortification policies – particularly folic acid – a century after the Pure Food and Drug Act? This commentary describes the difference between folate and folic acid, the level of evidence regarding the efficacy of mandatory fortification of cereal grains with folic acid, and possible repercussions of fortification – particularly in vulnerable populations related to maternal and child health.

Folate (vitamin B9) is a water-soluble vitamin found in leafy green vegetables, citrus fruits and beans. It is important for nucleotide and methionine biosynthesis, while deficiency is implicated in birth defects. The term folate refers to many related compounds, including folic acid, dihydrofolate (DHF), tetrahydrofolate (THF), 5-methyltetrahydrofolate (5-MTHF), and 5,10-methylenetetrahydrofolate (5,10-MTHF). The principal naturally occurring folates are in the THF form and polyglutamated. The synthetic folic acid used to fortify foods and found in most supplements is the fully oxidized monoglutamate form. MTHF reductase (MTHFR) is the final enzyme in a multistep pathway that converts folate and folic acid to the active metabolite 5-MTHF – the form that is transported across the intestinal mucosa – into cells and across the blood brain barrier where it functions as a coenzyme or cosubstrate in single-carbon transfers for the synthesis of nucleic acids and metabolism of amino acids. An example is the conversion of homocysteine to methionine in the synthesis of S-adenyl-methionine. When vitamin B12 is deficient, the conversion of homocysteine to methionine is inhibited, and folate is trapped as 5-MTHF, which cannot serve as a substrate for thymidine synthesis.

> While folic acid is water soluble and removed from the body through the urinary tract, high circulating levels of unmetabolized folic acid can accumulate in the blood, and vulnerable populations may be adversely affected by exceeding the tolerable upper intake limit.

Many nervous system disorders are associated with folate deficiency, including neural

tube defects during pregnancy, seizures and epilepsy, and neurodegeneration/cognitive decline. In 1996, the United States mandated national fortification of cereal grains with 140 µg folic acid per 100 g enriched product to prevent neural tube defects. Globally, countries are split on the decision to fortify cereal grains with folic acid. There are ethical issues regarding the risks to the larger portion of the population not receiving benefit.[2] In the United States, it was estimated that fortification would reduce neural tube defects by 50%. The prevalence of neural tube defects during the prefortification period of 1995-1996 averaged 7.3 per 10 000 for the White/non-Hispanic population in the Centers for Disease Control and Prevention National Center on Birth Defects and Developmental Disabilities study.[3] Another predominantly White/non-Hispanic population of 4783 subjects in the National Health and Nutrition Examination Study during 2007-2012 also exhibited a neural tube defect prevalence of 7.3 per 10 000 live births (range 5.5-9.4 per 10 000 live births).[4] While various studies report decreased postfortification prevalence of neural tube defects, the equivalent prevalence in these 2 studies spanning prefortification and postfortification periods argue against population level efficacy.

Major problems in assessing efficacy of national fortification policies include lack of prospective monitoring and absence of a nonfortification comparison group during the same time period. In 2020, neural tube defect risk at the population level was assessed in an article entitled, "Folic Acid Fortification and Neural Tube Defect Risk: Analysis of the Food Fortification Initiative Databset."[5] One would expect if national fortification was effective, then there should be decreased neural tube defects in response to fortification at the population level when comparing countries that fortify with countries that do not. This analysis demonstrates an equivalent average as well as range of high and low values for neural tube defects per 10 000 births in countries with and without fortification. Linear regression analysis indicates a very weak correlation between the prevalence of neural tube defects and the level of folic acid consumed from fortification.[6] Importantly, decreased prevalence of neural tube defects correlates strongly with better socioeconomic status,[5] which has been confirmed in another study.[7] A Cochrane systematic review found "very low certainty" regarding the efficacy of folic acid fortification in reducing neural tube defects.[8] The health benefits of vitamin B9 (folate) are well documented; however, there are numerous gaps in our understanding of the biology, physiology, and health effects of folate and folic acid.

The past century has witnessed tremendous advances with respect to food storage and safety. While there are subpopulations that experience food insecurity in the United States, the majority of the population is in a state of overconsumption versus underconsumption of food. Contrary to folic acid supplements, dosage cannot be controlled with food fortification.[9] Fortification of cereal grains with folic acid has increased the average intake double the projected level.[10] While folic acid is water soluble and removed from the body through the urinary tract, high circulating levels of unmetabolized folic acid can accumulate in the blood, and vulnerable populations may be adversely affected by exceeding the tolerable upper intake limit (UL). In regard to maternal and child health, the Maternal-Infant Research on Environmental Chemicals (MIREC) Pregnancy Cohort Study found that 25% of participants consumed more than the UL (>1000 µg/d) of folic acid.[11] Black children in the Boston Birth Cohort had a 10 times greater risk for autism spectrum disorder when they were in the highest versus the lowest quartile for unmetabolized folic acid in the umbilical cord.[12] Individuals with certain genetic polymorphisms that affect folic acid metabolism may have altered folate availability; for example, variants of the *MTHFR* gene affect about 40% of people worldwide and alter the conversion of folic acid to 5-MTHF. There are potential drug interactions between folic acid and numerous medications, such as proton pump inhibitors used to treat gastroesophageal reflux disease, anticonvulsants such as phenobarbital, the antibiotic tetracycline, and the cancer drug methotrexate.

Dr Wiley would concur with Paracelsus, 1538, who said, "All things are poison, and nothing is without poison; the dosage alone makes it so a thing is not a poison." Despite 26 years of fortification, a large portion of the target populations is deficient in folic acid, while a large segment is at risk for adverse health events in response to excess consumption. Could mandatory national fortification policies and overconsumption of folic acid be contributing to miscarriages, autism, Alzheimer's disease, and other health conditions? Why is neural tube defect prevalence still high in the United States if fortification policies are working? Why is folate insufficiency in women of reproductive age greater than 20%?[13] What is the best way to balance food insecurity and over consumption with public policy on fortification? Education and income are important predictors of the correct timing of supplement use in pregnancy.[14] A very low percentage of women receive nutrition information from their gynecologist prior to pregnancy.[14] The health of society would be better served if public health policy was targeted at prenatal care in women of reproductive age, for example, increased access to healthy foods and nutrition information as well as increased nutrition education in medical school curriculum. Other solutions include routine blood tests for folate levels; genetic screening for MTHFR variants; phone apps to track folic acid intake; avoidance of processed foods; and promotion of organic diets rich in leafy green vegetables, legumes, eggs, citrus fruits and beef liver.

Overall, the United States has not witnessed the projected 50% reduction in neural tube defects in response to national supplementation of cereal grains with folic acid, and current fortification levels present health concerns for large subgroups of the general population. The public health significance of fortification of cereal grains with folic acid is significant.[15] The father of the FDA in all likelihood would be opposed to national fortification with folic acid based on the lack of population-level efficacy data and the potential for harm to subpopulations. No doubt Dr Wiley's ghost haunts the halls of the FDA flabbergasted as to why at the turn of the 21st century a personalized medicine approach has not been implemented in regard to nutrient supplementation that targets women of reproductive age versus the currently employed national fortification policy with potential for harm to a large portion of the population.

Funding/Support: None declared.

Financial Disclosures: None declared.

continued on page 501

Insights Into Perinatal Mood and Anxiety Disorders: Addressing Treatment Gaps, Risk Factors, and Health Outcomes

Aneesh Kumar Sangtiani, MBBS; Manahil Mubeen, MBBS; Ayesha Irfan, MBBS

The transition to motherhood is a profound and complex experience, and when complicated by perinatal mood and anxiety disorders, it can lead to severe consequences for both the mother and her child, warranting an urgent need for increased awareness and comprehensive care strategies.

Perinatal mood and anxiety disorder (PMAD) is a term frequently used to describe mental health conditions that occur during pregnancy, following the birth of a baby, during adoption, or after experiencing the loss of a pregnancy or infant. These conditions include perinatal depression, anxiety disorders, obsessive-compulsive disorder, posttraumatic stress disorder, and postpartum psychosis.

PMADs are the most frequently occurring complications during pregnancy and the most frequently undiagnosed.[1] A systematic review of prevalent anxiety disorders during the perinatal period found that 20.7% of women (95% CI 16.7–25.4) experienced 1 or more anxiety disorders, with a slightly higher prevalence during pregnancy compared to the postpartum period (3.1%).[2] Significant evidence shows that the negative effects of PMADs are distributed unevenly, with Black women facing considerably higher rates of adverse outcomes than White women.[3]

Risk factors for PMADs are multifaceted and are classified into 5 domains: psychological, obstetric, biological, social, and lifestyle. Psychological factors include a history of depression, negative attitudes towards pregnancy, and past sexual abuse. Obstetric risk factors involve complications during delivery, such as emergency cesarean deliveries and when a woman's hopes or expectations about childbirth and motherhood don't reflect reality. Biological factors include young age, significant drops in estrogen and progesterone levels after childbirth, and low serotonin levels. Social factors involve inadequate support and domestic violence. Lifestyle factors include dietary habits, sleep patterns, and physical activity, with deficiencies in vitamins and minerals also influencing risk.[4]

Despite the prevalence of manifold risk factors, PMADs such as antenatal depression and postpartum depression are severely under diagnosed and inadequately treated. Studies show that these disorders go undetected in 50% to 70% cases, while approximately 85% of patients experiencing these conditions receive no treatment at all. Furthermore, 91% to 93% are inadequately treated, and 95% to 97% continue to suffer without remission. One study reports that only 8.6% of women with depression during pregnancy and 6.6% of women with postpartum depression receive adequate treatment,[5] and Black women are more frequently underdiagnosed or untreated for PMADs than White women.[3] This is extremely concerning as untreated PMADs could have disastrous effects on both maternal and infant health.

> By understanding the risk factors, recognizing the far-reaching effects on health and family dynamics, and addressing the disparities in treatment, we can create a supportive environment for all mothers.

Maternal mood and anxiety disorders are linked to a higher risk of preeclampsia and put the mother at long-term health risks for conditions such as hypertension and diabetes, increased risk of cardiovascular disease, maternal gestational weight retention, and overall morbidity/mortality.[5,6] Untreated antenatal depression has been observed to be a significant risk factor for developing postpartum depression—counted as the greatest risk factor for maternal suicide and infanticide.[5]

Untreated anxiety and depression during pregnancy also has been identified as a risk factor for increased labor inductions and cesarean delivery, leading to adverse health

Author Affiliations: Department of Medicine, Dow University of Heath Sciences, Karachi, Pakistan (Sangtiani, Mubeen, Irfan).

Corresponding Author: Ayesha Irfan, Dow University of Health Sciences, Baba-E-Urdu Rd, Karachi 74200, Pakistan; phone +923062873031; email belairfan4@gmail.com; ORCID ID 0009-0003-0546-7662

outcomes. It is associated with increased risk of low Apgar scores, neonatal hypoxia,[7] likelihood of premature delivery, and a reduction in breastfeeding initiation. Furthermore, women exhibiting depressive symptoms in the early postpartum period may face increased risks of negative infant-feeding outcomes, such as shorter breastfeeding duration, more breastfeeding difficulties, and lower levels of breastfeeding self-efficacy. Emerging evidence also indicates that depressed women might be less likely to breastfeed exclusively,[8,9] which can lead to poorer health outcomes for both the mother and the infant, including weakened immune function and increased risk of infections in the baby and delayed postpartum recovery for the mother.

Untreated PMADs are also linked to toxic stress in newborns. This severe stress response results in persistently elevated cortisol levels, leading to development of unhealthy lifestyles, socioeconomic inequalities like school failure and financial hardship, and result in poor health outcomes.[10] Per reports, PPD can lead to child abuse, neglect, discontinuation of breastfeeding, and family dysfunction, all harming early brain development. Families of individuals who experienced major depression before thirty are 3 to 5 times more likely to experience major depression themselves, suggesting a genetic component. Maternal PPD impairs mother-child bonding and attachment, vital for infant development. Infants in such neglectful settings due to maternal depression show adverse brain changes, impaired social interaction, and developmental delays, particularly attachment problems, which become less responsive to intervention over time. However, treating maternal depression reduces psychiatric symptoms and improves child functioning, highlighting the importance of addressing PMADS.[11]

Treating PMADs is of utmost importance for preventing any harm to women's mental health and physical well-being and for the growth and development of the infant. It is crucial for women suffering from these disorders to get screened and assessed by a skilled perinatal mental health specialist. This includes comprehensive planning in coordination with the obstetrics team, ideally prior to conception, and continues throughout the perinatal period.[12] First-line therapy for women suffering from mild to moderate depression are psychological and behavioral therapies.[12] Extensive research supports effectiveness of various psychological interventions, such as interpersonal therapy (IPT),[13] partner-assisted IPT,[14] cognitive behavioral therapy,[14] and psychoeducation.[15] Pharmacotherapy is also regarded as a suitable and effective therapeutic choice for women suffering from intense symptoms of depression and anxiety.[13]

Women with PMADs face many challenges in accessing health care. System-level barriers include unclear care pathways, poor communication between facilities, lack of protocols, gaps in care, limited educational resources, and bureaucratic hurdles. On the provider side, issues like inadequate training, time constraints, and confusion about roles often hinder effective diagnosis and treatment.

In conclusion, PMADs represent significant yet often overlooked challenges affecting mothers, infants, and families. By understanding the risk factors, recognizing the far-reaching effects on health and family dynamics, and addressing the disparities in treatment, we can create a supportive environment for all mothers. It is compulsory to invest in under-integrated mental health care, inclusive support structures, and racial equity-targeted interventions. Let us work together to ensure that all mothers have the opportunity to thrive during this crucial period of their life.

Funding/Support: None declared.
Financial Disclosures: None declared.

REFERENCES

1. Taiwo TK, Goode K, Niles PM, Stoll K, Malhotra N, Vedam S. Perinatal mood and anxiety disorder and reproductive justice: examining unmet needs for mental health and social services in a national cohort. *Health Equity.* 2024;8(1):3-13. doi:10.1089/heq.2022.0207

2. Fawcett EJ, Fairbrother N, Cox ML, White IR, Fawcett JM. The Prevalence of anxiety disorders during pregnancy and the postpartum period: a multivariate Bayesian meta-analysis. *J Clin Psychiatry.* 2019;80(4):18r12527. doi:10.4088/JCP.18r12527

3. Carrington CH. Clinical depression in African American women: diagnoses, treatment, and research. *J Clin Psychol.* 2006;62(7):779-791. doi:10.1002/jclp.20289

4. Ghaedrahmati M, Kazemi A, Kheirabadi G, Ebrahimi A, Bahrami M. Postpartum depression risk factors: a narrative review. *J Educ Health Promot*. 2017;6:60. doi:10.4103/jehp.jehp_9_16

5. Cox EQ, Sowa NA, Meltzer-Brody SE, Gaynes BN. The perinatal depression treatment cascade: baby steps toward improving outcomes. *J Clin Psychiatry.* 2016;77(9):1189-1200. doi:10.4088/JCP.15r10174

6. Qiu C, Williams MA, Calderon-Margalit R, Cripe SM, Sorensen TK. Preeclampsia risk in relation to maternal mood and anxiety disorders diagnosed before or during early pregnancy. *Am J Hypertens*. 2009;22(4):397-402. doi:10.1038/ajh.2008.366

7. Ogunyemi D, Jovanovski A, Liu J, et al. The contribution of untreated and treated anxiety and depression to prenatal, intrapartum, and neonatal outcomes. *AJP Rep*. 2018;8(3):e146-e157. doi:10.1055/s-0038-1661379

8. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. *J Clin Psychiatry*. 2013;74(4):e321-e341. doi:10.4088/JCP.12r07968

9. Dennis CL, McQueen K. The relationship between infant-feeding outcomes and postpartum depression: a qualitative systematic review. *Pediatrics*. 2009;123(4):e736-e751. doi:10.1542/peds.2008-1629

10. Garner AS, Shonkoff JP; Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. Early childhood adversity, toxic stress, and the role of the pediatrician: translating developmental science into lifelong health. *Pediatrics*. 2012;129(1):e224-e231. doi:10.1542/peds.2011-2662

11. Earls MF; Committee on Psychosocial Aspects of Child and Family Health AAP. Incorporating recognition and management of perinatal and postpartum depression into pediatric practice. *Pediatrics*. 2010;126(5):1032-1039. doi:10.1542/peds.2010-2348

12. Belbasis L, Bellou V, Evangelou E, Ioannidis JP, Tzoulaki I. Environmental risk factors and multiple sclerosis: an umbrella review of systematic reviews and meta-analyses. *Lancet Neurol.* 2015;14(3):263-273. doi:10.1016/S1474-4422(14)70267-4

13. Brandon AR, Ceccotti N, Hynan LS, Shivakumar G, Johnson N, Jarrett RB. Proof of concept: Partner-Assisted Interpersonal Psychotherapy for perinatal depression. *Arch Womens Ment Health*. 2012;15(6):469-480. doi:10.1007/s00737-012-0311-1

14. Chabrol H, Teissedre F, Saint-Jean M, Teisseyre N, Rogé B, Mullet E. Prevention and treatment of postpartum depression: a controlled randomized study on women at risk. *Psychol Med.* 2002;32(6):1039-1047. doi:10.1017/s0033291702006062

15. Kozinszky Z, Dudas RB, Devosa I, et al. Can a brief antepartum preventive group intervention help reduce postpartum depressive symptomatology? *Psychother Psychosom*. 2012;81(2):98-107. doi:10.1159/000330035

The Emptiness of Fetal Death – A Resident Physician's Struggle to Cope With Loss and Disappointment in Modern Medicine

Micaela Stevenson Wyszewianski, MD

I remember feeling like I had finally caught a break when "Ella," who was 39 weeks pregnant with her second baby, and her husband "Tom" came onto the labor and delivery unit. I thought I could finally take a nap, after having had multiple vaginal deliveries throughout the day and rounding on over 15 patients. I was alone on labor and delivery as the rest of my team was scattered throughout the hospital, but I felt fine as I perceived this was a normal laboring patient who I could deliver with ease.

When Ella's nurse, "Anne," called out for help, I walked in with an army of nurses. Perplexed by the number of people, she told us she only needed help with IV placement. I returned to our workroom, assured I would be called later. One of my favorite nurses looked up at me and said, "I heard something about decreased fetal movement."

I walked back to the room casually; decreased fetal movement was almost never a big deal. It usually resolved spontaneously before I made it to the room. But Anne told me she couldn't find fetal tones. I remained unconcerned but confused. A nurse grabbed an ultrasound machine, and I looked all over Ella's abdomen. I saw no fetal heart tones, but I remained unconvinced. I must just be bad at this. Why would this otherwise healthy baby at 39 weeks not have heart tones?

I broke Ella's membranes and put on a fetal scalp electrode. Thick meconium poured out, and I became more concerned. Her cervix was 9 cm dilated, and fetal heart tones were absent. I scanned Ella's abdomen again. I still saw no heartbeat. I called everyone I could think of and took Ella to the operating room.

As the chaos of preparing for an emergency cesarean delivery ensued, my attending physician whispered what I knew I had seen but was too shocked to believe: the baby had passed.

My attending physician met us in the operating room (OR) and scanned Ella's abdomen. As the chaos of preparing for an emergency cesarean delivery ensued, my attending physician whispered what I knew I had seen but was too shocked to believe: the baby had passed. We slowed our behavior. We stopped counting instruments, and we dimmed the lights. There was no need for sterile gowns. My attending physician told Ella that her baby had died. As I fought tears, Ella's husband Tom came to the OR, sobbing uncontrollably, screaming that his wife did not deserve this.

As Ella laid there, completely dilated and ready to push, I sat between her legs and silently begged God to help me deliver a live baby. I still wonder sometimes if I had been bold enough to open my mouth and pray aloud if I would have delivered a living baby. But instead, when the baby delivered, she was pink, simply appearing asleep, though her umbilical cord was pulseless. In standard, methodical fashion, I assessed Ella's vagina and perineum. I repaired a small vaginal laceration. I assessed bleeding. I grieved. I hoped. I stood there, in a stupor, watching my hands work – hoping every moment I would hear infant cries start. I hoped I would tell everyone about a miracle.

When we finished, my scrubs were soaked in thick meconium, my hair barely covered by a scrub cap. I stood, haunted by the emptiness in Ella's eyes as she held her baby, her husband sobbing loudly.

As soon as my attending and I were alone, she hugged me. I crumbled into her side, trying desperately to make sense of what had happened. She and I looked through the placenta, searching for any sign of abnormality. We stood there, both speechless, staring at a normal placenta and remembering the perfect-looking baby we had delivered.

continued on page 501

• • •

Author Affiliations: Department of Obstetrics and Gynecology, Medical College of Wisconsin, Milwaukee, Wisconsin (Stevenson).

Corresponding Author: Micaela Stevenson Wyszewianski, MD, Medical College of Wisconsin, Milwaukee, WI; email Micaelastevenson1@gmail.com.

Development of a Doctor: A Medical Student's Year Training in a Fetal Anomalies Clinic

Amanda Jentsch, BA

My preceptor began every appointment by asking expecting parents the same question: "What do you know about your baby's condition?" I listened carefully as families explained their understanding of the diagnosis, and I silently asked myself the same question. What did I know? I was two months into medical school, assigned to a fetal anomalies clinic to learn the basics of being a doctor, and every diagnosis was unfamiliar.

One of the very first skills I learned was how to take a history of present illness. My preceptor sent me into an exam room to ask the patient and her partner that key question, "What do you know about your baby's condition?" The patient had been referred to the clinic with imaging suggesting that her baby had echogenic kidneys. I had no idea what was normal for fetal kidneys, nor what "echogenic" meant. I walked into the room, nearly fell off the chair when I sat down, and opened my notebook with shaking hands. I asked the question, unsure of what they would say, or what I could offer in response.

The patient answered – a single sentence. A pause hung in the air. I was out of questions. The pair looked at me expectantly.

• • •

Author Affiliations: Medical College of Wisconsin, Milwaukee, Wisconsin (Jentsch).

Corresponding Author: Amanda Jentsch, Medical College of Wisconsin, 8701 W Watertown Plank Rd, Milwaukee, WI; email ajentsch@mcw.edu; ORCID ID 0009-0009-6807-275X

"Okay! Thank you," I said to break the silence. I winced at my overly perky tone. As I guided them to another room to meet with a specialist, the patient's partner asked, "So how long have you been doing this?" My cheeks burned with mortification.

January brought my sixth month of school and our cardiovascular system class. Most referrals to the clinic were for cardiac anomalies, with details about ventricles and outlet tracts I never quite grasped until the day after I attended a cardiac development lecture. Looking at the clinic whiteboard felt like I'd unlocked a new level in a video game. The words on the board had meanings that I knew! A sonographer allowed me to shadow an anatomy scan, and I was thrilled to be able to follow the blood flow through the heart. The assignment that week was to write a full visit note. I chose a patient whose baby was diagnosed with hypoplastic left heart syndrome and copied down imaging results to include, proudly noting the structures that I now recognized both in name and purpose.

Much of my learning came from observation. There was no physical exam for fetal anomalies, and imaging interpretation was far beyond my capabilities as a student. My history questions were usually limited to fetal movement, vaginal bleeding, and cramping – all aspects of an appointment that took mere minutes. Despite my new knowledge, I was not capable of contributing to the conversation about a baby's condition. It seemed that I was benefiting from the patients' presence in the clinic and giving nothing back. I longed to have a positive impact on my patients and their experience.

Despite my new knowledge, I was not capable of contributing to the conversation about a baby's condition... I longed to have a positive impact on my patients and their experience.

My ninth month of medical school found me shadowing in the birth center of the same hospital I had trained in all year. Sitting in the workroom and listening to the buzz of a busy night shift, I caught the tail end of a conversation about a patient being taken to the operating room for a cesarean delivery. Her baby had a complex congenital heart defect. I leapt at the chance to observe. I knew what to do: I stood quietly in the corner, out of the way. The patient lay on the table, prepped, alone except for the resident standing over her. I watched as the resident's brow furrowed, an ultrasound probe in her hand, and a silent machine next to her.

The resident would later explain to me that what happened next was called a "splash and crash." However, that moment was not the

time for teaching. The room burst into activity, and the anesthesiologist called out to me from across the room. Was I in the way? No – they needed me. The patient's partner hadn't arrived yet, so the anesthesia team gave me a stool and sat me down with instructions to keep her company while they worked. I slipped my hand into hers. While the surgeons worked on the other side of the drape, the patient and I talked quietly about the name she had picked out for the baby and her other children at home. From somewhere near us, her son began to cry, and she squeezed my hand tight.

In that moment, my limited knowledge and clinical capabilities weren't a concern. Once her partner arrived, I stepped back and watched as she greeted her baby before he was taken to the neonatal intensive care unit. Mother and son locked eyes through the incubator plastic, the lines hooked up to both of them, and the sea of people around. I might have missed it if I had been anything other than an observer.

Working with and learning from patients receiving fetal anomaly diagnoses was a privilege that reminded me why I entered medicine in the first place: to walk beside my patients in their journey. My preceptor asked her patients, "What do you know?" I often asked myself, "What do I know?" While I knew more than I did at the beginning of the year, I had always known how to hold a hand. How lucky I was to be there to do that.

Funding/Support: None declared.
Financial Disclosures: None declared.

Prophylactic or Poison: The Folic Acid Debate

continued from page 496

REFERENCES

1. Blum D. *The Poison Squad: One Chemist's Single-Minded Crusade for Food Safety at the Turn of the Twentieth Century.* Penguin Press; 2018.

2. Folic acid and the prevention of disease. Report of the Committee on Medical Aspects of Food and Nutrition Policy. *Rep Health Soc Subj (Lond).* 2000;50:i-101.

3. Williams J, Mai CT, Mulinare J, et al. Updated estimates of neural tube defects prevented by mandatory folic acid fortification - United States, 1995-2011. *MMWR Morb Mortal Wkly Rep.* 2015;64(1):1-5.

4. Crider KS, Qi YP, Devine O, Tinker SC, Berry RJ. Modeling the impact of folic acid fortification and supplementation on red blood cell folate concentrations and predicted neural tube defect risk in the United States: have we reached optimal prevention? *Am J Clin Nutr.* 2018;107(6):1027-1034. doi:10.1093/ajcn/nqy065

5. Murphy ME, Westmark CJ. Folic Acid fortification and neural tube defect risk: analysis of the Food Fortification Initiative dataset. *Nutrients*. 2020;12(1):247. doi:10.3390/nu12010247

6. Westmark CJ, Murphy ME. Reply to "The fallacy of using administrative data in assessing the effectiveness of food fortification. Comment on: Folic acid fortification and neural tube defect risk: analysis of the Food Fortification Initiative dataset. *Nutrients* 2020, 12, 247". Nutrients. 2020;12(5):1335. doi:10.3390/nu12051335

7. Pruitt Evans S, Ailes EC, Kramer MR, et al. Neighborhood deprivation and neural tube defects. *Epidemiology.* 2023;34(6):774-785. doi:10.1097/EDE.0000000000001655

8. Centeno Tablante E, Pachón H, Guetterman HM, Finkelstein JL. Fortification of wheat and maize flour with folic acid for population health outcomes. *Cochrane Database Syst Rev*. 2019;7(7):CD012150. doi:10.1002/14651858.CD012150.pub2

9. Maruvada P, Stover PJ, Mason JB, et al. Knowledge gaps in understanding the metabolic and clinical effects of excess folates/folic acid: a summary, and perspectives, from an NIH workshop. *Am J Clin Nutr.* 2020;112(5):1390-1403. doi:10.1093/ajcn/nqaa259

10. Choumenkovitch SF, Selhub J, Wilson PW, Rader JI, Rosenberg IH, Jacques PF. Folic acid intake from fortification in United States exceeds predictions. *J Nutr.* 2002;132(9):2792-2798. doi:10.1093/jn/132.9.2792

11. Patti MA, Braun JM, Arbuckle TE, MacFarlane AJ. Associations between folic acid supplement use and folate status biomarkers in the first and third trimesters of pregnancy in the Maternal-Infant Research on Environmental Chemicals (MIREC) Pregnancy Cohort Study. *Am J Clin Nutr.* 2022;116(6):1852-1863. doi:10.1093/ajcn/nqac235

12. Raghavan R, Selhub J, Paul L, et al. A prospective birth cohort study on cord blood folate subtypes and risk of autism spectrum disorder. *Am J Clin Nutr.* 2020;112(5):1304-1317. doi:10.1093/ajcn/nqaa208

13. Tinker SC, Hamner HC, Qi YP, Crider KS. U.S. women of childbearing age who are at possible increased risk of a neural tube defect-affected pregnancy due to suboptimal red blood cell folate concentrations, National Health and Nutrition Examination Survey 2007 to 2012. *Birth Defects Res A Clin Mol Teratol.* 2015;103(6):517-526. doi:10.1002/bdra.2337

14. Herter-Aeberli I, Wehrli N, Bärlocher K, Andersson M, Sych J. Inadequate status and low awareness of folate in Switzerland-a call to strengthen public health measures to ensure sufficient intakes. *Nutrients*. 2020;12(12):3729. doi:10.3390/nu12123729

15. Selhub J, Rosenberg IH. Public health significance of supplementation or fortification of grain products with folic acid. *Food Nutr Bull*. 2008;29(2 Suppl):S173-S176. doi:10.1177/15648265080292S120

The Emptiness of Fetal Death

continued from page 499

As my shift continued, powered by lattes and cola, the other staff surrounded me. My upper-level resident scrubbed into a cesarean delivery I normally would do. Nursing staff bought me comfort food. I was given time to try to recover. I was protected and surrounded as I felt a deep emptiness.

The morning came and I peeked my head into Ella's room. She was sleeping soundly with her husband, their baby between their two loving bodies, the first peace they had gotten throughout the night.

I dragged myself to our board sign out. I half whispered the information for all of the patients, haunted by the night's loss. I dragged myself out of the hospital, exhausted by every step. Once I made it out of the hospital, I stood in the nearly vacant parking lot, the brisk air hitting my face, and I shed a single tear. I felt alone, I felt sad, I felt hopeless. But what I felt more than anything was a deep sense of failure. I stood there knowing that I had failed to save a life I had promised to protect. I genuinely believed I would be called into my program director's office and would be fired. I feared I would be shamed and ridiculed by my colleagues. I feared I was a poor doctor and a danger to the community.

I drove home in a daze, experiencing my entire reality through the lens of a baby who would never grow up to see it. No crisp morning air across her lips. No autumn leaves. No warmth of lattes on cold winter mornings. As I climbed into bed, the last thing I thought about before I closed my eyes were Ella's eyes – bare and vacant.

Funding/Support: None declared.
Financial Disclosures: None declared.

Two Sides of the Same Coin: Mental Health

Mubashira Waseem

Acrylic on Watercolor Paper

Artist Statement:

Mental health can be either venom or a blossoming flower. Poor mental health is like a venomous snake, injecting poison that slowly deteriorates both mind and body. In contrast, good mental health is like a tree, steadily growing with every step of life, bringing peace, vitality and strength, offering solace even in the toughest times.

Pregnant Women Perceptions of Cannabinoid Use in Milwaukee, Wisconsin

Erica Marion, PhD; Matthew J. Dellinger, PhD; Francisco J. Enriquez, MD; Abbey R. Kruper, PsyD; Krista M. Lisdahl, PhD; Karen F. Lupa, CNM; Sarah Chilenski PhD; Erika L. Peterson, MD; Melissa L. Harris, MPH; Cecilia J. Hillard, PhD; Mary E. Homan, DrPH; Alexandra Skeeter, MD; Michael P. Anello, BA; Lora L. Daskalska, PhD; Fabrice Jotterand, PhD, MA

ABSTRACT

Introduction: There is an increased threat to pregnant women and their fetuses due to the lack of knowledge and current policies of cannabinoid use during pregnancy. Inconclusive evidence of cannabinoid use during pregnancy prevents the development of standard guidelines and education regarding risks on long-term maternal and child health outcomes. This observational study investigated pregnant women's attitudes and beliefs and the prevalence of clinician counseling on cannabinoid use during pregnancy.

Methods: A 45-item questionnaire was distributed to pregnant women receiving prenatal care at 2 obstetrics and gynecology clinics in Milwaukee, Wisconsin. Descriptive statistics were used to summarize pregnant women's attitudes and beliefs, sources of information, prevalence of cannabidiol (CBD) use, and prevalence of clinician counseling on tetrahydrocannabinol (THC) and CBD use during pregnancy.

Results: A total of 95 questionnaires were collected from pregnant women during prenatal care visits. The majority of participants were non-White (54%) with a high school diploma (30%) and average age of 29 years old. Pregnant women's beliefs related to the use of cannabinoids on their own physical, social, and emotional health was "somewhat better." In contrast, women's beliefs related to the impact of cannabinoids use on their fetus and on birth outcomes was negative. Participants reported a lack of knowledge of THC (55%) and CBD (77%) use during pregnancy. Since their first prenatal care visit, over 60% of participants reported that they did not receive counseling regarding cannabinoid use during pregnancy, and the internet was the preferred source for information on THC (73%) and CBD (80%) use during pregnancy.

Conclusions: Pregnant women lack informed guidance and education on the effect of cannabinoid use during pregnancy. The possibility of misinformation poses a risk to maternal and child health outcomes. Future research should focus on health communication and risk assessments on cannabinoid use during pregnancy for prevention and treatment.

• • •

Author Affiliations: Institute for Health and Equity, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Marion, Dellinger, Harris, Homan, Daskalska); Sixteenth Street Community Health Center, Milwaukee, Wisconsin (Enriquez, Lupa); Department of Obstetrics and Gynecology, MCW, Milwaukee, Wisconsin (Kruper, Peterson, Jotterand); Department of Psychology, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin (Lisdahl); Pennsylvania State University, State College, Pennsylvania (Chilenski); Pharmacology and Toxicology, MCW, Milwaukee, Wisconsin (Hillard); MCW, Milwaukee, Wisconsin (Skeeter); Clinical and Translational Science Institute, MCW, Milwaukee, Wisconsin (Anello).

Corresponding Author: Erica Marion, Institute for Health and Equity, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226-0509; email emarion@mcw.edu; ORCID ID 0009-0000-0989-044X

INTRODUCTION

The growing acceptance, accessibility, and use of cannabis and cannabis-derived molecules (cannabinoids) raise important public health concerns and a need to evaluate the health effects of cannabis use more thoroughly.[1] Policy changes in recent decades seem to have altered cannabis use patterns and perceived levels of risk. The relatively nascent status of cannabinoid uses also presents a public health concern for vulnerable populations, such as pregnant women and adolescents. There is mounting concern that, although cannabis could present therapeutic opportunities, developing fetuses could be affected by maternal use.[2,3] Unlike other substances whose use may confer risk, such as alcohol or tobacco, no accepted standards exist to help guide individuals as they make choices regarding either recreational or therapeutic use of cannabis.[1,4] Increasing legalization and use of cannabinoids coexist with mixed research on the risks and benefits. Given the presence of established therapeutic effects in adults, nuanced advice is necessary to ensure clear communication that cannabinoids are capable of imparting both risks and benefits to individuals.[1] Furthermore, the development of advice will serve as valuable contextualization to guide additional investigations on health effects by identifying priority areas, such as vulnerable populations, risk perceptions, and ethical considerations.

Potential Risk of Cannabinoid Use During Pregnancy

Despite widespread use of cannabinoids such as cannabidiol (CBD), there is limited research regarding their use during pregnancy.[5] Pregnant mice models have been used to investigate the effects of cannabinoids on offspring development. Gestating mice exposure to tetrahydrocannabinol (THC) has been linked to adverse effects on the neurological development and functionality of offspring throughout adolescence and adulthood.[6] Offspring can begin to experience abnormalities with emotional and cognitive functions, social behavior, and mobility. Furthermore, researchers who have used THC treatment with gestating mice reported a decrease in maternal and birth weights.[7] Recent studies found that prenatal exposure to CBD in gestating mice resulted in dysregulation of their offspring, suggesting that early communication is disrupted by CBD exposure.[8]

There are very few studies that have investigated the effects of cannabis use in pregnant women due to several limitations, including inconsistency or underreporting of results, the potency level of cannabis being consumed, and controlling for additional factors known to have adverse pregnancy outcomes. For example, a study in California explored the relationship between maternal mental health diagnosis and symptoms and intimate partner violence with cannabis use during pregnancy. Pregnant women were screened for cannabis use either by urine sample or self-reported cannabis use during their first prenatal care visit, with average gestational age at 8 weeks pregnant. Results from this study concluded that pregnant women were more likely to use cannabis if they were experiencing depression, anxiety, and/or intimate partner violence. However, there were inconsistencies in urine drug screening (6%), self-reporting (0.9%), and confirmatory toxicology testing (3.4%) for THC use. Differences in cannabis screening can be due to the frequency of use by a participant, which often is not captured in primary data collection. Another important limitation to consider within self-reporting is the potential of perceived legal implications of cannabis use during pregnancy,[9] as clinicians have reported discussing the legal implications of substance use for cessation efforts for pregnant women rather than counseling due to the lack of information regarding risks. Lastly, it is important to note that cannabis often is not used in isolation of other substances, alcohol, or tobacco, which have been associated with adverse pregnancy outcomes.[9]

Similar to mice models, studies investigating cannabis use for pregnant women have found significant associations with low birth weight, stillbirth, and long-term health consequences for their offspring. Despite limitations in self-reported cannabis use for pregnant women, one study found an significant of association with a 50% likelihood of low birth weight while controlling for maternal age, education level, and tobacco use.[10] Another study that explored a combination of prenatal cannabis and tobacco exposure found an increased risk of stillbirth in expectant mothers.[11] Additionally, the relationship between THC and tobacco prenatal exposure increases the likelihood of offspring using combustible cigarettes during adolescence, eventually becoming addicted to tobacco in adulthood.[12]

Lack of informed guidance may contribute to inadequate or ineffective communication between clinicians and pregnant women regarding the risk of cannabinoid use during pregnancy.[9] Currently, CBD is legalized in the state of Wisconsin, while THC is not. However, THC is accessible to Wisconsin residents through its neighboring state Illinois for individuals over the age of 21. It is important to recognize accessibility of cannabis products to increase the urgency of communicating risk to pregnant women to reduce adverse outcomes.

This observational study explored pregnant women's attitudes and knowledge about cannabinoids – specifically THC and CBD – in an urban city (Milwaukee, Wisconsin) to investigate whether they are receiving informed guidance and to gain insights into how to better inform pregnant women, especially those from vulnerable populations. This paper reports preliminary findings and baseline data to support further study, including educational interventions and clinician training.

METHODS

Setting

This observational study administered a 45-item written anonymous questionnaire in English and Spanish to pregnant women to learn about their perceptions regarding cannabinoid use – specifically THC and CBD. The questionnaire was administered at an academic medical setting and community health clinic. The community health clinic serves predominantly Spanish-speaking patients due to its location in the community. This project was reviewed and approved by the Medical College of Wisconsin Institutional Review Board (IRB).

Subjects

Subjects were recruited by medical assistants who asked patients who were seeing clinician about their pregnancy if they were interested in completing in the study questionnaire. Medical staff were not a part of the research team and did not share patient identifiable information with the research coordinators. Interested participants received a written informational letter for consent before the questionnaire was administered by a research coordinator. Participants could self-administer the questionnaire with the option to ask for more information and/or assistance from the research coordinator in the exam room. The questionnaire was translated before administration and approved by the Medical College of Wisconsin IRB for potential Spanish-speaking participants. In addition, medical interpreters were available to translate correspondence between Spanish-speaking participants and the research coordinator as needed to complete the questionnaire. All questionnaires were collected by the research coordinator and included in the analysis. Any questions that were not answered were analyzed as missing.

Table 1. Particpant Demographics (N = 95)

Median age (range)	29 (18 – 45)
Mean age (SD)	29.09 (6.49)
Race, n (%)	
Black or African American	20 (21)
White	39 (41)
Other[a]	26 (27)
Ethnicity, n (%)	
Hispanic	43 (45)
Education, n (%)	
< High school graduate	17 (18)
High school graduate	28 (29)
Some college	25 (26)
College graduate	21 (22)

[a]Other includes other unspecified race (n = 20), American Indian or Alaska Native (n = 1), Asian (n = 2), and multiracial (n = 2).

Table 2. Knowledge of Cannabinoid Use During Pregnancy and Sources of Information

	THC, N (%)	CBD, N (%)
Knowledge of use during pregnancy		
Yes	40 (43)	20 (21)
No	52 (55)	72 (77)
I don't know	2 (2)	2 (2)
Source of information		
Family or friends	18 (45)	10 (50)
Health care professional	18 (45)	4 (20)
Internet	29 (73)	16 (80)
Other	9 (23)	2 (10)

Abbreviations: THC, tetrahydrocannabinol; CBD, cannabidiol.

Table 3. Perceptions and Attitudes on the Impact of Cannabinoids During Pregnancy and Birth Outcome

	THC, N (%)	CBD, N (%)
Maternal		
Better	16 (18)	14 (16)
Somewhat better	31 (35)	31 (34)
No change	20 (22)	22 (24)
Somewhat worse	8 (9)	6 (7)
Worse	14 (16)	17 (19)
Birth Outcome		
Better	5 (5)	8 (9)
Somewhat better	6 (6)	11 (12)
No change	21 (23)	38 (41)
Somewhat worse	21 (23)	7 (8)
Worse	40 (43)	28 (30)

Abbreviations: THC, tetrahydrocannabinol; CBD, cannabidiol.

Survey Development

The survey was developed by a multidisciplinary translational research team with specialization in obstetrics, maternal fetal medicine, family medicine, cannabinoid neuroscience, community prevention coalitions, risk assessment and communication, substance use social services, and bioethics expertise in neuroethics and maternal/fetal ethics. The team developed the 45-item questionnaire by combining previously used survey tools and literature from similar studies.[13–16] Team members collaborated to create new questions and reviewed previously used questions. The completed questionnaire consisted of pregnant women's demographic information, overall knowledge of cannabinoid use, sources of information of cannabinoid use, clinician counseling for cannabinoid use during pregnancy, and the frequency and prevalence of CBD use before and during pregnancy. In addition, participants were asked about their perceptions/attitudes regarding how cannabinoid use would affect them physically, emotionally, and socially during pregnancy and their birth outcome. Physical characteristics included a pregnant woman's ability to move, sleep, and to manage morning sickness and cravings during pregnancy. Emotional characteristics included a pregnant woman's ability to concentrate, relax, unwind, feel calm, feel creative, and control anger. Lastly, social characteristics focused on a pregnant woman's ability to get along with others. Results were summarized with percentages and central tendency measures using Stata version 16 (StataCorp LLC).

RESULTS

A total of 95 pregnant women completed questionnaires on their attitudes and knowledge about the cannabinoids THC and CBD. Participants were mostly White women 41% (n = 39) with a high school diploma 29% (n = 28) and average age of 29 years old (Table 1).

THC

Only 45% (n=18) of participants endorsed discussing marijuana (cannabis) use during pregnancy with professional health care workers such as nurses or social workers (see Table 2). In addition, 68% of participants had not been counseled about cannabis use during pregnancy by any clinician since their first prenatal visit. When asked about their perceptions of the impact of THC during pregnancy, 53% (n = 47) of participants responded that THC would be beneficial for their pregnancy physically, emotionally, and socially. On the contrary, when asked about the health of the baby during birth, 66% (n = 61) of participants said they perceived the outcome would be worse after THC use (Table 3). More than half of the participants had not heard, read, or learned any information about using THC during pregnancy. For those who stated they had knowledge regarding THC use during pregnancy, their main source of information was the internet, specifically social media. Participants said they would judge whether the information regarding cannabis use during pregnancy is trustworthy by asking further questions with clinician or searching for additional information on the internet.

CBD

Only 4% (n=4) of respondents stated that they used CBD during pregnancy. Frequency of CBD use varied between less than 5 times

a year and weekly. However, 29% (n = 27) of respondents stated that they have used CBD while not pregnant less than 5 times a year. Overall, 77% (n = 72) of participants have not heard, read, or learned any information about using CBD products during pregnancy. Similar to results regarding THC use during pregnancy, participants' main source of CBD information was the internet and family or friends. Over 90% (n = 80) of participants did not receive information or counseling regarding CBD use during pregnancy from health care workers at the facilities or any clinician who provided treatment since their first prenatal visit. At 50% (n = 45), CBD use during pregnancy was perceived to be somewhat better physically, emotionally, and socially, such as relief from morning sickness, managing the ability to concentrate, and getting along with others. In addition, 41% (n = 38) of participants stated that there would be no change to the birth outcome if CBD is used during pregnancy.

DISCUSSION

Overall, this observational study supports the concept that pregnant women lack knowledge of the potential effects of cannabinoid use. Pregnant women's attitudes and beliefs on cannabinoid use varied regarding the risk and benefits on maternal health physically and emotionally. This supports previous research on women who reported cannabis use during pregnancy.[13] Some perceived THC as being more natural and safer than other illicit substances and prescribed medication. This can be an implication for women using cannabis to manage pregnancy symptoms, such as nausea and mood changes.[14]

Participants reported that their health care professionals did not provide counseling on the use of cannabinoids during pregnancy, which is consistent with previous studies investigating clinicians' counseling habits.[9] The lack of information available and inconsistent counseling from clinicians can increase the risk of ongoing cannabinoid use in pregnant women.[15] Inconsistent and potentially inaccurate sources of information regarding cannabinoid use during pregnancy pose a risk to patients' health literacy and violate bioethical protections for adverse outcomes for pregnant women and their offspring.

Like previous studies, pregnant women reported seeking medical information on cannabinoid use on the internet.[16] Our preliminary data suggest that social media is the most-used internet source of information regarding cannabis use during pregnancy. However, patients in other studies have reported a preference for clinicians to confirm the trustworthiness of information on cannabinoid use during pregnancy from any source.[17] This preference may be at odds with other research with pregnant women negatively reporting the quality of medical information from clinicians on cannabis use.[13]

In this study population, there was a low percentage of pregnant women who reported CBD use. Our study did not investigate cessation of cannabinoid use during pregnancy of previous users. However, pregnant women reported a decrease in usage of CBD during pregnancy compared to previous use. Motivating factors for discontinued cannabinoid use were not investigated, but women have reported social bias influencing their decision rather than adhering to clinicians' informed guidance.[18] Some pregnant women preferred to reduce cannabis use to manage risks of adverse pregnancy outcomes, which is consistent with our findings of pregnant women reporting that cannabinoid use will negatively impact birth outcomes.

This observational study has multiple limitations. First, we recognize sample bias, as participants who were recruited with linguistic needs were not recorded or addressed by staff when translating the questionnaire and assisting Spanish-speaking participants. Therefore, we cannot confirm participants' comprehension of information being translated. Second, self-reported data for cannabinoid use during pregnancy have been found to be underreported compared to collected urine samples.[19] Also, we did not collect data on participants' current pregnancy term or frequency of prenatal visits, which could have been used to compare differences in responses about cannabinoid impact on maternal characteristics and counseling from health care professionals. Another limitation is recall bias: depending on participants' gestational age, counseling from a health professional regarding cannabinoid use may not have occurred yet.

CONCLUSIONS

Our study found that pregnant women lack knowledge on the maternal impact of THC and CBD use. However, most pregnant women are aware that they may experience a negative birth outcome after THC and/or CBD use. Pregnant women often used the internet as a source of information regarding THC and CBD use, while reporting the absence of counseling from a health professional. Future research should focus on interventions to improve health communication about cannabinoid use between clinicians and pregnant women. Contradictions in sources and trustworthiness of information highlight inaccessibility of medical information on cannabis use. Established risk assessment and health communication practices should be employed, along with bioethical examination, to summarize ongoing research and synthesize advice. It may be possible to establish risk benchmarks using sensitive endpoints, such as birth outcomes, if robust observational studies can establish reliable exposure estimates. All evidence-based advice should be developed in partnership with stakeholder engagement from affected communities to maximize health-promoting messaging.

Funding/Support: The project described was supported by the National Center for Advancing Translational Sciences, National Institutes of Health (NIH), Award Number UL1TR001436. The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the NIH.

Financial Disclosures: None declared.

Acknowledgements: The authors wish to thank to the Sixteenth Street Clinic, Froedtert Hospital, and the Bioethics Ensemble Team.

REFERENCES

1. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research.* National Academies Press (US); January 12, 2017. Accessed June 6, 2023. doi:10.17226/24625

2. Roncero C, Valriberas-Herrero I, Mezzatesta-Gava M, Villegas JL, Aguilar L, Grau-López L. Cannabis use during pregnancy and its relationship with fetal developmental outcomes and psychiatric disorders: a systematic review. *Reprod Health*. 2020;17(1):25. doi:10.1186/s12978-020-0880-9

3. Singh S, Filion KB, Abenhaim HA, Eisenberg MJ. Prevalence and outcomes of prenatal recreational cannabis use in high-income countries: a scoping review. *BJOG*. 2020;127(1):8-16. doi:10.1111/1471-0528.15946

4. Peachman RR. Clinicians support medical marijuana use in children with cancer, but lack knowledge. *JAMA*. 2018;319(9):852-853. doi:10.1001/jama.2018.0089

5. NIDA. Nationwide Trends; 2015. Accessed January 6, 2025. https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.htm#tab6-72a.

6. Trezza V, Campolongo P, Manduca A, et al. Altering endocannabinoid neurotransmission at critical developmental ages: impact on rodent emotionality and cognitive performance. *Front Behav Neurosci.* 2012;6:2. doi:10.3389/fnbeh.2012.00002

7. Chang X, Bian Y, He Q, et al. Suppression of STAT3 signaling by Δ9-tetrahydrocannabinol (THC) induces trophoblast dysfunction. *Cell Physiol Biochem*. 2017;42(2):537-550. doi:10.1159/000477603

8. Iezzi D, Caceres-Rodriguez A, Chavis P, Manzoni OJJ. In utero exposure to cannabidiol disrupts select early-life behaviors in a sex-specific manner. *Transl Psychiatry.* 2022;12(1):501. doi:10.1038/s41398-022-02271-8

9. Holland CL, Rubio D, Rodriguez KL, et al. Obstetric health care providers' counseling responses to pregnant patient disclosures of marijuana use. *Obstet Gynecol.* 2016;127(4):681-687. doi:10.1097/AOG.0000000000001343

10. Crume TL, Juhl AL, Brooks-Russell A, Hall KE, Wymore E, Borgelt LM. Cannabis use during the perinatal period in a state with legalized recreational and medical marijuana: the association between maternal characteristics, breastfeeding patterns, and neonatal outcomes. *J Pediatr.* 2018;197:90-96. doi:10.1016/j.jpeds.2018.02.005

11. Varner MW, Silver RM, Rowland Hogue CJ, et al. Association between stillbirth and illicit drug use and smoking during pregnancy. *Obstet Gynecol.* 2014;123(1):113-125. doi:10.1097/AOG.0000000000000052

12. De Genna NM, Richardson GA, Goldschmidt L, Day NL, Cornelius MD. Prenatal exposures to tobacco and cannabis: associations with adult electronic cigarette use. *Drug Alcohol Depend*. 2018;188:209-215. doi:10.1016/j.drugalcdep.2018.03.045

13. Jarlenski M, Tarr JA, Holland CL, Farrell D, Chang JC. Pregnant women's access to information about perinatal marijuana use: a qualitative study. *Womens Health Issues*. 2016;26(4):452-459. doi:10.1016/j.whi.2016.03.010

14. Chang JC, Tarr JA, Holland CL, et al. Beliefs and attitudes regarding prenatal marijuana use: perspectives of pregnant women who report use. *Drug Alcohol Depend.* 2019;196:14-20. doi:10.1016/j.drugalcdep.2018.11.028

15. Weisbeck SJ, Bright KS, Ginn CS, Smith JM, Hayden KA, Ringham C. Perceptions about cannabis use during pregnancy: a rapid best-framework qualitative synthesis. *Can J Public Health*. 2021;112(1):49-59. doi:10.17269/s41997-020-00346-x

16. Jarlenski M, Tarr JA, Holland CL, Farrell D, Chang JC. Pregnant women's access to information about perinatal marijuana use: a qualitative study. *Womens Health Issues*. 2016;26(4):452-459. doi:10.1016/j.whi.2016.03.010

17. Satti MA, Reed EG, Wenker ES, et al. Factors that shape pregnant women's perceptions regarding the safety of cannabis use during pregnancy. *J Cannabis Res.* 2022;4(1):16. doi:10.1186/s42238-022-00128-x

18. Mark K, Gryczynski J, Axenfeld E, Schwartz RP, Terplan M. Pregnant women's current and intended cannabis use in relation to their views toward legalization and knowledge of potential harm. *J Addict Med.* 2017;11(3):211-216. doi:10.1097/ADM.0000000000000299

19. Young-Wolff KC, Sarovar V, Tucker LY, et al. Validity of self-reported cannabis use among pregnant females in northern California. *J Addict Med*. 2020;14(4):287-292. doi:10.1097/ADM.0000000000000581

Enablers and Challenges of Breastfeeding During the COVID-19 Pandemic

Caitlin J. Regner, MD; Aleksandra E. Zgierska, MD, PhD; Robert P. Lennon, MD, JD; Ellen Goldstein, PhD, MFT

ABSTRACT

Introduction: The COVID-19 pandemic greatly affected access to breastfeeding support. Limited research has evaluated the pandemic's impact on postpartum individuals' decisions to breastfeed during this time. This qualitative survey study described breastfeeding-related attitudes, decision-making, and experience of postpartum people early in the COVID-19 pandemic.

Methods: New mothers (<6 months postpartum) were identified via electronic health records at 2 academic health care systems located in Northeastern and Midwestern United States and were invited via mailings and phone to complete a cross-sectional online survey assessing the impact of COVID-19 on mental and physical health and coping. Thematic analysis was conducted to organize responses into categories of impact (positive, negative, neutral), highlighting the major themes of the influence of COVID-19 on breastfeeding.

Results: A total of 216 participants responded (66 Northeast, 150 Midwest), and the majority (64.6%) were age 31 to 45 years old. The predominance of positive themes associated with the pandemic that enabled participants' decisions to breastfeed were health benefits, convenience and ease, and changes in work routines, whereas the major challenges exacerbated by the pandemic were access to lactation support, mental health/stress, and COVID-19 restrictions. Breastfeeding decisions that were not explicitly affected by the pandemic included prior feeding intention and experience, as well as knowledge of importance and benefits.

Conclusions: Findings from this survey study enrich our understanding of the pandemic's impact on breastfeeding motivations and practices. As health care systems and policymakers seek to improve support for breastfeeding, feedback from postpartum mothers may suggest new ways to overcome barriers that arise in times of crisis.

• • •

Author Affiliations: Access Community Health Centers, Madison, Wisconsin (Regner); Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Regner); Department of Family and Community Medicine, College of Medicine, Penn State, Hershey, Pennsylvania (Zgierska, Lennon); Departments of Anesthesiology and Perioperative Medicine, and Public Health Sciences, College of Medicine, Penn State, Hershey, Pennsylvania (Zgierska); Department of Population Health Science Nursing Science, University of Illinois at Chicago, Chicago, Illinois (Goldstein).

Corresponding Author: Caitlin Regner, MD, Family Medicine Physician and Assistant Clinical Professor, Joyce & Marshall Erdman Clinic, 2202 S Park St, Madison WI 53713; email Caitlin.Regner@accesshealthwi.org; ORCID ID 0000-0002-5815-0306

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic placed a strain on the US health care system and led to dramatic changes in medical and social operations,[1] which affected pregnancy, postpartum, and infant care.[2,3] Early in the pandemic, support for breastfeeding initiation was affected by the separation of mothers from their infants in the case of COVID-19 infection, a higher frequency of early hospital discharges, and reduced inpatient lactation support.[4,5] For instance, the Centers for Disease Control and Prevention (CDC) showed a 17.9% reduction of in-person lactation support by the end of 2020.[4] Moreover, breastfeeding support outside of the hospital was limited due to lockdowns, disruptions in health care operations, and restrictions on services provided by peer- and community-based organizations,[2,6] resulting in reduced support for breastfeeding during several critical stages during the postpartum period.[5] In light of reduced lactation support, several studies have demonstrated reduced breastfeeding rates during the COVID-19 pandemic.[7,8]

Women's responses to these changes were mixed.[9] In some regions, women rated their breastfeeding experience as negative during the early pandemic compared to prepandemic.[10] Negative breastfeeding experience was particularly prevalent in mothers who were separated from their infant, struggled with breastfeeding,

or perceived decreased family and professional support. Other women noted a positive experience of breastfeeding, particularly in subsets who had greater partner support and more time at home.[11,12]

Given the varied breastfeeding experiences during the early COVID-19 pandemic in other regions, the purpose of this study was to contribute to the existing literature by describing the attitudes, decision-making, and experiences among postpartum people in the Northeastern and Midwestern United States. This information may allow for optimization of pregnancy and postpartum care and breastfeeding support in the future.

METHODS

This study analyzed data from a larger cross-sectional survey examining the impact of the COVID-19 pandemic on pregnant and postpartum persons at 2 independent sites, with study protocols that were approved by each Institutional Review Board. The aim of this qualitative analysis of the open-ended questions on breastfeeding was to understand how early responses to the COVID-19 pandemic affected breastfeeding-related attitudes, decisions, and experiences among pregnant and recently postpartum persons.

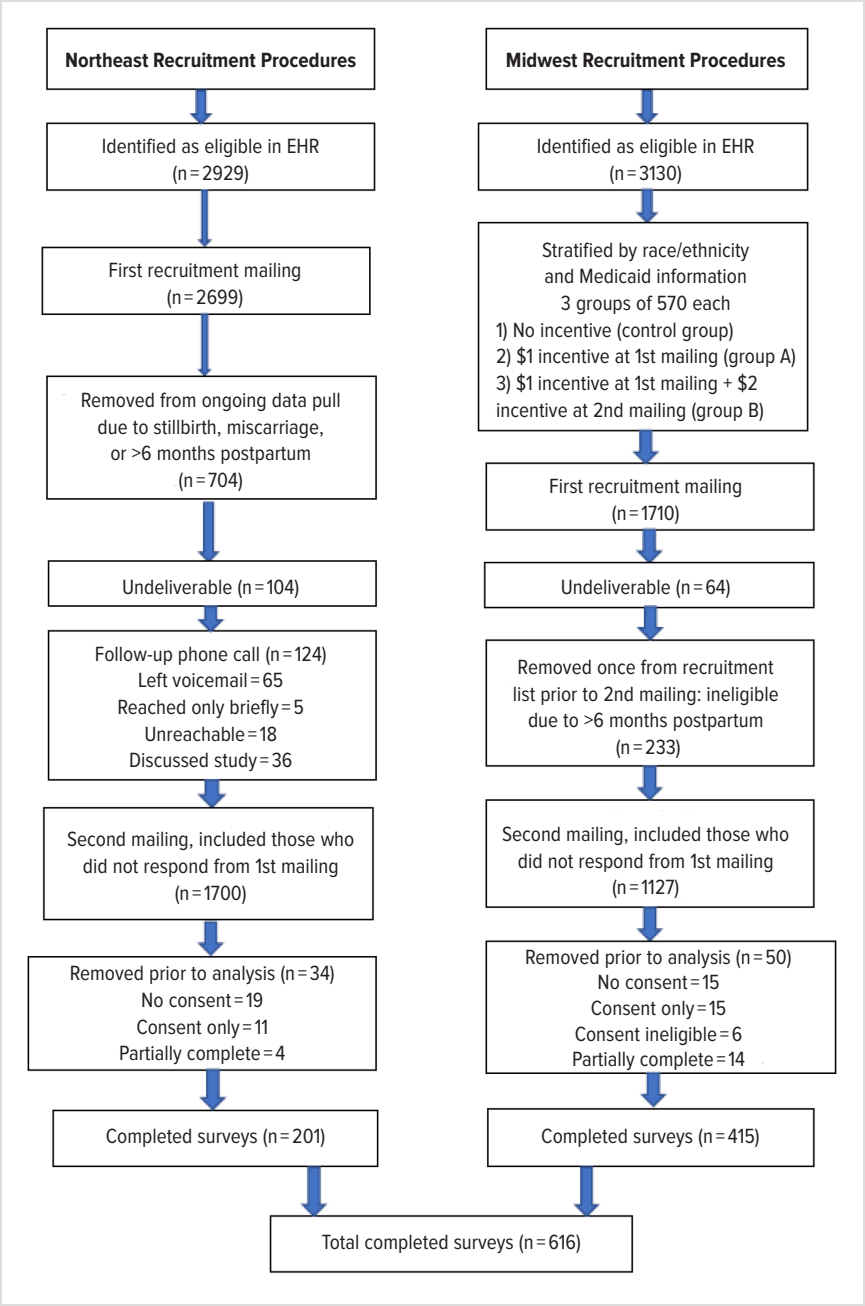
Study Design

The overall purpose of the survey was to assess the impact of COVID-19 on mental and physical health and coping, as well as to address social needs among pregnant and postpartum persons. Potentially eligible adults were identified by searching the electronic health records of the 2 participating academic health systems. Eligible persons were adults aged 18 years and older, English-speaking, and pregnant or postpartum (within 6 months of birth). The eligibility criteria and survey questions were identical at the 2 study sites; however, the study timing and recruitment methods differed slightly between the 2 geographical locations as reported elsewhere.[13] The Figure shows the recruitment flow chart by region.

Potentially eligible participants were mailed invitation letters containing their unique study identification (ID) number and a URL to access the survey. Once online, they were presented with a brief study summary and prompted to enter their ID number before proceeding to eligibility screening. Informed consent was obtained by directing participants to read the "Summary Explanation of Research" and agreeing to initiate the anonymous REDCap survey.

At the Northeast site, the survey was accessible from August 4, 2020, through November 24, 2020, with 201 persons completing the "parent" survey (94 pregnant, 107 postpartum). At the Midwest site, the survey was accessible from January 15, 2021, through April 15, 2021, with 415 individuals who completed the "parent" survey (209 pregnant, 206 postpartum). Only postpartum respondents who answered the optional open-ended ques-

Figure. Participant Recruitment by Region



Abbreviation: EHR, electronic health record.

Table. Sample Demographics and Breastfeeding Responses From Survey Participants, N = 216

	N (%)
Region	
Northeast	66 (31)
Midwest	150 (69)
Age range (years)	
19–30	77 (35.6)
31–45	139 (64.4)
Race (225 responses)[a]	
American Indian or Alaskan Native	5 (2.2)
Black or African American	8 (3.6)
White	191 (84.9)
Asian	12 (5.3)
Other Race	3 (1.3)
Prefer not to answer	6 (2.7)
Ethnicity	
Hispanic or Latino	9 (4.2)
Non-Hispanic or Latino	200 (92.6)
Prefer not to answer	5 (2.3)
Missing	2 (0.9)
Education	
High school diploma/GED	13 (6.0)
Partial college	20 (9.3)
Completed college	116 (53.7)
Graduate degree	65 (30.1)
Prefer not to answer	1 (0.5)
Missing	1 (0.5)
Marital status	
Married, or in a domestic partnership	207 (95.8)
Divorced or separated	1 (0.5)
Single	7 (3.2)
Missing	1 (0.5)
Employment status (217 responses)[a]	
Working	144 (66.4)
Maternity leave/sick leave/temporarily laid off	34 (15.7)
Homemaker	32 (14.7)
Disabled, permanently or temporarily	1 (0.5)
Student	6 (2.8)
How difficult is it for you to live on your total household income right now?	
Extremely difficult	1 (0.5)
Very difficult	3 (1.4)
Difficult	13 (6.0)
Somewhat difficult	49 (22.7)
Not at all difficult	150 (69.4)
Did you breastfeed or pump breast milk to feed your new baby after delivery, even for a short period of time?	
Yes	213 (98.6)
No	3 (1.4)
Did the COVID-19 pandemic influence your decision to breastfeed?	
Yes	16 (7.4)
No	200 (92.6)

[a]Some participants answered more than once.

tions on breastfeeding were included in the present analysis, producing a combined sample of 216 participants (66 Northeast, 150 Midwest).

Outcome Measures

The "parent" survey consisted of 52 questions on the socioeconomic, medical, and psychological well-being and needs of the participants. Three survey questions were related to breastfeeding, including 1 open-ended question ("Please consider sharing your thoughts about your decision regarding breastfeeding during the COVID-19 pandemic") and 2 closed-ended questions with yes/no answer choices ("Did you breastfeed or pump breast milk to feed your new baby after delivery, even for a short period of time?" and "Did the COVID-19 pandemic influence your decision to breastfeed?").

Data Analysis

Demographics and 2 closed-ended questions on breastfeeding were analyzed using Stata.[14] Qualitative data were analyzed thematically and entered into a Microsoft Excel spreadsheet for data sorting and coding.[15] The data were organized into 3 separate columns by meaning unit, theme, and category assigned as positive, negative, or neutral. The work of the primary coder (CR), a physician with experience in family medicine, obstetrics, and breastfeeding, was reviewed by a second coder (EG), a social and behavioral scientist. Any discrepancies were discussed and resolved via consensus. The calculated frequency of categories, domains, and themes demonstrated how often similar content was mentioned.

RESULTS

Sample Characteristics (n = 216)

The analysis sample included postpartum participants from the Northeast (N = 66) and Midwest (N = 150). There were no major differences in demographics by region. The majority of participants were between 31 to 45 years old (64.4%), White (84.9%), married or in a domestic partnership (95.8%), and working (66.4%), while 83.8% held at least a college degree, and 69.4% reported no difficulty living on their household income. In total, 213 (98.6%) reported having attempted breastfeeding or pumping breast milk postpartum, and 16 (7.4%) reported that their decision about breastfeeding was affected by the COVID-19 pandemic. See Table.

Participants' Perceptions

Responses from postpartum participants about the perceived impact of the pandemic on breastfeeding were categorized as positive (enablers), negative (challenges), and neutral (enablers and challenges not impacted by COVID-19). Descriptions of the most common themes and exemplar quotes are presented below.

Positive Impacts on Breastfeeding (122 responses, 6 themes): Six themes highlighted how the COVID-19 pandemic positively

affected participants' breastfeeding decisions or experiences and promoted its initiation or continuation.

Health Benefits (88 responses): Some participants placed an emphasis on their dedication to breastfeed—particularly considering the pandemic—due to the nutritional and immune-building benefits. "*I feel breastfeeding is even more important during the pandemic to provide the baby with even more protection with antibodies"* (Patient [P]-138). Several participants shared that pandemic-related uncertainty contributed to extended amounts of time breastfeeding and was often coupled with participants' desire to provide prolonged health benefits to their infant. For example, "*…because of the pandemic, I decided to breastfeed my baby longer and more for his immunity"* (P-167). At the time this study was conducted, the COVID-19 vaccine had recently been approved for use, and several women attributed the vaccine as a motivation to continue breastfeeding.

Convenience and Ease (19 responses): As a result of the pandemic, some participants described change in routine, increased support from partners, less time spent pumping, and increased ease of breastfeeding: *"[Breastfeeding] is easier this time around because I'm always home"* (P-186).

Changes in Work Routine (7 responses): Some noted changes in work settings and routines that affected breastfeeding during the pandemic: *"Working from home during COVID-19 has actually made breastfeeding easier"* (P-126).

Limited Formula Supply (4 responses): A few remarked that difficulties obtaining formula increased their motivation to breastfeed: *"I decided that I should attempt [breastfeeding] due to the uncertainty of formula available"* (P-152).

Lactation Support (2 responses): Though many experienced difficulties obtaining lactation support, a few respondents shared that they received good lactation support during the pandemic, which allowed them to breastfeed despite challenges. *"I received lots of [breastfeeding] support in the hospital and during our NICU [neonatal intensive care unit] stay"* (P-203).

Financial (2 responses): Participants also shared that COVID-19 positively influenced their decision to breastfeed as a means of *"saving money"* (P-42).

Negative Impacts of Pandemic on Breastfeeding (38 responses, 5 themes)

Five themes emphasized how the COVID-19 pandemic negatively affected participants' breastfeeding decisions or experiences.

Difficulty Accessing Lactation Support and Attending Medical Visits (17 responses): Many participants reported that the lack of in-person lactation support during the pandemic negatively affected their breastfeeding experience. While some people continued breastfeeding despite the challenges, others stopped altogether due to the lack of lactation support. *"We stopped breastfeeding after only a month or so because of not being able to get enough hands-on help to teach us and the baby how to breastfeed"* (P-19). One woman expressed her frustration when she finally had to go into the clinic due to a medical issue: *"I called the lactation hotline multiple times and had to go into the clinic for in-person treatment when I developed mastitis"* (P-202).

Apart from the challenges obtaining hands-on breastfeeding support, there was a general sentiment regarding the difficulties participants experienced when attending medical visits out of the home. *"I wasn't comfortable bringing a newborn into a doctor's office for extra visits…"* (P-64). In addition to having less lactation support, several expressed a more general lack of support from family, friends, or peers that affected their breastfeeding experience: *"Everyone seems too scared of everyone else (COVID-19 was continuing to spread at that time) to really help much so we ended up switching to formula"* (P-104).

Mental Health and Stress (11 responses): Several women noted increased anxiety about caring for their baby during the pandemic. Others were diagnosed with mental health disorders, which consequently affected infant feeding choices. One mother shared, *"Due to the pandemic, my mental health has not been well. I knew I needed medications that could possibly have an effect on my breastfeeding, so I decided to formula feed instead"* (P-143). Another mother's response highlights the impact of social changes from the pandemic on mental health: *"I think maternity leave/immediate postpartum periods are isolating for mothers. COVID-19 made this isolation more dramatic for some mothers, including myself, which led to worse postpartum depression than I have previously experienced after my first child"* (P-123).

COVID-19 Restrictions (5 responses): Some women shared their experience of being diagnosed with COVID-19 and its impact on breastfeeding. For instance, participants shared that they were not allowed to see their infant, while others had trouble caring for an infant while wearing a mask and face shield. In one instance, *"…I did find it more difficult to learn how to breastfeed as the mask limited my field of vision when trying to see how our baby was latching"* (P-69).

Several mothers expressed concern about breastfeeding due to being separated from their newborn: *"[The COVID-19 pandemic] made me afraid I potentially wouldn't be able to [breastfeed] for a couple weeks… For the moms who did separate from their children, they're strong as hell. But I couldn't mentally do it"* (P-16).

Social Isolation (3 responses): Some lamented the challenges that COVID-19 restrictions imposed on their postpartum experience, such as reduced opportunities for connection with other mothers and an increased sense of isolation. *"Mother-baby hour is only available virtually right now and does not provide the same opportunities for connections with other mothers that in-person meetings did"* (P-168).

Safety Concerns (2 responses): A few participants noted concerns about safety and hygiene of pumping outside of the home

that were related to the COVID-19 pandemic, such as"*[due to the COVID-19 pandemic] I worry about my pumping pieces and if it's still safe to pump"* (P-26).

Neutral Impacts of Pandemic on Breastfeeding (326 responses, 7 themes)

The majority of participants shared that the COVID-19 pandemic did not affect their breastfeeding choices and experiences, yet still provided rationale for their decisions related to breastfeeding. Seven themes on the neutral impact of the pandemic on breastfeeding were identified.

Advanced Decision-making About Breastfeeding (232 responses): The most common experience respondents expressed regarding breastfeeding was having a plan already in place. For most participants, this prior plan already included a decision to breastfeed: *"I always knew I'd want to try to breastfeed, pandemic or not, and did so for 12 weeks (P-65). Only a small proportion of respondents expressed they had made advanced plans not to breastfeed. "I didn't want to breastfeed to begin with"* (P-45).

Interestingly, even those with an advanced plan to breastfeed still had comments to share related to their pandemic experience. One mother said, *"I intended to breastfeed either way but feel it is even more important during this time"* (P-1). Another mother commented: *"I was going to breastfeed regardless of the pandemic; however, it did make me try maybe a little bit harder to make sure that my supply was good since formula was hard to come by in the beginning of the pandemic"* (P-207).

No Impact of Pandemic on Breastfeeding Choices and Experiences (60 responses): Many participants simply stated that COVID-19 did not impact their breastfeeding choices at all: *"I breast fed as long as I had milk supply; COVID-19 played no role in that"* (P-183).

Safety Planning (11 responses): *A*lthough many stated that the COVID-19 pandemic did not affect their breastfeeding decisions or experiences, their comments revealed that it was still on their mind, as indicated by contingency plans or anxieties related to choices they might make if diagnosed with COVID-19: *"We keep a strict quarantine, and I haven't had COVID (tested 8 times at the local testing center)"* (P-25).

Breastfeeding Challenges (9 responses): Some commented on the breastfeeding challenges they experienced that were unrelated to COVID-19: "*I'm not able to produce enough breast milk to feed my baby" (P-67).*

Pumping (6 responses): Despite participant comments that COVID-19 did not affect breastfeeding choices, several women shared specifically about plans for pumping. While not necessarily directly related to COVID-19, some comments suggested that pumping provided a helpful alternative for mothers who were unable to feed directly at the breast: *"Breastfeeding was challenging and my baby had difficulty latching, but I chose to exclusively pump so that she could have breastmilk for the first 6 months"* (P-162)

Medical Problems Unrelated to COVID-19 (5 responses): Several women commented on external medical factors that were unrelated to COVID-19, yet affected their breastfeeding choices: *"Baby had high bilirubin, so doctors made me put him on formula"* (P-81).

Issues with Formula (3 responses): Several participants commented on difficulties obtaining formula, even if they did not think it directly impacted their breastfeeding experience.

DISCUSSION

This study described breastfeeding attitudes, decision-making, and experiences among postpartum women during the early COVID-19 pandemic in the Northeastern and Midwestern United States. Participants noted that their breastfeeding decisions and experiences were affected by COVID-19 in a variety of ways. Pandemic-related factors that positively enabled participants' breastfeeding included additional health benefits (eg, immunity), convenience and ease, and changes in work routines, whereas impediments to breastfeeding exacerbated by the pandemic were access to lactation support and medical care, increased stress and negative effects on mental health, and COVID-19 restrictions. Factors that were unaffected by the pandemic included prior feeding intentions, as well as knowledge of the importance and benefits associated with breastfeeding.

Focusing more on the positive effects, our study findings were in accordance with other studies, in which women noted that the COVID-19 pandemic had given them more time at home to establish breastfeeding.[6,11] As of 2020, less than 20% of the female workforce had access to paid family leave following birth,[16] despite the fact that longer maternity leave is shown to increase the duration of breastfeeding.[17-19] Although these findings are not surprising, they highlight the need to review best practices to support breastfeeding for working parents. In addition to the importance of longer maternity leave, other studies have highlighted the positive effects on breastfeeding afforded by flexible work hours and lactation support in the workplace.[18,20-22] Specific workplace interventions shown to support breastfeeding include designated space for lactation and pumping, support from colleagues, and ability to work from home where possible.[22]

Similar to other studies evaluating postpartum social support during the COVID-19 pandemic,[2,6] participants in this study reported reduced support and increased stress and isolation as factors that negatively affected their breastfeeding experience. Many of the survey respondents commented on the importance of access to lactation support—especially for new parents—and yet medical support during the early pandemic was limited by early hospital discharges, reduced lactation support in hospital and outpatient settings, and limited availability of peer and community lactation support.[2,4,23] Recognizing how much these factors affect breastfeeding, the Baby-Friendly Hospital Initiative[24] provides

evidenced-based hospital practices that support lactation initiation. For their part, outpatient medical practices would do well to incorporate similar evidence-based practices[18,25] that promote and normalize breastfeeding in the office and provide immediate postpartum and lactation follow-up, with priority given to in-person lactation support.[11,26]

Unrelated to the effects of the pandemic, many participants commented on the potential immune benefits of breastfeeding. It is well known, for instance, that breastfeeding is associated with improved health outcomes in infants, including decreased rates of lower respiratory tract infection and severe diarrhea, as well as reduced obesity rates.[25] With regard to COVID-19 infection in particular, however, studies have found antibodies against the SARS-CoV-2 virus in breastmilk samples from women with a personal history of COVID-19[27,28] and those who were vaccinated against it, indicating that antibodies can be transferred to infants through breastmilk and may confer protection against infection.[29-31] This has been further substantiated by evidence that maternal receipt of 1 or more COVID-19 vaccines in pregnancy is associated with reduced risk for COVID-19-related hospitalization among infants <6 months.[32] In light of these data, which further augment participant comments on immune protection, clinicians are encouraged to have ongoing conversations about infant feeding choices with patients and to share data relevant to immune benefits that may impact breastfeeding and immunization decisions.

Limitations

This study had several limitations. Although recruitment included a variety of medical practices and diverse patient populations, respondents were mostly non-Hispanic, White, and married, with a high level of educational attainment and subjective social status, raising concern for participation bias. Despite this lack of diversity in respondents' backgrounds limiting generalizability, postpartum people comprise a vulnerable group that were negatively affected by potentially lasting challenges that were elicited from this study. Future studies should focus on a more targeted sampling from populations with greater racial, ethnic, and socioeconomic diversity. Furthermore, this study relied on participant self-report, which is an inherent limitation of survey research that can lead to response bias. Additional limitations include (1) the cross-sectional nature of the data, (2) self-selection bias, (3) only 1 independent data coder, and (4) limited survey questions with a lack of ability to follow-up or clarify responses.

CONCLUSIONS

Findings from this study offer important insights into the varied and complex ways the pandemic affected breastfeeding and related decisions. As health care institutions and policymakers look to improve breastfeeding initiation and duration rates, considering the experiences and perspectives of postpartum mothers during the COVID-19 pandemic may help shed light on potential ways to support breastfeeding in times of crisis.

Funding/Support: This study was supported by funds from the University of Wisconsin School of Medicine and Public Health and Department of Family Medicine and Community Health and from the Penn State Social Science Research Institute and the Huck Institutes of the Life Sciences.

Financial Disclosures: None declared.

Ethical Approval: The University of Wisconsin Health Sciences Institutional Review Board conducted an expedited review and approved this study (Submission ID: 2020-1350) as minimal risk on November 23, 2020. The Penn State Institutional Review Board conducted an expedited review and approved this study (Submission ID: 00015505) as minimal risk on July 22, 2020.

REFERENCES

1. Gribble K, Marinelli KA, Tomori C, Gross MS. Implications of the COVID-19 pandemic response for breastfeeding, maternal caregiving capacity and infant mental health. *J Hum Lact.* 2020;36(4):591-603. doi:10.1177/0890334420949514

2. Spatz DL, Froh EB. Birth and breastfeeding in the hospital setting during the COVID-19 pandemic. *MCN Am J Matern Child Nurs.* 2021;46(1):30-35. doi:10.1097/NMC.0000000000000672

3. Ng YPM, Low YF, Goh XL, Fok D, Amin Z. Breastfeeding in COVID-19: a pragmatic approach. *Am J Perinatol.* 2020;37(13):1377-1384. doi:10.1055/s-0040-1716506

4. Perrine CG, Chiang KV, Anstey EH, et al. Implementation of hospital practices supportive of breastfeeding in the context of COVID-19 - United States, July 15-August 20, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(47):1767-1770. doi:10.15585/mmwr.mm6947a3

5. Haiek LN, LeDrew M, Charette C, Bartick M. Shared decision-making for infant feeding and care during the coronavirus disease 2019 pandemic. *Matern Child Nutr.* 2021;17(2):e13129. doi:10.1111/mcn.13129

6. Snyder K, Worlton G. Social support during COVID-19: perspectives of breastfeeding mothers. *Breastfeed Med.* 2021;16(1):39-45. doi:10.1089/bfm.2020.0200

7. Koleilat M, Whaley SE, Clapp C. The impact of COVID-19 on breastfeeding rates in a low-income population. *Breastfeed Med*. 2022;17(1):33-37. doi:10.1089/bfm.2021.0238.

8. Latorre G, Martinelli D, Guida P, Masi E, De Benedictis R, Maggio L. Impact of COVID-19 pandemic lockdown on exclusive breastfeeding in non-infected mothers. *Int Breastfeed J.* 2021;16(1):36. doi:10.1186/s13006-021-00382-4

9. Bartick MC, Valdés V, Giusti A, et al. Maternal and infant outcomes associated with maternity practices related to COVID-19: the COVID mothers study. *Breastfeed Med.* 2021;16(3):189-199. doi:10.1089/bfm.2020.0353

10. Brown A, Shenker N. Experiences of breastfeeding during COVID-19: lessons for future practical and emotional support. *Matern Child Nutr.* 2021;17(1):e13088. doi:10.1111/mcn.13088

11. Lubbe W, Niela-Vilén H, Thomson G, Botha E. Impact of the COVID-19 pandemic on breastfeeding support services and women's experiences of breastfeeding: a review. *Int J Womens Health.* 2022;14:1447-1457. doi:10.2147/IJWH.S342754

12. Pacheco F, Sobral M, Guiomar R, de la Torre-Luque A, Caparros-Gonzalez RA, Ganho-Ávila A. Breastfeeding during COVID-19: a narrative review of the psychological impact on mothers. *Behav Sci (Basel).* 2021;11(3):34. doi:10.3390/bs11030034

13. Goldstein E, Brown RL, Lennon RP, Zgierska AE. Latent class analysis of health, social, and behavioral profiles associated with psychological distress among pregnant and postpartum women during the COVID-19 pandemic in the United States. *Birth*. 2023;50(2):407-417. doi:10.1111/birt.12664

14. StataCorp. Stata Statistical Software: Release 16; 2019. StataCorp LLC, College Station, TX.

15. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res.* 2005;15(9):1277-1288. doi:10.1177/1049732305276687

16. US Bureau of Labor Statistics. National Compensation Survey: employee benefits in

the United States, March 2020. Bulletin 2793. September 2020. Accessed January 8, 2024. https://www.bls.gov/ebs/publications/bulletin-24793-september-2020-landing-page-employee-benefits-in-the-united-states-march-2020.htm

17. Barraza L, Lebedevitch C, Stuebe A. The role of law and policy in assisting families to reach Healthy People's maternal, infant, and child health breastfeeding goals in the United States. US Department of Health and Human Services, Office of Disease Prevention and Health Promotion. May 4, 2020. Accessed January 8, 2024. https://odphp.health.gov/sites/default/files/2021-11/The%20Role%20of%20Law%20and%20Policy%20in%20Assisting%20Families%20to%20Reach%20Healthy%20People%e2%80%99s%20Maternal,%20Infant,%20and%20Child%20Health%20Breastfeeding%20Goals%20in%20the%20United%20States.pdf

18. Vanguri S, Rogers-McQuade H, Sriraman NK; Academy of Breastfeeding Medicine. ABM Clinical Protocol #14: breastfeeding-friendly physician's office-optimizing care for infants and children. *Breastfeed Med.* 2021;16(3):175-184. doi:10.1089/bfm.2021.29175.sjv

19. Hamad R, Modrek S, White JS. Paid family leave effects on breastfeeding: a quasi-experimental study of US policies. *Am J Public Health*. 2019;109(1):164-166. doi:10.2105/AJPH.2018.304693

20. Navarro-Rosenblatt D, Garmendia ML. Maternity leave and its impact on breastfeeding: a review of the literature. *Breastfeed Med.* 2018;13(9):589-597. doi:10.1089/bfm.2018.0132

21. Wicklund L, Epstein A, Szugye H, Schleicher M, Lam SK. Association between length of maternity leave and breastfeeding duration in the United States: a systematic review. *Obstet Gynecol.* 2024;143(4):e107-e124. doi:10.1097/AOG.0000000000000550

22. Vilar-Compte M, Hernández-Cordero S, Ancira-Moreno M, et al. Breastfeeding at the workplace: a systematic review of interventions to improve workplace environments to facilitate breastfeeding among working women. *Int J Equity Health.* 2021;20(1):110. doi:10.1186/s12939-021-01432-3

23. Kotlar B, Gerson EM, Petrillo S, Langer A, Tiemeier H. The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review. *Reprod Health.* 2021;18(1):10. doi:10.1186/s12978-021-01070-6

24. World Health Organization; UNICEF. Baby-Friendly Hospital Initiative: Revised, Updated and Expanded for Integrated Care. World Health Organization; 2009. Accessed January 8, 2024. https://www.who.int/publications/i/item/9789241594950

25. Meek JY, Noble L; Section on Breastfeeding. Policy statement: breastfeeding and the use of human milk. *Pediatrics*. 2022;150(1):e2022057988. doi:10.1542/peds.2022-057988

26. Meek JY, Hatcher AJ; Section on Breastfeeding. The breastfeeding-friendly pediatric office practice. *Pediatrics*. 2017;139(5):e20170647. doi:10.1542/peds.2017-0647

27. Pérez-Bermejo M, Peris-Ochando B, Murillo-Llorente MT. COVID-19: relationship and impact on breastfeeding-a systematic review. *Nutrients*. 2021;13(9):2972. doi:10.3390/nu13092972

28. Dong L, Tian J, He S, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *JAMA*. 2020;323(18):1846-1848. doi:10.1001/jama.2020.4621

29. Nir O, Schwartz A, Toussia-Cohen S, et al. Maternal-neonatal transfer of SARS-CoV-2 immunoglobulin G antibodies among parturient women treated with BNT162b2 messenger RNA vaccine during pregnancy. *Am J Obstet Gynecol MFM*. 2022;4(1):100492. doi:10.1016/j.ajogmf.2021.100492

30. Trostle ME, Aguero-Rosenfeld ME, Roman AS, Lighter JL. High antibody levels in cord blood from pregnant women vaccinated against COVID-19. *Am J Obstet Gynecol MFM*. 2021;3(6):100481. doi:10.1016/j.ajogmf.2021.100481

31. Yang YJ, Murphy EA, Singh S, et al. Association of gestational age at coronavirus disease 2019 (COVID-19) vaccination, history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and a vaccine booster dose with maternal and umbilical cord antibody levels at delivery. *Obstet Gynecol.* 2022;139(3):373-380. doi:10.1097/AOG.0000000000004693

32. Simeone RM, Zambrano LD, Halasa NB, et al. Effectiveness of maternal mRNA COVID-19 vaccination during pregnancy against COVID-19-associated hospitalizations in infants aged <6 months during SARS-CoV-2 omicron predominance - 20 states, March 9, 2022-May 31, 2023. *MMWR Morb Mortal Wkly Rep.* 2023;72(39):1057-1064. doi:10.15585/mmwr.mm7239a3

COVID-19 Pandemic-Related Perceived Loneliness as a Potential Risk Factor for Worse Outcomes Among People Who are Pregnant or Postpartum

Emma C. Allen, MD; Ellen Goldstein, PhD, MFT; Robert P. Lennon, MD, JD; Arthur Berg, PhD; Caitlin J. Regner, MD; Danielle Symons Downs, PhD; Jenae M. Neiderhiser, PhD; Rina Das Eiden, PhD; Aleksandra E. Zgierska, MD, PhD

ABSTRACT

Introduction: People in the perinatal period may be especially susceptible to the effects of social isolation and loneliness. We assessed the COVID-19 pandemic-related impact on loneliness and other outcomes in this population.

Methods: A cross-sectional anonymous survey was completed during August–November, 2020, and January–April, 2021, by people who were pregnant or postpartum in Pennsylvania and Wisconsin, respectively. Wilcoxon rank sum, Fisher exact, or chi-square tests were used to compare mental health, substance use, pregnancy-related and overall health, pandemic's life impact, and social status metrics between 2 groups of respondents: those who screened positive ("Lonely") versus negative ("Not Lonely") for loneliness. Multivariate logistic regression analysis assessed factors associated with Lonely versus Not Lonely status.

Results: Among 613 respondents, 48.8% were categorized as Lonely. Lonely individuals were more likely to be postpartum ($P = 0.01$); nulliparous ($P = 0.04$); have more pregnancy complications ($P = 0.049$); have a diagnosed mood disorder ($P < 0.001$); receive mental health care ($P < 0.001$); have elevated depression ($P < 0.001$), anxiety ($P < 0.001$), and stress ($P < 0.001$) scores; rate their social status as lower ($P < 0.001$); and endorse a worse pandemic-life impact ($P < 0.001$). A multivariate analysis identified that being postpartum (OR 0.59; 95% CI, 0.40-0.87) and having worse depression (OR 1.24; 95% CI, 1.13-1.36), stress (OR 0.41; 95% CI, 0.28-0.60), perceived social status (OR 0.83; 95% CI, 0.73-0.95), and pandemic-life impact (OR 1.79; 95% CI, 1.11-2.93) were associated with the Lonely status.

Conclusions: Early during the COVID-19 pandemic, screening positive for loneliness was associated with a worse biopsychosocial profile and more pregnancy complications among people in the perinatal period. Focusing efforts on preventing loneliness may help improve outcomes critical for maternal-fetal and child health.

• • •

Author Affiliations: Penn State College of Medicine, Hershey, Pennsylvania (Allen); University of Illinois Chicago College of Nursing, Department of Population Health Nursing Science, Chicago, Illinois (Goldstein); Penn State College of Medicine, Department of Family and Community Medicine, Hershey, Pennsylvania (Lennon, Zgierska); Penn State College of Medicine, Department of Public Health Sciences, Hershey, Pennsylvania (Berg, Zgierska); University of Wisconsin School of Medicine and Public Health, Department of Family Medicine and Community Health, and Access Community Health Centers, Madison, Wisconsin (Regner); Penn State, Departments of Kinesiology and Obstetrics and Gynecology, State College, Pennsylvania (Downs); Penn State, Department of Psychology, State College, Pennsylvania (Neiderhiser, Edien).

Corresponding Author: Aleksandra E. Zgierska, MD, PhD; Penn State College of Medicine, Department of Family and Community Medicine, 90 Hope Dr, Hershey, PA 17033; email azgierska@pennstatehealth.psu.edu; ORCID: 0000-0002-7773-6003

INTRODUCTION

Evidence from recent systematic reviews[1,2] documents the unique impact of the coronavirus disease-2019 (COVID-19) pandemic on people who are pregnant or postpartum. For example, nonessential health care services were altered, suspended, or, in some cases, canceled in an attempt to curb the spread of COVID-19 – especially among subgroups at higher risk for adverse outcomes, such as pregnant people and infants.[3] Medical professionals recommended telehealth for routine prenatal visits, postponement of nonurgent ultrasound appointments, cancellation of hospital tours, and limited access for spouses and other support persons to join patients during clinical visits, including births.[4] Although these efforts were necessary at the time to reduce morbidity and mortality, they also increased stress, anxiety, social isolation, and loneliness,[5,6] particularly among people who were pregnant or postpartum and their families.

Loneliness is a critical public health issue.[7] The detrimental effects of social isolation (ie, an objective lack of interaction with others) and loneliness (ie, the subjective feeling of the absence of a social network or companionship)[8] are well documented as having widespread prevalence.[7] These related yet distinct concepts have been associated with impaired immune responses, increased cortisol release, and

cardiovascular and overall mortality and morbidity and were further exacerbated by the COVID-19 pandemic, as underscored by the US Surgeon General's 2023 Advisory report.[7,8] Changes in family and personal health, responsibilities, lifestyle, and daily activities could make pregnancy and postpartum periods more vulnerable to the effects of social isolation and loneliness and their sequelae.[9] A systematic review by Isaacs et al found that people with high-risk pregnancies or birth complications were at increased risk for loneliness, isolation, fear, guilt, shock, grief, frustration, sadness, and anger, as well as posttraumatic stress disorder (PTSD) and depression.[10]

Overall, prepandemic research on loneliness during pregnancy and postpartum noted associations between loneliness and preterm delivery, low birthweight, and postpartum depression.[8] Studies on the COVID-19-related maternal health also suggested a negative correlation between pandemic-related stress and postpartum mental health.[11] While the growing body of evidence has examined the negative health effects of the COVID-19 pandemic in general, scant research has focused on people who are pregnant or postpartum and residing in both urban and rural communities in geographically different locations of the United States who may be at elevated risk for loneliness and its effects.

Therefore, the goal of this cross-sectional survey study was to explore the impact of pandemic-related restrictions on perceived loneliness and other health determinants and outcomes, including self-reported pregnancy complications, early during the COVID-19 pandemic when the social distancing and isolation had been most enforced. Understanding these factors can provide important insight for better supporting vulnerable perinatal people during future times of crisis in an effort to promote improved maternal and child health outcomes.

MATERIALS AND METHODS

Study methods are detailed elsewhere[11] and briefly summarized below.

Design

Adult pregnant and postpartum patients of 2 large academic health systems were invited to an participate in an online, anonymous, single-time survey inquiring about COVID-19 pandemic-related health and experiences. The survey was administered by 2 separate study sites serving a blend of urban and rural communities, one in south-central Pennsylvania (August 4–November 24, 2020) and another in south-central Wisconsin (January 15–April 15, 2021). Deidentified data from both sites were merged for analyses. The study procedures were approved by each site's Institutional Review Board.

Population

Potentially eligible individuals were identified via an electronic health record (EHR). Inclusion criteria were as follows: adult (18 years or older) patients from the participating health systems, able to read or speak English, and reporting current pregnancy or birth within the prior 6 months. Potential participants were excluded if they had a recent diagnosis of miscarriage or stillbirth.

Across both study sites, invitation letters were sent to a total of 7220 people (4409 in the first and 2811 in the second mailings). In this group, 700 individuals accessed the online survey (9.6% response rate), of which 694 were eligible and 660 (95% of eligible individuals) consented to participate in the survey. The final sample, used for the present analysis, consisted of 613 respondents (200 from Pennsylvania, 413 from Wisconsin; 92.3% of eligible participants) who completed the loneliness-focused study measures.

Survey

The study survey was drawn from prior research[12] and was designed to assess several domains: (1) health and health behaviors; (2) pregnancy and, if relevant, birth and postpartum experiences and outcomes; (3) coping, adjustment, loneliness, emotions, and feelings; (4) social support; (5) economic stability and access to and need for specific resources; (6) the impact of COVID-19 pandemic on health, health behaviors, and life events; and (7) demographic information. The measures were obtained via REDCap, a secure online research electronic data capture platform. The survey included algorithms to identify people in need of resources based on their positive screen for financial insecurity, domestic violence, depressive and anxiety symptoms, substance misuse, or inadequate health care access. The algorithm triggered the provision of "handouts" with relevant resources to those with a positive screen; the full list of all resources also was available to all interested participants.

Measures

The data for the present analysis included perceived loneliness, mental health, substance use, pregnancy-related and overall health, pandemic's life impact, social status, and demographics (eg, age, race, ethnicity, education, marital status).

Perceived loneliness, the primary outcome measure, was assessed by the UCLA 3-Item Loneliness Scale,[13] a tool validated across different populations.[14] This scale consists of 3 questions, with 1-3 Likert scale responses (1 = hardly ever, 3 = often) that yield a summary score ranging from 3 (least lonely) to 9 (most lonely); a score ≥ 6 is considered a "positive screen" for loneliness and a risk factor for worse health/well-being.[15] The Loneliness Scale's total score served as a basis for categorizing the study sample into 2 groups: Not Lonely (score <6) versus Lonely (score ≥ 6).

Mental health components were evaluated in several ways. Perceived stress was assessed by asking a single question: "What is your overall level of stress related to the COVID-19 pandemic?", with Likert scale-based responses from 1 (no stress) to 7 (extreme stress). Depressive and anxiety symptom severity were measured by the validated Edinburgh Postnatal Depression Scale (EPDS),[16]

which uses Likert scale-based responses from 0 (no, not at all) to 3 (yes, all of the time). The EPDS total score measures the severity of depressive symptoms and ranges from 0 to 30; the total score >12 constitutes a positive screen for depressive symptoms. The EPDS questions 3 through 5 comprise the anxiety subscale, with a score >5 constituting a positive screen for anxiety.[16] One question asked about the presence (yes/no) of chronic mental health conditions (mood, anxiety, or other mental health disorders), and another asked about current receipt (yes/no) of treatment for mental health disorders.

Substance use was assessed with several questions about the use of drugs in the last 3 months. For this analysis, we compiled the answers to 4 separate questions asking about the following substances (yes/no): (1) "smoked cigarettes," (2) "used e-cigarettes or vaped," (3) "excessively drinking alcohol," or (4) "regularly using other drugs." With this approach, if a participant answered "yes" to any of these 4 questions, the response was marked as "yes," and if they answered "no" to all the questions, they were marked as answering "no" to substance use.

General Health was assessed by asking about the presence ("check all that apply") of chronic conditions identified as risk factors for COVID-19 complications. The chronic medical conditions included chronic lung disease, moderate-to-severe asthma, heart condition, obesity with body mass index >40 kg/m^2, diabetes, chronic kidney disease on dialysis, liver disease, and immunocompromised status. Therefore, the number of chronic medical conditions per responder could range from zero to 8. The chronic mental health conditions included mood, anxiety, or other mental health disorders, as described above (see mental health).

Table 1. Sample Characteristics by Lonely Versus Not Lonely Status

	Overall n = 613	Lonely n = 299	Not Lonely n = 314	*P* value[a]
Age, years, mean (SD)	31.6 (4.5)	31.2 (4.5)	32.0 (4.4)	0.056
Race, yes, n (%)				0.52
Asian	25 (4.1%)	10 (3.3%)	15 (4.8%)	
Black or African American	10 (1.6%)	3 (1.0%)	7 (2.2%)	
White	529 (86.3%)	261 (87.3%)	268 (85.4%)	
Multiracial[b]	24 (3.9%)	14 (4.7%)	10 (3.2%)	
Other	25 (4.1%)	11 (3.7%)	14 (4.5%)	
Hispanic or Latino ethnicity, yes, n (%)	33 (5.4%)	15 (5.0%)	18 (5.7%)	0.69
Partnered/married, yes, # (%)	575 (93.8%)	277 (92.6%)	298 (94.9%)	0.25
Highest level of education, n (%)				0.86
Some college and above	570 (93.0%)	277 (92.6%)	293 (93.3%)	
High school degree or less	40 (6.5%)	20 (6.7%)	20 (6.4%)	
Perceived social status, mean (SD)	7.0 (1.6)	6.7 (1.7)	7.2 (1.5)	**<0.001**
Pandemic life impact, negative, n (%)	483 (78.8%)	262 (87.6%)	221 (70.4%)	**<0.001**
Pregnancy vs postpartum status, n (%)				**0.005**
Pregnant	300 (48.9%)	129 (43.1%)	171 (54.5%)	
Postpartum	313 (51.1%)	170 (56.9%)	143 (45.5%)	
Nulliparous status, yes	265 (43.2%)	142 (47.5%)	123 (39.2%)	**0.038**
Number of pregnancy complications,[c] mean (SD)	0.7 (0.9)	0.8 (1.0)	0.6 (0.8)	**0.049**
Mental Health				
Mental health disorder,[d] yes, n (%)	188 (30.7%)	121 (40.5%)	67 (21.3%)	**<0.001**
Mental health treatment, yes, n (%)	121 (19.7%)	78 (26.1%)	43 (13.7%)	**<0.001**
Depression (EPDS total score), mean (SD)	7.1 (4.7)	9.0 (4.8)	5.2 (3.8)	**<0.001**
Anxiety (EPDS subscale score), mean (SD)	3.6 (2.2)	4.4 (2.1)	2.8 (2.0)	**<0.001**
Any substance use[e] (past 3 months), yes, n (%)	19 (3.1%)	10 (3.3%)	9 (2.9%)	0.73
No. of chronic medical conditions,[f] mean (SD)	0.2 (0.5)	0.2 (0.5)	0.2 (0.4)	0.48
Perceived stress, score, mean (SD)	4.3 (1.4)	4.8 (1.2)	3.8 (1.4)	**<0.001**

Abbreviation: EPDS, Edinburgh Postnatal Depression Scale.

[a]Wilcoxon rank sum test, Fisher exact test, or chi-square test.

[b]Checked more than 1 race.

[c]Top 5 pregnancy complications (n = 613): elevated blood pressure, hypertension or preeclampsia (n = 88; 14.4%); severe nausea, vomiting, dehydration (n = 64; 10.4%); vaginal bleeding (n = 57; 9.3%); gestational or other diabetes (n = 52; 8.5%); and small fetal size or growth restriction (n = 28; 4.6%).

[d]At least 1 mental health disorder (mood, anxiety or other).

[e]Cigarettes, e-cigarettes, alcohol, and/or other drugs.

[f]Top 5 chronic medical conditions (n = 613): moderate-to-severe asthma (n = 52, 8.5%); obesity with body mass index >40 kg/m^2 (n = 38, 6.2%); immunocompromised status (n = 25, 4.1%); diabetes (n = 3, 2.1%); and chronic lung disease (n = 2, 0.3%).

Pregnancy-related health was evaluated by asking participants about their current obstetrical status (pregnant now vs being within 6 months postpartum) and whether the current/recent pregnancy was their first (nulliparous status) versus not (multiparous status). All participants were asked about complications or medical problems during their pregnancy: "Have you experienced any of the following problems during your pregnancy?" They were instructed to "check all that apply" to the following options: gestational or other diabetes; vaginal bleeding; urinary tract infection; severe nausea, vomiting, or dehydration; cervical cerclage; elevated blood pressure, hypertension, or preeclampsia; placental problems, such as placenta previa or placental abruption; blood transfusion; motor vehicle accident; small fetal size or growth restriction; and large fetal size or macrosomia. The number of complications per responder ranged from 0 to 11.

Pandemic life impact was measured by a single question: "Please indicate the extent to which you view the COVID-19 pandemic as having either a positive or negative impact on your whole life – now and for years to come," with response choices ranging from 1 through 7 (1 = extremely negative impact, 4 = no impact, 7 = extremely positive impact); responses 1 through 3 were considered to signify pandemic's negative life impact.

Perceived social status was assessed with the MacArthur Scale of Subjective Social Status, a validated measure that accounts for economic and social factors and uses 1-10 Likert-scale responses (1 = being "worst off," 10 = being "best off") to assess a person's perceived social rank relative to others in their social/societal group.[17] Perceived socioeconomic status has shown associations with health outcomes across a variety of domains.[18]

Data Analysis

All analyses were performed using R statistical analysis software (R Core Team, Version 4.0.5). Descriptive statistics (mean ± SD or frequencies) were used to characterize the total sample and the Lonely and Not Lonely groups. Bivariate comparisons of all variables were completed using Wilcoxon rank sum, Fisher exact, or chi-square tests. Variables that differed in the bivariate analyses (2-tailed $P < 0.05$) between Lonely and Not Lonely groups were included in a multivariate logistic regression analysis, which yielded odds ratios (OR), 95% confidence intervals, and *P* values to better assess factors associated with the likelihood of screening positive for loneliness. Since the EPDS anxiety subscale score is a part of the total EPDS score, the anxiety subscale score was not included in the multivariate analysis.

RESULTS

Sample Characteristics

The sample (n = 613) consisted predominantly of White (86.3%), non-Hispanic (94.6%), married/partnered (93.8%) individuals with at least some college education (93.0%) who were, on average, 31.6 ± 4.5 years old. Close to half (48.8%) screened positive for loneliness and formed the Lonely group; the remaining respondents (51.2%) formed the Not Lonely group. Approximately half of the sample reported being currently pregnant and nulliparous; one-third reported presence of a mental health disorder diagnosis; and one-fifth noted a receipt of mental health treatment. A small proportion of the respondents (3.1%) reported use of substances (eg, cigarettes, e-cigarettes, or other drugs). The majority (78.8%) noted a negative pandemic life impact and higher social status (7.0 ± 1.6). See Table 1.

The Lonely group had a higher percentage ($P < 0.05$) of nulliparous (47.5%) than multiparous (39.2 %) and postpartum (56.9 %) than pregnant (45.5 %) participants. The Lonely group reported overall worse mental health and well-being ($P < 0.05$) than the Not Lonely group, with a higher average number of reported pregnancy complications (0.8 ± 1.0 vs 0.6 ± 0.8) and more frequent reports of the presence of mental health condition (40.5% vs 21.3 %) and mental health care receipt (26.1% vs 13.7%). The Lonely group also had higher scores of depression (9.0 ± 4.8 vs 5.2 ± 3.8), anxiety (4.4 ± 2.1 vs 2.8 ± 2.0), and perceived stress (4.8 ± 1.2 vs 3.8 ± 1.4); lower perceived social status scores (6.7 ± 1.7 vs 7.2 ± 1.5); and was more likely to report a negative life impact of the pandemic (87.6 % vs 70.4 %). The groups did not statistically significantly differ in demographic characteristics, the average number of reported chronic medical conditions, or the frequency of substance use.

Table 2. Multivariate Analysis: Predictors of the Positive Loneliness Screen (Lonely Group Status)

	Odds Ratio (95% CI)	*P* value[a]
Perceived social status, score	0.86 (0.77 – 0.98)	**0.019**
Pandemic life impact, negative	1.78 (1.10 – 2.90)	**0.020**
Pregnant (vs postpartum)	0.62 (0.42 – 0.90)	**0.013**
Nulliparous, yes	1.27 (0.87 – 1.85)	0.210
Pregnancy complications, number	0.99 (0.80 – 1.22)	0.922
At least 1 mental health diagnosis, yes	1.19 (0.71 – 2.00)	0.503
Mental health treatment, yes	1.21 (0.68 – 2.16)	0.509
Depression (EPDS), total score	1.17 (1.11 – 1.23)	**< 0.001**
Stress, score	1.45 (1.24 – 1.70)	**< 0.001**

Abbreviation: EPDS, Edinburgh Postnatal Depression Scale.
[a]Wilcoxon rank sum test, Fisher exact test, or chi-square test

Factors Associated With Lonely Status

A multivariate logistic regression analysis included all variables that differed in bivariate comparisons between the Lonely and Not Lonely groups (Table 1) to better assess the correlates of a positive screen for loneliness. Those in the Lonely group were more likely to be postpartum than pregnant (OR 0.59; 95% CI, 0.40-0.87) and to have higher EPDS-based depressive symptoms (OR 1.24; 95% CI, 1.13-1.36), stress (OR 0.41; 95% CI, 0.28-0.60), and negative pandemic's life impact (OR 1.79, 95% CI, 1.11-2.93) scores, as well as a lower perceived social status score (OR 0.83; 95% CI, 0.73-0.95). See Table 2.

DISCUSSION

During the first year of the COVID-19 pandemic, among people who were pregnant or postpartum and resided in urban and rural communities of Pennsylvania and Wisconsin, those who screened positively for loneliness versus those with a negative screen reported worse subjective social status and pandemic life impacts, more pregnancy complications, worse depression/anxiety and stress symptoms, and being more likely to have a mood disorder and receive mental health treatment. They were also more likely to be first-time parents and postpartum. These findings are important as they illustrate the associations between perceived loneliness and numerous negative health measures with documented relevance to pregnancy outcomes and the well-being of pregnant/postpartum persons, their families, and children.[19] The fact that first-time mothers seemed to be more affected is also concerning, as early parenthood is the time marked in general by parental worries and increased risk of postpartum depression.[20]

Research Implications

Whether the subjective feeling of loneliness changed for individu-

als before versus during versus after the pandemic is unclear.[21] However, it is possible the pandemic could have served as an extreme exacerbating event that brought to light a condition already experienced during the perinatal period.[21] Although the prepandemic data on loneliness/social isolation in pregnancy are limited, prior studies confirm that the pandemic increased social isolation and, in turn, loneliness in this population.[22] Future research could assess the loneliness and its correlates now, after the acute effects of the COVID-19 pandemic have subsided. Although our study did not include a racially or ethnically diverse sample, existing evidence documents the negative effect of loneliness during the COVID-19 pandemic on maternal mental health, with higher levels of loneliness associated with worse depression,[23] perceived stress, and social supports—particularly for women of color[24]—calling for more research in this population. In turn, an increase in maternal psychiatric distress has been implicated in worse maternal-fetal and child outcomes.[25]

Clinical Implications

People who are pregnant or postpartum are at increased risk for mental health disorders; our results further underscore the need for close monitoring and screening for mental health problems—especially among those experiencing loneliness—and during the times of increased isolation, such as the COVID-19 pandemic. Traditional screening tools used in the perinatal setting include the Patient Health Questionnaire (PHQ)-9[26] and EPDS[16] for depression and the GAD-7[27] for anxiety; screening for loneliness also should be considered. The 3-item Loneliness Scale[13-15] could be a time-saving, cost-effective, and user-friendly addition to the maternal screening toolbox to help identify individuals at higher risk for adverse pregnancy and/or postpartum complications. Referrals to social services early during pregnancy could be considered for individuals who screen positive for loneliness. According to the US Surgeon General's 2023 Advisory,[7] a National Strategy to Advance Social Connection is a critical next step in making strides to strengthen social connections and rebuild community and to enhance our overall health and well-being. The Advisory's agenda is a whole-societal approach, envisioning equitable access and distribution of resources, that will require sustained investment and an evidence-based approach to kindle and renew a sense of shared and common kinship.

Strengths and Limitations

This study was strengthened by the robust sample size and geographic distribution. Sampling from 2 different regions of the US, including from both rural and urban communities, may support the generalizability to the rest of the US population. However, the lack of sample diversity, with the vast majority of respondents identifying as White, non-Hispanic females with a college education, may limit result generalizability to other demographic populations. Although we did not collect demographic details that would allow us to utilize participant-level geocoding and urbanicity status determination, our results are likely applicable to rural residents because the service catchment of the collaborating health systems include robust representation of rural patients in central Wisconsin and south-central Pennsylvania. Our survey included multiple validated surveys targeting specific domains, eg, depression/anxiety and loneliness, that can further increase the generalizability of our findings.

We recognize this study also had important limitations. The survey was administered early during the pandemic (August 2020-April 2021) when mask mandates, online schooling, and remote work were still widely practiced and before COVID-19 vaccines were available to the public. If it had been administered later—especially after the vaccination rollout and social distancing restrictions had been lifted—it could have influenced the findings; it is unknown if the between-group differences would have persisted. Another limitation involved the subjective nature of the clinical and obstetric health reports. Depending on the participant's health literacy, they may have incorrectly reported the pregnancy complications or health problems they experienced. However, the overall readability score of the survey was 6.3, which can be interpreted as a 6th grade reading level, and 93.4% of the sample reported completed high school and had at least some college education.

CONCLUSIONS

Early during the COVID-19 pandemic, many people during their perinatal period screened positively for loneliness, which, in turn, was associated with a worse biopsychosocial profile and more pregnancy complications. Focusing efforts on preventing and mitigating loneliness may help improve outcomes critical for maternal-fetal and child health. Future studies should further assess this relationship—especially any potential causality—and investigate perceived loneliness and its impact on birth outcomes and newborn care, particularly in rural and underserved communities to inform future clinical services, research funding, strategic initiatives, and policy agendas.

Funding/Support: This project was supported by funding from Penn State Social Science Research Institute and Huck Institutes of the Life Sciences and the University of Wisconsin School of Medicine and Public Health. Content is the responsibility of the authors and does not represent the views of the funders.

Financial Disclosures: None declared.

REFERENCES

1. Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM*. 2020;2(2):100107. doi:10.1016/j.ajogmf.2020.100107

2. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *CMAJ*. 2021;193(16):E540-E548. doi:10.1503/cmaj.202604

3. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019

(COVID-19) on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol.* 2020;56(1):15-27. doi:10.1002/uog.22088

4. Boelig RC, Saccone G, Bellussi F, Berghella V. MFM guidance for COVID-19. *Am J Obstet Gynecol MFM*. 2020;2(2):100106. doi:10.1016/j.ajogmf.2020.100106

5. Rumas R, Shamblaw AL, Jagtap S, Best MW. Predictors and consequences of loneliness during the COVID-19 pandemic. *Psychiatry Res.* 2021;300:113934. doi:10.1016/j.psychres.2021.113934

6. Ernst M, Niederer D, Werner AM, et al. Loneliness before and during the COVID-19 pandemic: a systematic review with meta-analysis. *Am Psychol.* 2022;77(5):660-677. doi:10.1037/amp0001005

7. Office of the Surgeon General (OSG). Our Epidemic of Loneliness and Isolation: The U.S. Surgeon General's Advisory on the Healing Effects of Social Connection and Community. US Dept of Health and Human Services; 2023. Accessed December 11, 2024. https://www.hhs.gov/sites/default/files/surgeon-general-social-connection-advisory.pdf

8. Leigh-Hunt N, Bagguley D, Bash K, et al. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health.* 2017;152:157-171. doi:10.1016/j.puhe.2017.07.035

9. Rokach A. Self-perception of the antecedents of loneliness among new mothers and pregnant women. *Psychol Rep.* 2007;100(1):231-243. doi:10.2466/pr0.100.1.231-243

10. Isaacs NZ, Andipatin MG. A systematic review regarding women's emotional and psychological experiences of high-risk pregnancies. *BMC Psychol.* 2020;8(1):45. doi:10.1186/s40359-020-00410-8

11. Goldstein E, Brown RL, Lennon RP, Zgierska AE. Latent class analysis of health, social, and behavioral profiles associated with psychological distress among pregnant and postpartum women during the COVID-19 pandemic in the United States. *Birth*. 2023;50(2):407-417. doi:10.1111/birt.12664

12. Thomason ME, Graham A, VanTieghem MR. The COPE-IS: Coronavirus Perinatal Experiences – Impact Survey. PhenX Toolkit. Updated April 7, 2020. Accessed December 11, 2024. https://www.phenxtoolkit.org/toolkit_content/PDF/COS_COPE_IS.pdf

13. Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A short scale for measuring loneliness in large surveys: results from two population-based studies. *Res Aging.* 2004;26(6):655-672. doi:10.1177/0164027504268574

14. Russell DW. UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. *J Pers Assess.* 1996;66(1):20-40. doi:10.1207/s15327752jpa6601_2

15. Matthews T, Bryan BT, Danese A, Meehan AJ, Poulton R, Arseneault L. Using a loneliness measure to screen for risk of mental health problems: a replication in two nationally representative cohorts. *Int J Environ Res Public Health.* 2022;19(3):1641. doi:10.3390/ijerph19031641

16. Smith-Nielsen J, Matthey S, Lange T, Væver MS. Validation of the Edinburgh Postnatal Depression Scale against both DSM-5 and ICD-10 diagnostic criteria for depression. *BMC Psychiatry.* 2018;18(1):393. doi:10.1186/s12888-018-1965-7

17. Galvan MJ, Payne BK, Hannay J, Georgeson AR, Muscatell KA. What does the MacArthur Scale of Subjective Social Status measure? Separating economic circumstances and social status to predict health. *Ann Behav Med*. 2023;57(11):929-941. doi:10.1093/abm/kaad054

18. Donahoe JT, McGuire TG. The vexing relationship between socioeconomic status and health. *Isr J Health Policy Res.* 2020;9(1):68. doi:10.1186/s13584-020-00430-0

19. Kent-Marvick J, Simonsen S, Pentecost R, Taylor E, McFarland MM. Loneliness in pregnant and postpartum people and parents of children aged 5 years or younger: a scoping review. *Syst Rev.* 2022;11(1):196. doi:10.1186/s13643-022-02065-5

20. Leonard KS, Evans MB, Kjerulff KH, Symons Downs D. Postpartum perceived stress explains the association between perceived social support and depressive symptoms. *Womens Health Issues.* 2020;30(4):231-239. doi:10.1016/j.whi.2020.05.001

21. Murthy VH. COVID-19 pandemic underscores the need to address social isolation and loneliness. *Public Health Rep*. 2021;136(6):653-655. doi:10.1177/00333549211045425

22. Basu A, Kim HH, Basaldua R, et al. A cross-national study of factors associated with women's perinatal mental health and wellbeing during the COVID-19 pandemic. *PLoS One*. 2021;16(4):e0249780. doi:10.1371/journal.pone.0249780

23. Perzow SED, Hennessey EP, Hoffman MC, Grote NK, Davis EP, Hankin BL. Mental health of pregnant and postpartum women in response to the COVID-19 pandemic. *J Affect Disord Rep*. 2021;4:100123. doi:10.1016/j.jadr.2021.100123

24. Giurgescu C, Wong AC, Rengers B, et al. Loneliness and depressive symptoms among pregnant Black women during the COVID-19 pandemic. *West J Nurs Res.* 2022;44(1):23-30. doi:10.1177/01939459211043937

25. Bernard-Bonnin, AC; Canadian Paediatric Society, Mental Health and Developmental Disabilities Committee. Maternal depression and child development. *Paediatr Child Health.* 2004;9(8):575-598. doi:10.1093/pch/9.8.575

26. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16(9):606-613. doi:10.1046/j.1525-1497.2001.016009606.x

27. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097. doi:10.1001/archinte.166.10.1092

Fish Consumption Advisory Awareness and Behavior Among Asian Women of Childbearing Age — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023

Elizabeth J. Polter, PHD, MPH;* Matthew Schinwald, MS;* Amanda Haban, MPH; Jon Meiman, MD; Carrie Tomasallo, PhD, MPH

ABSTRACT

Introduction: Asian persons in the Milwaukee, Wisconsin, area might be more susceptible to contaminant exposure because of high consumption of local sportfish and store-purchased fish. This is a particular risk to women who are pregnant or might become pregnant and breastfeeding women because of health risks to the developing fetus or child's neurological system.

Methods: We conducted a survey among women of childbearing age from 4 Asian ethnic groups (Hmong, Karen, Chinese, and Filipino) residing in the Milwaukee area to assess self-reported fish consumption from different sources, fish preparation behaviors, fish consumption behaviors during pregnancy and breastfeeding, and awareness of local and national fish consumption advisories and limits.

Results: Participants included 153 women aged 18 to 50 years. Seventy-one (46%) had consumed ≥1 sport-caught or store-purchased species at levels above a local, state, or federal advisory. Participants reported consuming a median of 11 Wisconsin sportfish and 24 store-purchased fish meals each year. Approximately half of participants reported reducing fish consumption or changing fish preparation methods to avoid contaminants. Overall, 62 (41%) were aware of any fish consumption advisory.

Conclusions: Self-reported fish consumption habits among certain Hmong, Karen, Chinese, and Filipino women of child-bearing age were higher than local, state, or federal advisories, and approximately half of participants self-reported awareness of local or federal fish consumption advisories. Reaching Asian diaspora communities with culturally appropriate educational materials regarding safe fish consumption might help reduce contaminant exposure.

INTRODUCTION

Despite well-documented health benefits,[1,2] consumption of certain sport-caught and store-purchased fish can also increase exposure to contaminants such as mercury, perfluoroalkyl and polyfluoroalkyl substances (PFAS), and polychlorinated biphenyls (PCB).[3] High levels of contaminants in the freshwaters of Milwaukee, Wisconsin, could pose a particular risk to residents. The 1987 Great Lakes Water Quality Agreement designated the Milwaukee Estuary an Area of Concern (AOC).[4] The Milwaukee AOC includes Milwaukee's major rivers (Kinnickinnic, Menomonee, and Milwaukee), inner and outer harbors, and nearshore area of Lake Michigan.[4] To protect anglers from high levels of contaminants in these waters, the Wisconsin Department of Natural Resources (DNR) recommends limited consumption of certain species caught in the Milwaukee AOC.[5]

The US Food and Drug Administration (FDA) and US Environmental Protection Agency (EPA) also have published advisories to help consumers maximize the health benefits of fish consumption while reducing contaminant exposure. Federal advisories include limiting consumption of store-purchased fish species with high contaminant levels and avoiding specific preparation methods (eg, boiling and poaching) and fish parts (eg, skin and head).[1,6]

Exposure to contaminants in fish is a particular risk to women who are pregnant or might become pregnant[7] and breastfeeding women, because of health risks to the developing fetus's or child's neurological system.[8] Prenatal exposure to mercury, PCBs, and/or

Author Affiliations: Wisconsin Department of Health Services, Madison, Wisconsin (Polter, Schinwald, Haban, Meiman, Tomasallo); Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia (Polter). *Denotes co-first authors.

Corresponding Author: Elizabeth Polter, Wisconsin Department of Health Services, 1 W Wilson St, Ste 150, Madison, WI 53703; phone 608.266.7480; email Ura1@cdc.gov; ORCID ID 0000-0001-7336-3492

PFAS may lead to low birthweight[9,10] and neurodevelopmental disorders.[11,12] Thus, it is particularly important that women of childbearing age know and follow fish consumption advisories.

In 2021, an estimated 74 977 persons of Asian descent resided in the 4 counties of the Milwaukee AOC (Milwaukee, Ozaukee, Washington, and Waukesha counties). Over half (40 418; 54%) were born outside the United States.[13] To capture the experiences of heterogeneous Asian communities in Milwaukee, we focused on 4 groups: Hmong, Karen, Chinese, and Filipino. Approximately 24% of Asian people in the Milwaukee area are Hmong, of whom one-third were born in the United States.[13] Additionally, approximately 6029 refugees from Burma arrived in the area between 2000 and 2021,[14] many of whom are of Karen ethnicity. Two additional ethnic groups, Chinese and Filipino, also have large, primarily foreign-born populations in the Milwaukee area.[13]

Previous studies reported that Asian immigrants residing in urban areas of North America consume fish more often and have higher blood and hair levels of mercury than non-Asian residents of the same areas.[15-20] Our prior study assessing fish consumption and advisory awareness among Burmese refugees residing in the 4 counties of the Milwaukee AOC found that most were unaware of local and state safe-eating fish advisories and limits.[21] During 2021, our team conducted a focus group to understand the influence of culture, attitudes, and beliefs on the fish consumption habits of Asian women of childbearing age (WCBA) who resided in the 4 counties of the Milwaukee AOC.[22] Focus group participants reported eating local sportfish (fish caught in local waters by participants or persons they knew) because of availability, taste, and cost savings. All participants were aware of contaminant risks in fish. However, only a limited number had specific knowledge of fish consumption advisories, and many believed they did not have the self-efficacy to avoid contaminants. Focus group participants who reported high self-efficacy were more willing to follow health messages.[22]

As a quantitative complement to our focus group study, we conducted a cross-sectional survey to better understand fish consumption choices and fish advisory awareness among Asian WCBA who reside in the Milwaukee area.

Table 1. Demographic Characteristics of 153 Asian Women of Childbearing Age by Ethnicity — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023

	Total (N = 153)	Chinese (N = 37)	Filipino (N = 12)	Hmong (N = 52)	Karen (N = 52)
Age, years; mean (SD)	34 (8.3)	38 (9.3)	37 (6.1)	34 (8.1)	29 (6.5)
Years in the United States, mean (SD)	20 (13)	18 (11)	22 (13)	33 (7.3)	8.3 (3.2)
Years in Milwaukee area, mean (SD)	14 (11)	9.8 (8.5)	14 (7.2)	25 (11)	7.2 (3.2)
Household income,[a] No. (%)					
≤ $24,999	21 (14)	4 (11)	1 (8)	5 (10)	11 (21)
$25,000–$$49,999	51 (33)	1 (3)	2 (17)	10 (19)	38 (73)
$50,000–$74,999	19 (12)	5 (14)	2 (17)	10 (19)	2 (4)
$75,000–$99,999	22 (14)	5 (14)	4 (33)	12 (23)	1 (2)
≥ $100,000	40 (26)	22 (59)	3 (25)	15 (29)	0
Education, No. (%)					
No high school diploma	27 (18)	1 (3)	0	1 (2)	25 (48)
High school diploma or GED	29 (19)	3 (8)	1 (8)	7 (13)	18 (35)
Some college	15 (10)	1 (3)	1 (8)	10 (19)	3 (6)
Associate or bachelor's degree	56 (37)	16 (43)	7 (58)	27 (52)	6 (12)
Postgraduate, professional, or doctoral degree	26 (17)	16 (43)	3 (25)	7 (13)	0
Employment, No. (%)					
Full-time	82 (54)	18 (49)	7 (58)	42 (81)	15 (29)
Part-time	30 (20)	11 (30)	1 (8)	6 (12)	12 (23)
Unemployed	41 (26)	8 (22)	4 (33)	4 (8)	25 (48)
Does anyone in your household use SNAP or WIC services, No. (%)					
Yes	51 (33)	2 (5)	3 (25)	11 (21)	35 (67)
No	102 (67)	35 (95)	9 (75)	41 (79)	17 (33)
Cigarette use, No. (%)					
Every day	3 (2)	0	0	3 (6)	0
Some days	1 (1)	0	0	1 (2)	0
Not at all	149 (97)	37 (100)	12 (100)	48 (92)	52 (100)

Abbreviations: GED, General Educational Development; SNAP, Supplemental Nutrition Assistance Program; WIC, Women, Infants, and Children.

[a]Participants were asked whether their per year income was < $15,000; $15,000–$24,999; $25,000–$34,999; $35,000–$49,999; $50,000–$74,999; $75,000–$99,999; or ≥$100,000. Categories were collapsed as shown above based on sample size.

METHODS

Recruitment and Eligibility

The Wisconsin Department of Health Services (DHS) conducted this survey during January 1, 2022–January 31, 2023. Participants were recruited through community-based convenience and snowball sampling. Community advisory group members, schools, DNR listservs, and community organizations distributed recruitment materials to potentially eligible persons. We also asked participants who completed the survey to recruit additional participants within their social networks.

Eligible participants must have met the following criteria: (1) residing ≥1 year in the following Wisconsin counties: Milwaukee, Waukesha, Washington, or Ozaukee; (2) female; (3) self-identified as 1 of 4 major Asian ethnicities in the Milwaukee area: Chinese, Filipino, Hmong, or Karen; (4) aged 18 to 50 years; (5) had consumed ≥1 meal of fish caught from waterbodies in Wisconsin in the last 12 months by the participant or someone the participant knows; (6) the only member of their household to participate in

Table 2. Fish Consumption During the Preceding Year of 153 Asian Women of Childbearing Age by Ethnicity – Milwaukee, Wisconsin, January 1, 2022–January 31, 2023

	Total[a] (N = 153)		Chinese (N = 37)		Filipino (N = 12)		Hmong (N = 52)		Karen (N = 52)	
	Median Annual Meals (IQR)	No. (%) Who Exceeded Consumption Advisories	Median Annual Meals (IQR)	No. (%) Who Exceeded Consumption Advisories	Median Annual Meals (IQR)	No. (%) Who Exceeded Consumption Advisories	Median Annual Meals (IQR)	No. (%) Who Exceeded Consumption Advisories	Median Annual Meals (IQR)	No. (%) Who Exceeded Consumption Advisories
Wisconsin sport-caught	11 (5–23)	12 (8)	10 (4–20)	1 (3)	24 (14–33)	0	10 (5–26)	7 (13)	10 (4–19)	2 (4)
Milwaukee sport-caught	6 (2–18)	50 (33)	6 (2–12)	15 (41)	11 (2–21)	3 (25)	5 (1–14)	12 (23)	7 (3–19)	20 (38)
Store-purchased	20 (9–46)	33 (22)	54 (27–80)	13 (35)	33 (20–62)	3 (25)	14 (6–25)	7 (13)	16 (9–31)	10 (19)
All fish[b]	40 (18–64)	71 (46)	63 (39–90)	22 (59)	72 (46–89)	5 (42)	29 (15–51)	18 (35)	31 (17–49)	26 (52)

Abbreviation: IQR, interquartile range.

[a]The total number of fish meals per participant was calculated as a tally of self-reported meals eaten of all species from each source in the preceding year.

[b]The total number of all fish meals was the sum of Wisconsin sportfish (including Milwaukee Estuary Area of Concern sportfish) and store-purchased fish). The total number of participants exceeding advisories was the number reporting consumption of any Wisconsin, Milwaukee area, or store-purchased fish above advisory levels.

the telephone survey; and (7) had not participated in a previous project about fish consumption with Wisconsin DHS.

Interested participants completed a screening survey to determine eligibility. Screening surveys written in English, Chinese, and Hmong were administered through REDCap instruments hosted by DHS. Based on community feedback, Filipino participants received information in English. As many persons in the Karen community do not have reliable access to email, screening forms written in Karen were administered by mail.

Data Collection

Trained interviewers administered the survey in each participant's preferred language (English, Chinese, Hmong, or Karen) by telephone. Prior to each interview, we mailed or emailed visual aids to participants that included a map of the waterbodies in the Milwaukee AOC and photographs of each fish species or variety evaluated. Survey items assessed participant demographics, fish consumption habits, health beliefs about fish, and awareness of fish advisories. Participants received a $50 gift card for completing the survey.

Table 3. Fish Consumption Behaviors and Behavior Changes Among Asian Women of Childbearing Age — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023

	Total (N = 153)	Chinese (N = 37)	Filipino (N = 12)	Hmong (N = 52)	Karen (N = 52)
	No. Responding "Yes" (%)				
Have you ever made the following changes to avoid mercury or polychlorinated biphenyls (PCBs)?					
Eaten fewer fish meals	60 (39)	13 (35)	4 (33)	27 (52)	16 (31)
Eaten different types or species of fish	76 (50)	23 (62)	6 (50)	22 (42)	25 (48)
Avoided eating certain parts of fish (head, fat, belly, skin)	80 (52)	17 (46)	3 (25)	27 (52)	33 (63)
Avoided eating fish from some fishing locations	78 (51)	21 (57)	4 (33)	26 (50)	27 (52)
	No. Responding "Sometimes," "Very Often," or "Always" (%)				
When preparing fish, how often do you or the person who prepares your fish use:					
Skin of the fish	132 (86)	34 (92)	11 (92)	42 (81)	45 (87)
Head of the fish	119 (78)	28 (76)	8 (67)	42 (81)	41 (79)
Guts, organs, or other innards of the fish	20 (13)	1 (3)	1 (8)	7 (13)	11 (21)
Belly fat of the fish	20 (13)	1 (3)	1 (8)	7 (13)	11 (21)
When cooking fish, how often do you or the person who prepares your fish:					
Smoke or dry fish	41 (27)	7 (19)	5 (42)	12 (23)	17 (33)
Pickle fish	9 (6)	2 (5)	0	3 (6)	4 (8)
Use fish to make fish paste	7 (5)	2 (5)	1 (8)	1 (2)	3 (6)
Pan fry	129 (84)	29 (78)	11 (92)	47 (90)	42 (81)
Grill, or roast fish	106 (69)	21 (57)	11 (92)	41 (79)	33 (63)
Deep fry fish	109 (71)	15 (41)	9 (75)	44 (85)	41 (79)
Boil or poach fish	98 (64)	22 (59)	7 (58)	46 (88)	23 (44)
Braise fish	55 (36)	18 (49)	2 (17)	14 (27)	21 (40)
Use fish or fish parts to make broth, stock, curry, or soup	90 (59)	15 (41)	6 (50)	27 (52)	42 (81)

Self-Reported Fish Consumption During Preceding Year

We assessed consumption of 27 sportfish species and 13 store-purchased fish varieties. For each sportfish species, interviewers asked, "In the past 12 months, how many times did you eat [species] from Wisconsin waterbodies?" Then, if participants reported any consumption of the species in Wisconsin waterbodies, the question was repeated for the Milwaukee AOC. Participants also reported their consumption of several store-purchased fish species.

Fish Preparation and Consumption Behaviors, and Fish Consumption Advisory Awareness

Participants reported whether they had made fish consumption changes to avoid contaminants, including eating fewer fish meals, eating different types of fish, avoiding certain parts of fish, or avoiding fish caught in certain locations. Using a 5-point Likert scale, participants reported how often they consumed parts of fish that might increase contaminant exposure (ie, skin, head, guts, organs or other innards, or belly fat). They reported which preparation methods they used to grill or roast fish, including an EPA-recommended

option to reduce contaminant exposure. Additionally, the EPA recommends avoiding several fish preparation options, including pan frying, deep frying, boiling or poaching, braising, or using fish or fish parts to make broth, stock, curry, or soup. Finally, 3 options without an associated EPA recommendation, including smoking or drying fish, pickling fish, and using fish to make fish paste were included.[23]

Participants who indicated a prior pregnancy described any changes to their fish consumption during pregnancy and breastfeeding. Finally, all participants reported their awareness of sportfish advisories for Wisconsin and the Milwaukee AOC and FDA or EPA limits for store-purchased fish. Those who were aware of any fish advisory answered items assessing attitudes towards the advisories.

Fish Consumption Limits

For Wisconsin sportfish, we used limits provided by the Wisconsin DNR for the Milwaukee AOC, and for general Wisconsin Inland Waters.[5] For store-purchased fish, we used fish consumption limits set by the FDA and EPA.[1] For fish consumption advisories' limits for consuming fish of the same species but different sizes (eg, ≤6 meals per year for walleye >22 inches and ≤1 meal per month for walleye <22 inches), we used the more restrictive limit. For species that did not have a specific limit for the Milwaukee AOC, we used the Wisconsin Inland Waters limit.[5]

Statistical Analysis

We summarized participant characteristics and self-reported beliefs, behaviors regarding fish consumption during pregnancy and while breastfeeding, and knowledge of fish consumption advisories. We calculated means and standard deviations for continuous variables and frequencies and percentages for categorical variables. We dichotomized Likert scale items for analysis (eg, "extremely effective" or "very effective" vs "somewhat effective," "a little effective," and "not at all effective").

For fish consumption in the preceding

Table 4. Fish Consumption Behavior During Most Recent Pregnancy Among Asian Women of Childbearing Age — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023

	Total (N = 153)	Chinese (N = 37)	Filipino (N = 12)	Hmong (N = 52)	Karen (N = 52)
Have you ever been pregnant?					
Yes, n (%)	113 (74)	25 (68)	12 (100)	36 (69)	40 (77)
If you have ever been pregnant, did you eat fish during your most recent pregnancy?					
Yes, n (%)	89 (79)	22 (88)	10 (83)	21 (58)	36 (90)
If you reported consuming fish during your most recent pregnancy, what was the frequency of your fish consumption during that pregnancy vs before pregnancy?					
Decrease, n (%)	26 (30)	5 (23)	4 (40)	8 (38)	9 (26)
Same, n (%)	55 (63)	13 (59)	6 (60)	10 (48)	26 (74)
Increase, n (%)	7 (8)	4 (18)	0 (0)	3 (14)	0 (0)
In the time before your most recent pregnancy, did you eat the same fish species?					
Yes, n (%)	79 (89)	19 (86)	8 (80)	18 (86)	34 (94)
Did you avoid eating certain fish species during your most recent pregnancy?					
Yes, n (%)	31 (35)	7 (32)	6 (60)	10 (48)	8 (22)
I didn't eat fish during my most recent pregnancy because (n)	24	3	2	15	4
I was concerned that the chemicals in fish were harmful to my baby's health, n (%)	19 (79)	2 (67)	2 (100)	13 (87)	2 (50)
I did not like the taste of fish meals, n (%)	1 (4)	0 (0)	0 (0)	0 (0)	1 (25)
I was concerned that eating fish during pregnancy can make delivery difficult, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
I did not have time to clean and prepare fish, n (%)	3 (13)	1 (33)	0 (0)	2 (13)	0 (0)

Table 5. Fish Consumption Behavior While Breastfeeding Among Asian Women of Childbearing Age by Ethnicity — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023

	Total	Chinese	Filipino	Hmong	Karen
Of participants who reported a previous pregnancy (n):	112	25	12	36	39
Did you breastfeed after your last pregnancy?[a]					
Yes, n (%)	75 (67)	23 (92)	8 (67)	21 (58)	23 (59)
Of participants who reported breastfeeding after most recent pregnancy (n):	75	23	8	21	23
Did you eat fish when you were breastfeeding?					
Yes, n (%)	57 (76)	22 (96)	7 (88)	9 (43)	19 (83)
Of participants who reported eating fish while breastfeeding after most recent pregnancy (n):	57	22	7	9	19
Fish consumption frequency while breastfeeding vs before pregnancy					
Decrease, n (%)	8 (14)	5 (23)	0 (0)	3 (33)	0 (0)
Same, n (%)	43 (75)	12 (55)	7 (100)	6 (67)	18 (95)
Increase, n (%)	6 (11)	5 (23)	0 (0)	0 (0)	1 (5)
While you were breastfeeding, did you eat the same fish species?					
Yes, n (%)	50 (88)	18 (82)	6 (86)	8 (89)	18 (95)
Did you avoid eating certain fish species while breastfeeding?					
Yes, n (%)	39 (68)	8 (36)	3 (43)	2 (22)	5 (26)
Of participants who breastfed after their most recent pregnancy and reported not eating fish while breastfeeding (n):	18	1	1	12	4
I didn't eat fish while breastfeeding because I was concerned that chemicals in fish were harmful to my baby's health.					
Yes, n (%)	9 (50)	1 (100)	1 (100)	5 (42)	2 (50)
I didn't eat fish while breastfeeding because I did not have time to clean and prepare fish.					
Yes, n (%)	2 (11)	0 (0)	1 (100)	1 (8)	0 (0)
I didn't eat fish while breastfeeding because I did not like the taste.					
Yes, n (%)	3 (17)	0 (0)	0 (0)	2 (17)	1 (25)

[a]One participant selected "prefer not to answer."

year, we calculated the median and range for each sport-caught and store-purchased species. For each individual species, we compared self-reported consumption to advisories to determine the number of participants reporting consumption above the advisory. For all species, limits for weekly or monthly consumption were multiplied by 52 or 12, respectively, to calculate limits for annual consumption.

We compared the proportion of Asian WCBA aware of Milwaukee, Wisconsin, and EPA and FDA advisories with consumption over advisory limits for any Milwaukee or store-purchased species, respectively. We conducted chi-square tests to determine whether awareness of advisories was associated with consumption over advisory limits in the preceding year. Analyses were completed using R version 4.1.3 (R Core Team, 2021). This activity was reviewed by the Centers for Disease Control and Prevention (CDC), deemed not research, and conducted consistent with applicable federal law and CDC policy (45 CFR part 46.102(l)(2), 21 CFR part 56; 42 USC Sect 241(d); 5 USC Sect 552a; 44 USC Sect 3501 et seq).

RESULTS

A total of 153 Asian WCBA participated, including 37 Chinese, 12 Filipino, 52 Hmong, and 52 Karen. The average participant age was 34 years (SD = 8.3 years) (Table 1). Overall, participants had resided in the Milwaukee area and United States for an average of 14.4 years (SD = 11.1 years) and 19.9 years (SD = 12.9 years), respectively. Hmong participants had resided in the Milwaukee area an average of 25 years, whereas Karen participants had resided in the Milwaukee area an average of 7.2 years. Compared with Chinese and Filipino participants, a higher proportion of Hmong and Karen participants were in lower income and education categories. Approximately three-quarters of Chinese, Filipino, and Hmong participants were employed full- or part-time, whereas approximately half (48%) of Karen participants were unemployed (Table 1).

Fish Consumption

Overall, participants reported annually consuming a median of 11 (interquartile range [IQR] 5-23) Wisconsin sportfish meals, including 6 (IQR 2-18) from the Milwaukee AOC, and a median of 20 store-purchased fish meals (IQR 9-46). Among the 4 ethnic groups, Chinese participants reported the highest store-purchased fish consumption, and Filipino participants reported the highest sportfish consumption (Table 2). One-third of participants (n=50, 33%) reported consumption above advisory levels for ≥1 species from the Milwaukee AOC (Table 2). For store-purchased fish, 33 participants (22%) reported consumption above advisory levels for ≥1 store-purchased species (Table 2). However, average self-reported consumption for each individual fish species was low; only 1 sport-caught species (total Wisconsin white bass) and 2 store-purchased species (salmon and tilapia) had median consumption above zero (Supplemental Tables 1 and 2). Most participants who reported fish consumption exceeding advisory levels reported a limited number of meals for a fish species with zero limit (ie, species listed as, "do not eat" or "choices to avoid"). For example, 44 (29%) participants reported eating carp (listed "do not eat") from the Milwaukee AOC (Supplemental Table 1). However, among this group, the median annual carp consumption was only 2 meals (Supplemental Table 1). For store-purchased fish, 23 participants ate king mackerel, 4 ate shark, 10 ate swordfish, and 3 ate tilefish – all of which were classified as fish "choices to avoid" (Supplemental Table 2).

Fish Preparation Behaviors

Certain participants reported they had made behavior changes to avoid harmful contaminants from fish. Sixty (39%) participants reported eating fewer fish meals, 76 (50%) reported eating different species of fish, and 80 (52%) avoided eating certain parts of the fish. However, most participants reported keeping the skin (86%) or head (78%) of fish at least some or most of the time while preparing fish. Additionally, 146 (95%) participants reported sometimes using cooking methods that can trap fat (and consequently, contaminants) within the fish. This included pan-frying (n = 129, 84%), boiling or poaching (n = 98, 64%), or using the fish in a broth or soup (n = 90, 59%). Hmong participants (n = 27, 52%) reported eating fewer fish meals to reduce contaminant exposure, compared with approximately one-third of Chinese, Filipino, and Karen participants. Other behavior changes varied across ethnic groups. For example, 21 (57%) Chinese participants reported avoiding certain types of fish or fish caught at certain locations, whereas 27 (52%) Karen participants reported avoiding eating certain parts of the body (Table 3).

Fish Consumption Changes During Pregnancy and Breastfeeding

Among 113 participants who reported a previous pregnancy, 89 (79%) reported eating ≥1 fish meal during their most recent pregnancy. Of these 89 women who did consume fish, 62 (70%) reported that fish consumption remained the same or increased during pregnancy. Although 79 (89%) did not change the species of fish they consumed during pregnancy, 31 (35%) of 89 reported that they avoided certain fish species while pregnant.

Among 24 participants who did not eat fish during their most recent pregnancy, 19 (79%) reported that they avoided fish because of concerns that chemicals in fish were harmful (Table 4). Among 75 participants who reported breastfeeding after their last pregnancy, 57 (76%) consumed fish while breastfeeding. Of those, 49 (86%) reported fish consumption the same or higher while breastfeeding than before pregnancy, and most did not change the species they were eating. However, 39 (68%) reported avoiding certain species while breastfeeding (Table 5).

Awareness and Attitudes Regarding Fish Advisories

Only 29 (19%) respondents were aware of local fish consumption advisories, 39 (25%) were aware of Wisconsin sportfish advisories, and 34 (22%) were aware of FDA or EPA advisories. Karen participants had the lowest advisory awareness, with 2 (4%) aware of local advisories, 1 (2%) aware of state advisories, and zero aware of FDA or EPA advisories. Awareness was highest for Chinese and Filipino participants, of whom approximately 33% (16/49) were aware of local advisories, 47% (23/49) were aware of state advisories, and 33% (17/49) were aware of FDA or EPA advisories (Supplemental Figure). Among 29 respondents who were aware of local advisories, 10 (34%) reported that they knew "some," "quite a bit," or "a great deal" about the advisories. Of 39 respondents who were aware of Wisconsin sportfish advisories, 10 (26%) reported that they knew at least "some," "quite a bit," or "a great deal" about the advisories. Among 34 participants who were aware of FDA or EPA advisories, 11 (32%) reported that they knew "some," "quite a bit," or "a great deal" about the advisories.

Overall, sportfish consumption did not vary meaningfully by advisory awareness. Eight (28%) participants who were aware of Milwaukee advisories and 41 (34%) participants who were not aware of Milwaukee advisories consumed ≥1 meal above Milwaukee AOC advisories ($P = 0.74$). Few participants reported consumption above Wisconsin sportfish advisory limits, including 4 (10%) of 39 participants who were aware of Wisconsin advisories and 8 (7%) of 114 who were not aware of Wisconsin advisories ($P = 0.48$). For store-purchased fish, 14 (41%) of 35 participants who reported awareness of FDA or EPA fish advisories ate ≥1 "choices to avoid" fish meal, compared with 19 (16%) of 114 participants who were not aware of store-purchased fish advisories ($P = 0.28$).

DISCUSSION

From our survey of a multiethnic cohort of Asian WCBA in the Milwaukee area, we found that approximately half of participants reported consumption of ≥1 store-purchased or sportfish meal above recommended levels. Approximately a quarter of participants were aware of any fish consumption advisory. Although approximately half of participants reported past changes to their fish consumption to avoid contamination, many also reported using unsafe fish cooking methods that can trap contaminants in fish.

Fish are a good source of important nutrients and can improve overall health.[24] In the United States, non-Hispanic Asian persons are approximately 3 times as likely as any other racial and ethnic group to eat seafood at least twice per week.[25] However, risks can be associated with fish consumption, because chemical pollutants from the environment can accumulate in the tissues of fish, such as in fat tissue.[26,27] Both risks and benefits of sportfish consumption are enhanced in WCBA.[24] In Milwaukee's Asian communities, clinicians should engage with communities to ensure that the highest-risk groups are aware of advisories. Partnership with community groups and leaders was instrumental to our recruitment efforts for this survey, and these same groups may be essential for future educational efforts.

Most participants were not aware of local, state, or national fish consumption advisories. By comparison, in a survey of mostly White, male anglers, 72.8% were aware of Wisconsin advisories, and 60.1% were aware of Milwaukee advisories.[28] Low advisory knowledge—even among those who were familiar with advisories—might explain why awareness of advisories was not associated with sportfish consumption behavior. For store-purchased fish, those who reported advisory awareness reported higher consumption of high-contaminant fish. Despite these findings, participants who were aware of advisories reported that they were easy to understand and follow. Health care providers and public health practitioners can share advisory information (Supplemental Table 3) to increase awareness of fish consumption advisories among Milwaukee's Asian WCBA.

Strengths and Limitations

This project has multiple limitations. First, we recruited participants by convenience and snowball sampling, and findings might not represent their overall WCBA communities. Second, food frequency questionnaires have been shown to underestimate overall consumption.[29,30] We attempted to increase the reliability and validity of our survey by providing pictures of fish species and a map of the Milwaukee AOC. However, misclassification of fish consumption data was likely. Third, participant recruitment fell short of recruitment goals for the Chinese and Filipino communities. Findings for these groups might not represent community views or behaviors. However, although the limited number of Filipino participants in this study reported higher average consumption than Hmong or Karen participants, community feedback suggests that their recruitment shortfall occurred because sportfishing is not common among Milwaukee's Chinese and Filipino communities. Thus, the findings of this survey might not be as relevant to them as it is to Hmong and Karen communities. Despite its limitations, however, our findings provide disaggregated insight into the fish consumption behaviors of Milwaukee's heterogeneous Asian communities. With multilingual surveys conducted over the phone and screening surveys conducted both on paper and online, we were able to conduct a representative evaluation.

CONCLUSIONS

This study provides new insight into the fish consumption habits, health beliefs, and advisory awareness among a multiethnic sample of Asian WCBA in Milwaukee. Approximately half of participants reported ≥1 fish meal above advised levels for the species and location. We also found limited awareness of fish advisories, increased risk for exposure to contaminants during pregnancy, and limited

adherence to safe fish preparation practices among all groups. These findings underscore the need for educational materials on safe fish consumption tailored to heterogeneous Asian WCBA communities.

Acknowledgement: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Funding/Support: None declared.

Financial Disclosures: None declared.

Appendix: Supplemental materials are available at www.wmjonline.org.

REFERENCES

1. Advice about eating fish: for those who might become or are pregnant or breastfeeding and children ages 1-11 years. US Food and Drug Administration. Updated March 5, 2024. Accessed September 30, 2023. https://www.fda.gov/food/consumers/advice-about-eating-fish

2. Kosti RI, Kasdagli MI, Kyrozis A, et al. Fish intake, n-3 fatty acid body status, and risk of cognitive decline: a systematic review and a dose-response meta-analysis of observational and experimental studies. *Nutr Rev*. 2022;80(6):1445-1458. doi:10.1093/nutrit/nuab078

3. Christensen KY, Raymond M, Blackowicz M, et al. Perfluoroalkyl substances and fish consumption. *Environ Res*. 2017;154:145-151. doi:10.1016/j.envres.2016.12.032

4. Milwaukee estuary area of concern. Wisconsin Department of Natural Resources. Accessed November 16, 2023. https://dnr.wisconsin.gov/topic/GreatLakes/Milwaukee.html

5. Wisconsin Department of Health Services – Division of Public Health; Great Lakes Consortium for Fish Consumption Advisories; Wisconsin Department of Natural Resources. Choose wisely: a health guide for eating fish in Wisconsin 2024-2026. Wisconsin Department Natural Resources. February 2024. Accessed April 16, 2024. https://moenlakechain.org/docs/PFOS/24feb08-WI-DNR-PUB_FH_824_ChooseWisely.pdf

6. US Department of Agriculture. *Dietary Guidelines for Americans: 2020-2025*. 9th ed. December 2020. Accessed July 14, 2024. https://www.dietaryguidelines.gov/sites/default/files/2021-03/Dietary_Guidelines_for_Americans-2020-2025.pdf

7. Chen B, Dong S. Mercury contamination in fish and its effects on the health of pregnant women and their fetuses, and guidance for fish consumption-a narrative review. *Int J Environ Res Public Health*. 2022;19(23):15929. doi:10.3390/ijerph192315929

8. Find the advice for eating fish from Wisconsin waters. Wisconsin Department of Natural Resources. Accessed November 16, 2023. https://apps.dnr.wi.gov/fishconsumptionadvisoryquery/

9. Dack K, Fell M, Taylor CM, Havdahl A, Lewis SJ. Mercury and prenatal growth: a systematic review. *Int J Environ Res Public Health*. 2021;18(13):7140. doi:10.3390/ijerph18137140

10. Govarts E, Nieuwenhuijsen M, Schoeters G, et al. Birth weight and prenatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE): a meta-analysis within 12 European birth cohorts. *Environ Health Perspect.* 2012;120(2):162-170. doi:10.1289/ehp.1103767

11. Yoshimasu K, Kiyohara C, Takemura S, Nakai K. A meta-analysis of the evidence on the impact of prenatal and early infancy exposures to mercury on autism and attention deficit/hyperactivity disorder in the childhood. *Neurotoxicology*. 2014;44:121-131. doi:10.1016/j.neuro.2014.06.007

12. Spratlen MJ, Perera FP, Lederman SA, et al. The association between prenatal exposure to perfluoroalkyl substances and childhood neurodevelopment. *Environ Pollut.* 2020;263(pt B):114444. doi:10.1016/j.envpol.2020.114444

13. American Community Survey: ACS 5-year estimates detailed tables. Table B05010: ratio of income to poverty level in the past 12 months by nativity of children under 18 years in families and subfamilies by living arrangements and nativity of parents. United States Census Bureau. 2021. Accessed April 16, 2024. https://data.census.gov/table/ACSDT5Y2021.B05010?q=B05010&y=2021

14. Statistics and data. Wisconsin Department of Children and Families. Accessed May 13, 2024. https://dcf.wisconsin.gov/refugee/statistics-population

15. Dix-Cooper L, Kosatsky T. Blood mercury, lead and cadmium levels and determinants of exposure among newcomer South and East Asian women of reproductive age living in Vancouver, Canada. *Sci Total Environ*. 2018;619-620:1409-1419. doi:10.1016/j.scitotenv.2017.11.126

16. Liu Y, Buchanan S, Anderson HA, Xiao Z, Persky V, Turyk ME. Association of methylmercury intake from seafood consumption and blood mercury level among the Asian and non-Asian populations in the United States. *Environ Res.* 2018;160:212-222. doi:10.1016/j.envres.2017.09.031

17. Buchanan S, Targos L, Nagy KL, Kearney KE, Turyk M. Fish consumption and hair mercury among Asians in Chicago. *J Occup Environ Med*. 2015;57(12):1325-1330. doi:10.1097/JOM.0000000000000560

18. Silver E, Kaslow J, Lee D, et al. Fish consumption and advisory awareness among low-income women in California's Sacramento-San Joaquin Delta. *Environ Res.* 2007;104(3):410-419. doi:10.1016/j.envres.2007.03.003

19. Tsuchiya A, Hinners TA, Krogstad F, et al. Longitudinal mercury monitoring within the Japanese and Korean communities (United States): implications for exposure determination and public health protection. *Environ Health Perspect.* 2009;117(11):1760-1766. doi:10.1289/ehp.0900801

20. Li A, Tang Q, Kearney KE, et al. Persistent and toxic chemical pollutants in fish consumed by Asians in Chicago, United States. *Sci Total Environ.* 2022;811:152214. doi:10.1016/j.scitotenv.2021.152214

21. He X, Raymond M, Tomasallo C, Schultz A, Meiman J. Fish consumption and awareness of fish advisories among Burmese refugees: a respondent-driven sampling study in Milwaukee, Wisconsin. *Environ Res*. 2021;197:110906. doi:10.1016/j.envres.2021.110906

22. Shaw S, He X, Haban A, Tomasallo C, Meiman J. A focus group study of fish consumption behaviors among Asian women in Milwaukee, Wisconsin. *Prev Med Rep.* 2023;36:102528. doi:10.1016/j.pmedr.2023.102528

23. US Environmental Protection Agency; Agency for Toxic Substances and Disease Registry, US Public Health Service. Should I eat the fish I catch? A guide to healthy eating of the fish you catch. US Environmental Protection Agency. September 1997. Accessed April 16, 2024. https://www.epa.gov/sites/default/files/2019-05/documents/should-i-eat-fish-1997.pdf

24. Starling P, Charlton K, McMahon AT, Lucas C. Fish intake during pregnancy and foetal neurodevelopment—a systematic review of the evidence. *Nutrients*. 2015;7(3):2001-2014. doi:10.3390/nu7032001

25. erry AL, Herrick KA, Afful J, Ahluwalia N. Seafood consumption in the United States, 2013-2016. *NCHS Data Brief.* 2018;(321):1-8. https://www.cdc.gov/nchs/products/databriefs/db321.htm

26. Huang H, Li Y, Zheng X, Wang Z, Wang Z, Cheng X. Nutritional value and bioaccumulation of heavy metals in nine commercial fish species from Dachen Fishing Ground, East China Sea. *Sci Rep*. 2022;12(1):6927. doi:10.1038/s41598-022-10975-6

27. James MO, Kleinow KM. Seasonal influences on PCB retention and biotransformation in fish. *Environ Sci Pollut Res Int*. 2014;21(10):6324-6333. doi:10.1007/s11356-013-1611-3

28. He X, Tomasallo C, Li Z, et al. Fish consumption, awareness of fish advisories, and body burden of contaminants among the Milwaukee urban anglers: a biomonitoring study. *J Toxicol Environ Health Sci.* 2022;14(2):20-35. doi:10.5897/JTEHS2022.0506

29. Subar AF, Thompson FE, Kipnis V, et al. Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires: the Eating at America's Table Study. *Am J Epidemiol.* 2001;154(12):1089-1099. doi:10.1093/aje/154.12.1089

30. Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? *Cancer Epidemiol Biomarkers Prev.* 2005;14(12):2826-2828. doi:10.1158/1055-9965.EPI-12-ED1

The Perceptions of Infertility Patients Regarding the COVID-19 Vaccine: A Mixed Methods Analysis of Patient Readiness

David Eggert, DO; Amy Pan, PhD; Cassandre R. Krier; Kate Schoyer, MD; Kristina Kaljo, PhD; Stephanie Gunderson, MD

ABSTRACT

Introduction: We sought to elucidate infertile patient perceptions regarding the novel COVID-19 vaccine as it pertained to fertility treatments and future pregnancies.

Methods: Patients visiting the Froedtert North Hills Health Center for Fertility and Reproductive Medicine in Menomonee Falls, Wisconsin from July 1, 2020, through June 6, 2021, were invited to participate in a mixed methods survey assessing infertile patient perceptions regarding clinic closures, delays in treatment, and the COVID-19 vaccine. The main outcomes measured were readiness to receive the COVID-19 vaccine in the setting of trying to conceive.

Results: There were 760 surveys sent with a total of 192 completed surveys (response rate = 25.3%). Respondents who reported having a college or post graduate education were more likely to consider the COVID-19 vaccine when it became available to them ($P < 0.001$). When participants' responses were stratified by the number of previous completed fertility treatments (either embryo transfers or intrauterine inseminations), there was a statistically significant trend of increasing willingness to receive the COVID-19 vaccine as the number of completed fertility treatments increased even when considering a pregnancy or while breastfeeding ($P = 0.004$ and $P = 0.001$, respectively). Qualitative themes included participants' fear of the unknown due to existing perceptions, beliefs, and mistrust; interpretations of medical knowledge, and desire for provider guidance and mindful communication.

Conclusions: This study suggests that despite identified hesitancy of the COVID-19 vaccine, patients with higher levels of education and those who completed an increasing number of infertility treatments were more willing to consider the COVID-19 vaccine.

INTRODUCTION

Infertility is defined as trying to conceive for at least 1 year without a successful pregnancy. It is well established that the diagnosis of infertility and the need for infertility treatments can result in significant psychosocial distress.[1-5]

• • •

Author Affiliations: Department of Obstetrics and Gynecology, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Eggert, Schover, Kaljo, Gunderson); Department of Pediatrics, Qualitative Health Sciences, MCW, Milwaukee, Wisconsin (Pan); MCW, Milwaukee, Wisconsin (Krier).

Corresponding Author: Stephanie Gunderson, MD, 8701 W Watertown Plank Rd, Milwaukee, WI 53226; phone 414.805.6600; email sgunderson@mcw.edu; ORCID ID 0000-0003-2703-5169

The SARS-CoV-19 virus (COVID-19) pandemic started in late 2019 and caused disruptions on a global scale. This disease led to mandated physical distancing, widespread enforcement of personal protective equipment, and closures of institutions worldwide. The pandemic also delayed medical treatments that were considered elective, including infertility treatments.

On March 17, 2020, the American Society for Reproductive Medicine (ASRM) published guidelines recommending the cessation and suspension of new and ongoing fertility treatments, except for urgent, medically indicated fertility preservation procedures.[6] This included intrauterine insemination (IUI) and in vitro fertilization (IVF), including egg retrievals and frozen embryo transfers.

Recently, data have shown that fertility clinic closure during the COVID-19 pandemic was associated with a sharp increase in the prevalence of anxiety and depression among infertile patients undergoing treatment and was perceived as an uncontrollable and stressful event.[7-8]

On April 24, 2020, ASRM released an update on its recommendations that included resumption of care in individual clinics based on state and disease risk.[9] On December 11, 2020, the Pfizer-Biotech COVID-19 vaccine was authorized by the US Food and Drug Administration under an emergency use authorization for limited populations, with public-wide release shortly after.[10] Although numerous studies have shown statistically significant increased levels of anxiety and depression in infertility patients whose evaluations and treatments were delayed, these studies did not include questions regarding patient perceptions of the

COVID-19 vaccine.[7-8] Studies in general populations showed that pregnant women are less likely to receive the COVID-19 vaccine than nonpregnant and breastfeeding women.[11] The most common reasons for "declining" the vaccine included concern for short- or long-term side effects, the speed of the development of the vaccine, fear of harming the pregnancy, previous allergy or anaphylaxis, lack of sufficient research, and potential interaction with other medical comorbidities.[11] Online rumors about the vaccine's potential negative impact on fertility regularly appeared after the vaccine rollout—particularly during its early phases—which was a source of hesitancy to the vaccine, specifically in patients seeking treatment for infertility and those of reproductive age.[12] To the best of our knowledge, prior to this study, there has been no data to represent the patient perspective towards the COVID-19 vaccine among those seeking infertility treatment.

The primary aim of this study was to assess the readiness of infertility patients to receive the COVID-19 vaccine in the setting of trying to conceive.

METHODS

Study Design

This survey study is a single-center convergent mixed methods study that involved the distribution of a 60-question survey assessing infertile patient perceptions regarding clinic closures, treatment delays, and the COVID-19 vaccine.

Recruitment and Data Collection

The study was performed at the Froedtert North Hills Health Center for Fertility and Reproductive Medicine in Menomonee Falls, Wisconsin. All patients who visited this clinic from July 1, 2020, through June 30, 2021, were invited to participate in the survey. Exclusion criteria included any patient under the age of 18 and prior completion of the survey. This survey was developed based on an existing survey out of Stanford University elucidating perceptions of how the COVID-19 pandemic affected the care of patients with cancer.[13] Three different versions of the survey were offered to patients including a hard copy paper survey, online Google form survey, and Qualtrics survey. Initially, the survey was conducted in person only starting February 22, 2021. Given the limited availability of researchers to present the survey study to in-person patients on March 22, 2021, it was expanded to online platforms. Two reminders were sent to participants if they had not completed the survey during the study period. The survey was offered to a total of 760 patients resulting in 192 responses (25.3% response rate). Online surveys were distributed to patients through MyChart Messaging system (a patient portal) through the electronic medical record (Epic Systems Corporation, Verona, Wisconsin). No patient identifiers were obtained in this anonymous survey. Approval was obtained from the Medical College of Wisconsin's Institutional Review Board, IRB Reference Number PRO00039946.

Table 1. Demographic Data, N=192

Variable	n	%[a]
Age		
≤35	86	44.8
>35	85	44.3
Did not answer	21	10.9
Gender		
Male	5	2.6
Female	187	97.4
Ethnicity/race		
White	177	92.2
Hispanic	7	3.6
African American	3	1.6
Asian	2	1.0
Jewish	1	0.5
Prefer not to answer	1	0.5
Did not answer	1	0.5
Marital status		
Married	178	92.7
Never married	8	4.2
Member of an unmarried family	6	3.1
Education		
No college degree	32	16.7
College degree	90	46.9
Postgraduate degree	67	34.9
Did not answer	3	1.6
Employment status		
Employed	178	92.7
Unemployed/disabled	11	5.7
Student	1	0.5
Did not answer	2	1.0
Health insurance		
Private	187	97.4
Badgercare	1	0.5
Obamacare	1	0.5
Military	1	0.5
Medicare	2	1.0
Household income		
<$30 000	3	1.6
$30 001–$50 000	4	2.1
$50 001–1$00 000	47	24.5
>$100 000	96	50.0
Did not answer	42	21.9
Infertility diagnosis[b]		
Polycystic ovary syndrome/anovulation	23	12.0
Endometriosis	9	4.7
Male factor	21	10.9
Low ovarian reserve	17	8.9
Same sex couple	2	1.0
Uterine abnormality	3	1.6
Tubal abnormality	4	2.1
Genetic	2	1.0
Unexplained	22	11.5
Did not answer	89	46.4

[a]Percentages may not add up to 100 due to rounding.

[b]Qualitative data from survey that was summarized after data collection.

Data Analysis

Quantitative Analysis Methods

Data were presented as n (%). Chi-square or Fisher exact tests were used to examine the associations between categorical variables. Linear trend in proportion was tested by Cochran-Armitage trend test. SAS version 9.4 (SAS Institute Inc, Cary, North Carolina) and SPSS version 28.0 (IBM Corporation, Armonk, New York) were used for statistical analyses. $P<0.05$ was considered statistically significant.

Qualitative Analysis

The survey questions analyzed included 2 free-text questions to further ascertain the perspectives and insights of those participating in the study. These qualitative questions aimed to explore patients' underlying motivations and were used to help amplify the patient experience. Written responses were extracted verbatim from the survey and inserted into an Excel document. Using inductive content analysis of the free-text survey responses, 2 members of the research team assigned individual codes to capture and classify recurring patterns. The same team members compared responses to negotiate discrepancies and ensure trustworthiness of analysis. Those patterns were grouped together into 3 themes to elucidate the individual perceptions and beliefs regarding the COVID-19 vaccine.

Table 2. Education as Variable Affecting Respondents' Willingness to Receive COVID-19 Vaccine

	No/Unknown, n (%)	Yes, n (%)	Total N	*P* value
Question: Would you like to get the coronavirus (COVID-19) vaccine when it is available?			187	0.0010[a]
No college degree	14 (47)	16 (53)		
College degree	25 (28)	65 (72)		
Postgraduate degree	10 (15)	57 (85)		

[a]Cochran-Armitage trend test.

Table 3. Number of Infertility Treatments Associated With Respondents' Willingness to Receive COVID-19 Vaccine

	No/Unknown, n (%)	Yes, n (%)	Total N	*P* value
Would you like to get the coronavirus (COVID-19) vaccine when it is available?			188	0.040[a]
0 infertility treatments	1 (50)	1 (50)		
1 infertility treatment	42 (30)	100 (70)		
2 infertility treatments	7 (18)	31 (82)		
≥3 infertility treatments	0 (0)	6 (100)		
If you are pregnant or breastfeeding when the vaccine becomes available to you will you get it?			180	0.0010[a]
0 treatments	1 (50)	1 (50)		
1 treatment	82 (61)	53 (39)		
2 treatments	18 (49)	19 (51)		
≥3 treatments	0 (0)	6 (100)		

[a]Cochran-Armitage trend test.

RESULTS

Quantitative Analysis

A total of 192 patients responded to the survey. Of those who responded, 187 identified as female, and 5 identified as male. A large majority identified as White, married individuals. Many respondents had a college or postgraduate degree and private health insurance. Not all questions were answered by all respondents. Therefore, to accurately convey the response rate, each question shows the total number of responses (Table 1).

Participant willingness to accept the COVID-19 vaccine was analyzed in conjunction with different demographic variables to see if there was an association between these variables and vaccine acceptance. The survey results suggest that respondents' age, marital status, income level, and insurance status did not correlate with willingness to accept the vaccine in any significant way (Supplementary Table 1). Participants with a higher educational level (college or postgraduate degree) were more likely to accept the COVID 19 vaccine when it became available to them (Cochran-Armitage trend test $P=0.001$) (Table 2). Interestingly, when asked to consider a future pregnancy or breastfeeding and the COVID-19 vaccine, the significant trend between level of education of vaccine acceptance disappeared ($P=0.92$) (Supplementary Table 2). When the number of completed treatment cycles (either IUI or embryo transfer) were analyzed with the respondents' willingness to accept the vaccine, there was a statistically significant trend of increasing willingness to receive the COVID-19 vaccine as the number of infertility treatments increased (Cochran-Armitage trend test $P=0.040$), even when considering future pregnancy or breastfeeding (Cochran-Armitage trend test $P=0.0010$) (Table 3).

Qualitative Analysis

From the analysis of free-text responses, we identified 3 primary themes: (1) fear of the unknown due to perceptions, beliefs, and historical mistrust; (2) patient interpretations of medical knowledge and self-generated benefit-risk assessments; and (3) seeking provider guidance and mindful communication.

Theme 1: Fear of the Unknown

Patients report a multifaceted fear of the unknown. Between concerns about harming a future child or fetus, the impact on fertility, and worries regarding breastfeeding risks, respondents described inadequate counseling on what to expect during a vulnerable time. Specifically, a female patient, age 34, said, *"After all we have been through to get pregnant, it is not worth the risk."* Another female patient, age 36, agreed, *"I have been trying to become pregnant for*

over 2 years, and I would be devastated if a reaction to the vaccine affected my pregnancy." Additionally, patients describe how negative outcomes due to COVID-19 may influence their response and cited a lack of guidance or communication from medical professionals during the pandemic. Stemming from historical medical mistrust, a male patient, age 40, said, *"[I am] not comfortable with how it [the vaccine] was developed and being targeted to minorities."*

Theme 2: Patient Interpretations of Medical Knowledge, and Self-Generated Benefit-Risk Assessments

Many patients provide insight into the their experience when developing an understanding of new medical information, whether disseminated by their clinican or obtained through outside means. Primarily, patients cited a lack of clinical evidence for the use of the COVID-19 vaccine in pregnancy. A female patient, age 41, said, *"[the] vaccine is new and hurriedly made, so I don't trust it."* Other patients shared similar sentiments of mistrust due to the seemingly rapid production and dissemination of the COVID-19 vaccine. *"Not enough time has passed to determine potential long-term effects,"* said another female respondent, age 35. Regarding fertility specifically, a female respondent, age 43, said, *"[I'm] worried about effects on fertility. Other members of my family will get the vaccine to protect me."*

For patients who are in higher-risk categories at baseline during their pregnancy, respondents described a greater sense of unpredictability and concern with COVID-19. A female patient, age 43, said, *"I have an autoimmune disorder, and I worry about sufficient studies having been done with women who were pregnant and doubly with my disorder."* Another female patient, age 31, reported similar worries, stating *"I am waiting until after I deliver to get the vaccine, as my husband had a significant reaction to the vaccine, and I do not know if that would affect my baby."*

Respondents also indicated that they perceived the lack of clinical research as harmful, advancing their mistrust surrounding COVID-19. *"I'm not a lab rat, and my unborn child won't be either,"* said a female patient, age 39. Less explicitly, another female patient, age 32, agreed, stating that they would not receive the vaccine due to *"the unknowns involved, and the fact that pregnant women were not a part of the testing."*

Without access to clinical trials that include pregnant women, patients reported creating a self-generated benefit-risk assessment based on their emotions and insufficient evidence. Respondents detailed an increased risk of being within a vulnerable population, as well as feelings of inadequacy and guilt that may arise if their pregnancy is unsuccessful due to the consequences of COVID-19. One female patient, age 41, said, *"Infertility is a rollercoaster. If I did become pregnant, got the vaccine, and then lost the baby, I would feel immense guilt."*

Theme 3: Seeking Provider Guidance and Mindful Communication

Patients described an increase in desire to communicate with their clinicians during COVID-19. They reported wanting direct information and individualized assessments tailored to their needs. As illustrated by this response from a female patient, age 33, *"I would consult with my doctor, and if they said it was safe, I would [receive the vaccine],"* patients are influenced by trust in their clinician's recommendations. Another female patient, age 32, said, *"I'm not sure I want to get the vaccine while pregnant. I will need to discuss with my doctor before I will decide."* Many patients additionally detailed that these conversations are important and have changed their opinion on receiving the vaccine. For example, a female respondent, age 37, said, *"I'm pregnant and got vaccinated yesterday. OB was supportive."*

DISCUSSION

This study took place at the height of the COVID-19 pandemic and at the beginning stages of vaccine release to the public. Therefore, this timely study sheds light for fertility providers on patient hesitancies regarding the COVID-19 vaccine and provides insights into evidence-based practice and targeted education regarding the vaccine. While education and number of completed infertility treatments appeared to significantly increase acceptance of the vaccine, it is evident there is still vaccine hesitancy—especially when related to pregnancy and breastfeeding—among the infertility population.

Previous studies have shown that less than 1 in 4 pregnant people were vaccinated against COVID-19, despite retrospective data showing safety, efficacy, and vaccine-generated antibody passage through umbilical cord blood and breastmilk.[14-18] Our results suggest that as the number of infertility treatments increased, the acceptance of the vaccine also increased. The likely explanation for this is that participants in this study may do more to secure a viable and safe pregnancy. It is also possible that patients who have undergone more treatment cycles have spent more time with their clinician and have established a stronger rapport and level of trust. Further noted in our qualitative responses, patients appreciated detailed guidance and conversations with clinicians regarding the COVID-19 vaccine to help them make informed decisions regarding vaccine acceptance. However, many respondents who received 1 to 2 fertility treatments altered their answer from "yes" to "no or don't know" responses when considering the COVID-19 vaccine during a pregnant state or breastfeeding, which highlights the hesitancy of respondents to accept the vaccine while pregnant or breastfeeding (Table 3). This perceived hesitancy correlates with the themes of fearing the unknown, mistrust in health care, and patient-driven benefit-risk assessments as found in our qualitative analysis. Patients who received less guidance were less likely to receive the vaccine.

Higher education significantly increased overall acceptance of the vaccine. However, when considering vaccination while pregnant or breastfeeding, the impact of education was no longer significant (Table 2 and Supplemental Table 2). This transition occurred in all

3 categories of education. Vaccine hesitancy in health care workers (the majority of individuals having at least some college degree) considering pregnancy/lactation and the COVID-19 vaccine has been reported previously.[14] In that study, while the majority of respondents were not hesitant about the vaccine, respondents who were pregnant, breastfeeding, or actively pursuing pregnancy were significantly more hesitant to receive the vaccine.[14] This suggests that education does not fully combat the hesitancy of the vaccine in pregnancy or breastfeeding and suggests that other factors play a role in helping patients make informed decisions regarding the vaccine. In our study, income, insurance status, age, and marital status showed no impact on vaccine acceptance.

There were a few limitations to our study. The survey distributed to participants was long (60 questions), which may have contributed to survey fatigue, variability between questions, and potentially lower response rate. Also, the study population was limited to a single academic center located in a state without an insurance mandate to cover infertility treatments. With this in mind, the authors recognize that the patient population surveyed was likely skewed with patients having higher levels of education and more resources to support infertility treatments.

To our knowledge, this is the first mixed method study elucidating the perspectives of the COVID-19 vaccine in an infertile population. Our study was timely in that it was initiated when most of the public were not eligible to receive the COVID-19 vaccine and continued until the vaccine was widely available.

CONCLUSIONS

This study demonstrates that despite identified hesitancy regarding the COVID-19 vaccine, patients with higher levels of education and those who completed an increasing number of infertility treatments were more willing to consider the vaccine. Patients unwilling to receive the vaccine reported mistrust in health care, lack of communication with clinicians, and medical misunderstanding while formulating benefit-risk assessments. Our study highlights the ongoing hesitancies regarding the COVID-19 vaccination in patients seeking infertility evaluation and those undergoing treatment. Higher quality patient-clinician communication is essential for infertility patients with less than a college degree and for patients in the early stages of their fertility journey.

Acknowledgements: The authors would like to acknowledge and thank Pippa Simpson, PhD, for her work on the statistical analysis.

Funding/Support: None declared.

Financial Disclosures: None declared.

Appendix: Supplemental Tables are available at www.wmjonline.org.

REFERENCES

1. Rooney KL, Domar AD. The relationship between stress and infertility. *Dialogues Clin Neurosci*. 2018;20(1):41-47. doi:10.31887/DCNS.2018.20.1/klrooney

2. Greil AL. Infertility and psychological distress: a critical review of the literature. *Soc Sci Med*. 1997;45(11):1679-1704. doi:10.1016/s0277-9536(97)00102-0

3. Greil AL, Shreffler KM, Schmidt L, McQuillan J. Variation in distress among women with infertility: evidence from a population-based sample. *Hum Reprod*. 2011;26(8):2101-2112. doi:10.1093/humrep/der148

4. Greil AL, Slauson-Blevins K, McQuillan J. The experience of infertility: a review of recent literature. *Sociol Health Illn*. 2010;32(1):140-162. doi:10.1111/j.1467-9566.2009.01213.x

5. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA*. 2020;324(8):782-793. doi:10.1001/jama.2020.12839

6. American Society for Reproductive Medicine COVID-19 Task Force. Patient management and clinical recommendations during the coronavirus (COVID-19) pandemic as of March 17, 2020. American Society for Reproductive Medicine. 2020. Accessed May 26, 2022. https://www.asrm.org/globalassets/_asrm/practice-guidance/covid-19/patient-management-updates/covidtaskforce.pdf

7. Boivin J, Harrison C, Mathur R, Burns G, Pericleous-Smith A, Gameiro S. Patient experiences of fertility clinic closure during the COVID-19 pandemic: appraisals, coping and emotions. *Hum Reprod*. 2020;35(11):2556-2566. doi:10.1093/humrep/deaa218

8. Lawson AK, McQueen DB, Swanson AC, Confino R, Feinberg EC, Pavone ME. Psychological distress and postponed fertility care during the COVID-19 pandemic. *J Assist Reprod Genet*. 2021;38(2):333-341. doi:10.1007/s10815-020-02023-x

9. American Society for Reproductive Medicine COVID-19 Task Force. Patient management and clinical recommendations during the coronavirus (COVID-19) pandemic. Update no. 3. (April 24, 2020 through May 11, 2020). American Society for Reproductive Medicine; 2020. Accessed May 26, 2022. https://www.asrm.org/globalassets/_asrm/practice-guidance/covid-19/patient-management-updates/covidtaskforceupdate3.pdf

10. FDA takes key action in fight against COVID-19 by issuing emergency use authorization for first COVID-19 vaccine. News release. US Food and Drug Administration. December 11, 2020. Accessed June 07, 2022. https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19

11. Sutton D, D'Alton M, Zhang Y, et al. COVID-19 vaccine acceptance among pregnant, breastfeeding, and nonpregnant reproductive-aged women. *Am J Obstet Gynecol MFM*. 2021;3(5):100403. doi:10.1016/j.ajogmf.2021.100403

12. Abbasi J. Widespread misinformation about infertility continues to create COVID-19 vaccine hesitancy. *JAMA*. 2022;327(11):1013-1015. doi:10.1001/jama.2022.2404

13. Rodriguez GM, Ferguson JM, Kurian A, Bondy M, Patel MI. The impact of COVID-19 on patients with cancer: a national study of patient experiences. *Am J Clin Oncol*. 2021;44(11):580-587. doi:10.1097/COC.0000000000000865

14. Perez MJ, Paul R, Raghuraman N, et al. Characterizing initial COVID-19 vaccine attitudes among pregnancy-capable healthcare workers. *Am J Obstet Gynecol MFM*. 2022;4(2):100557. doi:10.1016/j.ajogmf.2021.100557

15. Beharier O, Plitman Mayo R, Raz T, et al. Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine. *J Clin Invest*. 2021;131(19):e154834. doi:10.1172/JCI154834

16. Gray KJ, Bordt EA, Atyeo C, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstet Gynecol*. 2021;225(3):303.e1-303.e17. doi:10.1016/j.ajog.2021.03.023

17. Kelly JC, Carter EB, Raghuraman N, et al. Anti-severe acute respiratory syndrome coronavirus 2 antibodies induced in breast milk after Pfizer-BioNTech/BNT162b2 vaccination. *Am J Obstet Gynecol*. 2021;225(1):101-103. doi:10.1016/j.ajog.2021.03.031

18. Razzaghi H, Meghani M, Pingali C, et al. COVID-19 vaccination coverage among pregnant women during pregnancy - eight integrated health care organizations, United States, December 14, 2020-May 8, 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(24):895-899. doi:10.15585/mmwr.mm7024e2

Vaping During Pregnancy in Northern Wisconsin

Jeffrey J. VanWormer, PhD; Richard L. Berg, MS; Aditya Joshi, MD

ABSTRACT

Introduction: The use of electronic cigarettes during pregnancy is an emerging health risk. This study estimated use of electronic cigarettes and associated risk factors in pregnant women in a predominantly rural population.

Methods: Surveys on e-cigarette use and sociodemographics, linked to medical records, were administered to women in the third trimester of pregnancy. Participants were Marshfield Clinic Health System patients in northern and central Wisconsin.

Results: There were 391 respondents. The prevalence of e-cigarette use during pregnancy was 5% (95% CI, 2-8). Women who were younger, lower gestational age, unmarried, had lower education, lower income, and lower body mass index were more likely to use e-cigarettes.

Discussion: Use of e-cigarette in pregnant women in rural Wisconsin was 5 times greater than that observed nationally. Prenatal e-cigarette prevention interventions may need to focus on women who are younger, not married, and with lower education/income.

INTRODUCTION

Electronic cigarettes (e-cig) are battery-powered devices that generate an inhaled aerosol (ie, vaping). These aerosols include nicotine and flavorings, as well as solvents and phenolic compounds, some of which are carcinogens.[1] Given their potential to cause adverse fetal outcomes in animal models,[2] the toxicity of these compounds is a concern during pregnancy. Research in humans is developing, but the principal risk is fetal size for gestational age. Compared to nonusers, the odds of delivering a low birthweight baby are over twice as high – both for pregnant mothers who continue to smoke conventional cigarettes or those who use e-cigs in late pregnancy.[3] Low birth weight is a strong risk factor for metabolic disorders in adulthood.[4] The US Surgeon General considers vaping a fetal risk factor.[5]

Vaping has increased widely in the US since 2007.[5] Some surveys found as many as 10% of mothers regularly vape just prior to pregnancy,[6] though more recent national estimates suggest vaping is lower in later pregnancy stages.[7] Most prior studies, however, represent primarily urban populations. There is a higher rate of conventional smoking in the rural US, which is linked to rural sociodemographics, such as higher rates of unemployment, lower income, and decreased access to health care.[8]

Vaping is an emerging health risk during pregnancy. No known studies have examined vaping during pregnancy among women in rural Wisconsin, where the burden of many lifestyle risk factors (eg, smoking) is greater than more affluent areas. The purpose of this study was to estimate the prevalence of e-cig use in pregnant mothers in north-central Wisconsin and to identify sociodemographic and other factors associated with vaping.

METHODS

Design and Setting

A cross-sectional survey was used, with linkage of existing sociodemographic and clinical characteristics of pregnant women from Marshfield Clinic Health System (MCHS) electronic health records (EHR). The source population included adults with reasonably complete capture of their medical care within MCHS data systems, including patients who reside within a 20-county region of north-central Wisconsin and are members of Security

Author Affiliations: Center for Clinical Epidemiology and Population Health, Marshfield Clinic Research Institute, Marshfield, Wisconsin (VanWormer); Office of Research Computing and Analytics, Marshfield Clinic Research Institute, Marshfield, Wisconsin (Berg); Division of Neonatology, Department of Pediatrics, Marshfield Clinic, Marshfield, Wisconsin (Joshi).

Corresponding Author: Jeffrey J. VanWormer, PhD, Center for Clinical Epidemiology and Population Health, Marshfield Clinic Research Institute, 1000 N Oak Ave, Marshfield, WI 54449; phone 715.221.6484; email vanwormer.jeffrey@marshfieldresearch.org; ORCID ID 0000-0002-8733-8703

Health Plan of Wisconsin and/or residents of the Marshfield Epidemiologic Study Area.[9]

Sample

Inclusion criteria for survey invitees were (1) living in the source population, (2) age ≥18 years, (3) female, (4) currently pregnant in the third trimester (per pregnancy diagnostic codes) or ≥24 weeks' gestation, (5) ≥1 encounter with an MCHS clinician over the previous year, and (6) ability to read the English language survey. Known institutional residents (eg, medical, penal) were excluded. The requirement of having a recent medical encounter helped ensure current study eligibility. Given the limited prior research on e-cig use in pregnant mothers, guidance on assumptions for precise sample size calculations was unavailable. Thus, all known pregnant mothers from the source population over a 1-year timeframe were invited to complete the study survey. Procedures were approved in advance by the MCHS Institutional Review Board, including a request to waive documentation of informed consent and HIPAA authorization.

Recruitment

Contact information for study-eligible individuals was extracted from the EHR. For each enumerated individual, survey recruitment methods included (1) a mailed invitation packet, which included a cover letter, study information sheet, survey instrument, return mailer, and $5 cash incentive; (2) a mailed reminder/thank you postcard; (3) follow-up telephone calls for nonrespondents (plus a verbal survey response option); and (4) final mailed follow-up packet, which included the same elements as the mailed invitation packet, sent to all remaining nonrespondents. By completing the survey, participants consented to have their survey data linked to their EHR data for analyses.

Measures

The outcome was current use of e-cigs during third trimester pregnancy. This was assessed in the survey using validated questions from the Pregnancy Risk Assessment Monitoring System (PRAMS), with supplemental questions on e-cig use.[6] Clinical data, such as number of clinical encounters over the past year, medical comorbidities, and conventional cigarette smoking nearest to the date of pregnancy, were extracted from the EHR. In addition, self-report surveys (and EHR data if available) captured basic pregnancy characteristics (eg, gestation), knowledge/beliefs in e-cig risks, and sociodemographic measures, such as age, race/ethnicity, education, income, and health insurance coverage.

Analyses

To assess possible respondent biases, available basic EHR characteristics were compared between survey respondents and nonrespondents. Univariate regression was used to examine associations between each sociodemographic/clinical exposure and e-cig use. The univariate model findings were considered hypothesis generating, as multivariable regression was not performed given the small sample size and exploratory nature of our study design. However, propensity score weighting (using inverse probability weights) was used to account for imbalances between survey respondents and nonrespondents. Regression analyses included propensity scores to better reflect the full target population, adjusting final estimates to help minimize the influence of imbalances in potentially confounding characteristics in survey respondents.

Table 1. Descriptive Characteristics of Pregnant Women in Northern and Central Wisconsin Who Were Invited to a Survey on Vaping, Including Propensity Score Weighted Characteristics of Survey Respondents

	All Invitees (n = 1199)	Respondents (n = 391)	
Characteristics		**Unadjusted**	**Weighted**
Age (years)	28.6 ± 0.2	29.4 ± 0.3	28.4 ± 0.3
Gestational age (months)	31.2 ± 0.1	30.4 ± 0.2	31.2 ± 0.3
Gravida			
≥2	131 (11%)	37 (9%)	9%
<2 or unknown	1068 (89%)	354 (91%)	91%
Race/Ethnicity			
White, non-Hispanic	975 (81%)	337 (86%)	81%
Non-White or Hispanic	224 (19%)	54 (14%)	19%
Health insurance			
Medicaid	485 (40%)	111 (28%)	42%
Not Medicaid	714 (60%)	280 (72%)	58%
Smoking status at start of pregnancy			
Smoker	360 (30%)	65 (17%)	32%
Non-smoker	839 (70%)	326 (83%)	68%
Medical encounters in prior 3 years (n)	69.1 ± 1.6	66.3 ± 2.2	69.5 ± 2.9
Body mass index (kg/m^2)	29.3 ± 0.2	29.5 ± 0.4	29.7 ± 0.4
Depression			
Yes	402 (34%)	115 (29%)	37%
No	797 (66%)	276 (71%)	63%
Anxiety			
Yes	628 (52%)	172 (44%)	55%
No	571 (48%)	219 (56%)	46%

Values are reported as mean ± SE or frequency (% of total). Among respondents, the unadjusted values are as-observed from the surveys. Weighted values reflect the rebalanced exposure characteristics after propensity score weighting (using inverse probability weights) was applied.

RESULTS

There were 1199 individuals invited to take the survey over the 1-year study period. Of these, 423 (35%) responded. Thirty-two respondents were no longer pregnant at the time of survey completion and were excluded from analyses, yielding a final analytical sample of 391 participants. Descriptive characteristics of survey invitees and respondents are outlined in Table 1. The most notable differences were that respondents were less likely to be current smokers or on Medicaid, but the propensity score weighting adequately balanced the respondent sample to better reflect the underlying source population.

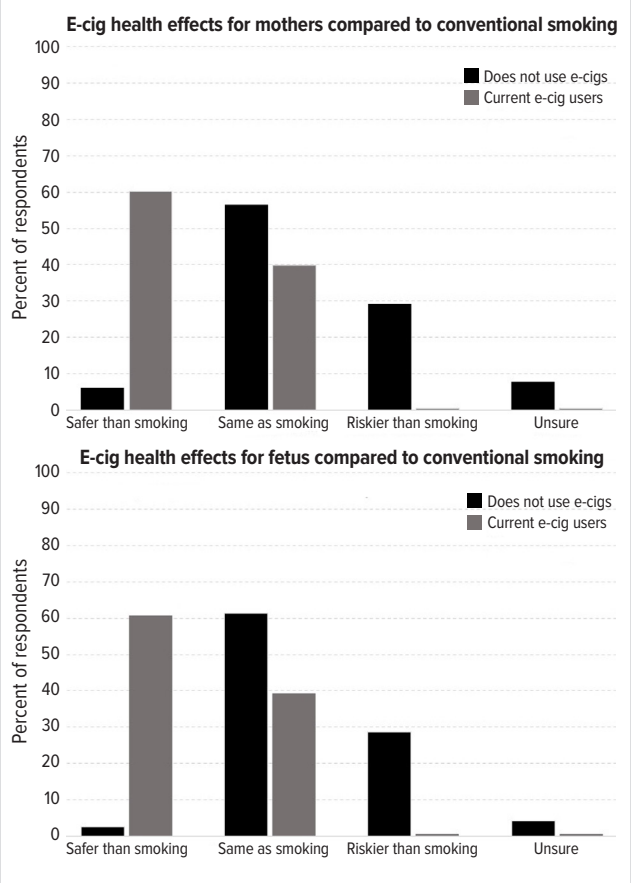
The model-estimated prevalence of current e-cig use during

Table 2. Univariate Associations Between Sociodemographic/Clinical Exposures and Current E-cig Use Among Pregnant Women in Northern and Central Wisconsin (n = 391)

Exposures	Current E-cig Use (95% CI)	*P* value
Maternal age (years)	0.74 (0.64–0.90)	0.002
Gestational age (months)	0.87 (0.79–0.95)	0.002
Gravida		
≥2 vs <2 or unknown (ref)	0.53 (0.05–5.52)	0.594
Children in the household		
Any vs none (ref)	0.19 (0.05–0.68)	0.011
Marital status		
Married/living with partners vs not married (ref)	0.08 (0.02–0.28)	< 0.001
Race/ethnicity		
White, non-Hispanic vs non-white or Hispanic (ref)	1.15 (0.31–4.27)	0.834
Health insurance		
Medicaid vs not Medicaid (ref)	0.83 (0.22–3.14)	0.784
Education		
College vs high school or less (ref)	0.10 (0.03–0.40)	0.001
Annual household income		
≥ $60 000 vs < $60 000 (ref)	0.09 (0.01–0.92)	0.042
Smoking status at start of pregnancy		
Smoker vs nonsmoker (ref)	3.12 (0.75–13.01)	0.118
Medical encounters in prior 3 years (n)	0.99 (0.98–1.01)	0.484
Body mass index	0.84 (0.74–0.96)	0.008
Depression		
Yes vs no (ref)	0.69 (0.20–2.42)	0.559
Anxiety		
Yes vs no (ref)	3.09 (0.82–11.64)	0.095

Values are reported as odds ratio (95% CI, *P* value) of current E-cig use. Odds ratio values >1.0 indicate that the odds of e-cig use increase as compared to the reference group (or a 1-unit increase for continuous exposures). Odds ratio values <1.0 indicate that the odds of e-cig use decrease as compared to the reference group (or a 1-unit increase for continuous exposures). For example, the predicted odds of e-cig use was 0.74 (or 26% lower) for each 1 year increase in maternal age. Exposures with $P < 0.05$ were considered to have a statistically significant association with e-cig use.

Figure. Beliefs in the Health Effects of Electronic Cigarettes for (a) Mother and (b) Fetus, as Compared to Conventional Smoking, in Pregnant Women in Northern and Central Wisconsin (n = 391).



third trimester pregnancy was 5% (95% CI, 2.0-8.0), with 16% (95% CI, 11.4-19.6) reporting e-cig use within the 3 months prior to pregnancy. In the subset of respondents who reported ever using e-cigs (n = 119), the most-used brands were Juul (26%), Vuse (21%), and Blu (5%). The most common reasons cited for using e-cigs included initial curiosity (54%), pleasing flavors (36%), and to help reduce use of conventional tobacco products (27%).

As outlined in Table 2, seven exposure variables were significantly associated with current e-cig use. Pregnant women who were younger, at a lower gestational age, not married, without other children in the home, had lower education, lower income, and lower body mass index (BMI) were significantly more likely to report current use of e-cigs (all *P* values < 0.05). In addition, compared to pregnant women who did not use e-cigs, significantly more current e-cig users viewed e-cigs as just as safe or safer than conventional cigarettes, both for the mother and the fetus (all *P* values < 0.00, see Figure).

DISCUSSION

This was the first known study to examine the basic epidemiology of e-cig use in pregnant women in this predominantly rural area of Wisconsin. About 1 of every 20 pregnant women in this region used e-cigs during their third trimester of pregnancy. This was considerably higher than national estimates, where just 1% of pregnant women reported e-cig use in the third trimester.[7] This may reflect differences in the underlying characteristics of our source population, including a higher proportion of non-Hispanic White respondents – a group that was more likely to use e-cigs in the national study. Several other exposures that predicted e-cig use in our study also were observed in national data,[7] including individuals who were younger, lower income, and not married.

Cigarette smoking just prior to pregnancy, while trending in the expected direction in that e-cig use was somewhat more common among cigarette smokers, was not as strong of a risk factor for current e-cig use in our study as has been observed nationally.[7] This was somewhat surprising, as 27% of (ever) e-cig users in our

study still indicated e-cigs were used to help reduce use of conventional tobacco products, and current e-cig users near-uniformly believed that e-cigs were just as safe or safer for the mother and fetus relative to cigarettes. Despite evidence that smokers who also use e-cigs are less likely to quit smoking compared to those who do not use e-cigs,[10] beliefs that e-cigs are a safer alternative to tobacco and/or can help with smoking cessation seem to persist in pregnant e-cig users.

Strengths of this study included the linkage of EHR and survey data to identify e-cig risk factors in an understudied population of rural pregnant mothers, as well as use of a propensity score method to help control for imbalances in the respondent sample. Limitations included the small sample size, which precluded multivariable modeling, as well as the cross-sectional design, which limits causal conclusions. In addition, the e-cig use outcome from the PRAMS and several exposure variables were self-reported. Other limitations included the racially homogenous sample, which limits generalizability. In addition to addressing these limitations, future research should examine both maternal and child outcomes of e-cig use after pregnancy in rural populations.

Findings from this study indicate the prevalence of e-cig use in pregnant women in north-central Wisconsin could be 5 times greater than that observed nationally.[6] Several influential social, economic, and demographic risk factors for e-cig use were confirmed, namely younger age, low education and income, and unmarried status. If confirmed in larger studies, this could inform better targeted screening, education, and e-cig prevention strategies during the course of prenatal care in rural areas.

Funding/Support: This project was funded by philanthropic support of the Marshfield Clinic Research Institute's General Medical Research Fund.

Financial Disclosures: None declared.

REFERENCES

1. England LJ, Aagaard K, Bloch M, et al. Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products. *Neurosci Biobehav Rev.* 2017;72:176-189. doi:10.1016/j.neubiorev.2016.11.013

2. Orzabal MR, Lunde-Young ER, Ramirez JI, et al. Chronic exposure to e-cig aerosols during early development causes vascular dysfunction and offspring growth deficits. *Transl Res*. 2019;207:70-82. doi:10.1016/j.trsl.2019.01.001

3. Wang X, Lee NL, Burstyn I. Smoking and use of electronic cigarettes (vaping) in relation to preterm birth and small-for-gestational-age in a 2016 U.S. national sample. *Prev Med*. 2020;134:106041. doi:10.1016/j.ypmed.2020.106041

4. Liao L, Deng Y, Zhao D. Association of low birth weight and premature birth with the risk of metabolic syndrome: a meta-analysis. *Front Pediatr*. 2020;8:405. doi:10.3389/fped.2020.00405

5. *U.S. Department of Health and Human Services. E-cigarette use among youth and young adults. A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2016.

6. Kapaya M, D'Angelo DV, Tong VT, et al. Use of electronic vapor products before, during, and after pregnancy among women with a recent live birth – Oklahoma and Texas, 2015. *MMWR Morb Mortal Wkly Rep*. 2019;68(8):189-194. doi:10.15585/mmwr.mm6808a1

7. Liu B, Du Y, Wu Y, Sun Y, Santillan MK, Santillan DA, Bao W. Prevalence and distribution of electronic cigarette use before and during Pregnancy among women in 38 states of the United States. *Nicotine Tob Res*. 2021;23(9):1459-1467. doi:10.1093/ntr/ntab041

8. Buettner-Schmidt K, Miller DR, Maack B. Disparities in rural tobacco use, smoke-free policies, and tobacco taxes. *West J Nurs Res*. 2019;41(8):1184-1202. doi:10.1177/0193945919828061

9. DeStefano F, Eaker ED, Broste SK, et al. Epidemiologic research in an integrated regional medical care system: the Marshfield Epidemiologic Study Area. *J Clin Epidemiol*. 1996;49(6):643-652. doi:10.1016/0895-4356(96)00008-x

10. Weaver SR, Huang J, Pechacek TF, Heath JW, Ashley DL, Eriksen MP. Are electronic nicotine delivery systems helping cigarette smokers quit? Evidence from a prospective cohort study of U.S. adult smokers, 2015-2016. *PLoS One*. 2018;13(7):e0198047.

Effectiveness of Educational and Psychological Messaging Interventions to Improve Safe Fish Consumption Knowledge and Behaviors Among Asian Women of Childbearing Age

Elizabeth Polter, PhD, MPH; Amanda Haban, MPH; Jon Meiman, MD; Carrie Tomasallo, PhD, MPH

ABSTRACT

Background: We evaluated the effectiveness of an intervention to reduce contaminant exposure from fish consumption among Asian women of childbearing age residing in the Milwaukee, Wisconsin, area.

Methods: Women of childbearing age were randomized to group 1, no intervention; group 2, educational messaging only; or group 3, educational messaging plus a motivational self-affirmation component. Then, we compared safe fish consumption knowledge, intentions, and behaviors among groups.

Results: Among 123 participants, groups 2 and 3 were more likely than group 1 to report "eating fewer fish meals" to reduce exposure to contaminants (group 2 odds ratio [OR] 1.42; 95% CI, 0.59–3.44; group 3 OR 2.76; 95% CI, 1.12–7.03).

Discussion: Self-affirmation messaging can enhance educational messaging to increase safe fish consumption among Asian women of childbearing age.

BACKGROUND

Fish contain key nutrients and are recommended as part of a healthy diet to support fetal neurodevelopment during pregnancy.[1] However, fish consumption might result in fetal exposure to contaminants, including mercury, perfluoroalkyl and polyfluoroalkyl substances (PFAS), and polychlorinated biphenyls (PCBs).[1] The US Food and Drug Administration (FDA), Environmental Protection Agency (EPA),[1] and Wisconsin Department of Natural Resources (DNR)[2,3] have issued advisories to practice safe fish preparation methods and avoid consuming certain fish species. Several freshwater bodies near Milwaukee, Wisconsin, are designated as an Area of Concern because of contaminant levels and have additional consumption advisories.[3]

Asians individuals residing in the United States had higher reported fish consumption than other racial/ethnic groups[4] and might be at higher risk for mercury, PFAS, or PCB contaminant exposure from fish.[5] To better understand fish advisory awareness and consumption behaviors among Asian women of childbearing age (WCBA), we conducted a focus group and quantitative survey. Most focus group participants had not heard of specific advisories.[6] Those who expressed greater self-efficacy (ie, the belief that they could make desired changes to their behavior) were more willing to follow advisories.[6] Among survey respondents, only 40.5% had heard of any fish consumption advisories.[7] These findings demonstrated a need for interventions to increase Asian WCBA's awareness of fish advisories and willingness to follow them.

In this evaluation, we assessed whether educational messaging with or without a motivational self-affirmation component can increase perceived self-efficacy[8] and lead to improved fish advisory awareness and safer fish consumption behaviors.

METHODS

Eligibility and Recruitment

We recruited participants through convenience and snowball sampling. Community advisory group members, schools, DNR listservs, and community organizations distributed recruitment materials to potentially eligible persons. We also asked participants who completed the survey to recruit additional participants within their social networks.

• • •

Author Affiliations: Wisconsin Department of Health Services, Madison, Wisconsin (Polter, Haban, Meiman, Tomasallo); Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia (Polter).

Corresponding Author: Elizabeth Polter, Wisconsin Department of Health Services, 1 W Wilson St, Ste 150, Madison, WI 53703; phone 608.266.7480; email Ura1@cdc.gov; ORCID ID 0000-0001-7336-3492

Interested persons used a hyperlink on the recruitment materials to complete a REDCap (Research Electronic Data Capture) screening survey. Eligible participants must have met the following screening criteria: (1) resided ≥1 year in Milwaukee, Waukesha, Washington, or Ozaukee counties; (2) female; (3) self-identified as Chinese, Filipino, Hmong, or Karen; (4) aged 18 to 50 years; (5) had consumed ≥1 meal of fish caught by the participant or by someone the participant knows from waterbodies in Wisconsin in the last 12 months; (6) the only member of their household to participate in the telephone survey; and (7) had not participated in a previous project about fish consumption with the Wisconsin Department of Health Services. Participants completed survey instruments in their preferred language, which included English, Chinese, Hmong, or Karen.

Table 1. Demographic Characteristics and Baseline Fish Consumption and Preparation Behavior Among 123 Asian Women of Childbearing Age by Intervention Condition – Milwaukee, Wisconsin, June 7, 2023–February 24, 2023

	Overall (n = 123)	Group 1[a] (n = 38)	Group 2[b] (n = 43)	Group 3[c] (n = 42)
Age, years; mean (SD)	32 (7.7)	31 (6.9)	33 (8.2)	33 (7.8)
Years living in the Milwaukee area, mean (SD)	3.5 (0.87)	3.5 (0.86)	3.5 (0.88)	3.5 (0.89)
Household size, mean (SD)	4.3 (2.0)	4.7 (2.3)	4.1 (1.7)	4.1 (2.0)
Number of children in household, mean (SD)	1.5 (1.6)	1.4 (1.7)	1.6 (1.6)	1.6 (1.4)
Ethnicity, n (%)				
Chinese	15 (12)	3 (8)	9 (21)	3 (7)
Filipino	14 (11)	5 (13)	5 (12)	4 (10)
Hmong	77 (63)	25 (66)	22 (51)	30 (71)
Karen	17 (14)	5 (13)	7 (16)	5 (12)
Survey language, n (%)				
English	111 (90)	37 (97)	34 (79)	40 (95)
Karen	6 (5)	1 (3)	5 (12)	0 (0)
Chinese	1 (1)	0 (0)	1 (2)	0 (0)
Hmoob or Hmong	5 (4)	0 (0)	3 (7)	2 (5)
Educational attainment, n (%)				
Some college or less	46 (39)	11 (31)	17 (40)	18 (44)
Associate degree or more	72 (61)	24 (69)	25 (60)	23 (56)
Fish consumption and behaviors				
Local wild-caught fish meal frequency in the last month, n (%)				
1 time in the last month	105 (85)	31 (82)	38 (88)	36 (86)
2 or 3 times in the last month	17 (14)	6 (16)	5 (12)	6 (14)
Storebought fish meal frequency in the last month, n (%)				
1 time in the last month	89 (72)	28 (74)	29 (67)	32 (76)
2 or 3 times in the last month	33 (27)	9 (24)	14 (33)	10 (24)
Have you ever: n (%)				
Eaten fewer fish meals	66 (54)	20 (53)	24 (56)	22 (52)
Eaten different types or species of fish	73 (59)	25 (66)	23 (53)	25 (60)
Avoided eating certain parts of fish (head, fat, belly, skin)	61 (50)	20 (53)	19 (44)	22 (52)
Avoided eating fish from some fishing locations	75 (61)	24 (63)	25 (58)	26 (62)
Consuming fish parts that contain more fat (sometimes or more frequently), n (%)				
Skin	96 (78)	28 (74)	33 (77)	35 (83)
Head	83 (67)	26 (68)	29 (67)	28 (67)
Guts, organs, or other innards	20 (16)	9 (24)	4 (9)	7 (17)
Belly fat	51 (41)	16 (42)	15 (35)	20 (48)
Fish preparation methods that can trap fat and increase contaminant exposure (sometimes or more frequently), n (%)				
Use fish or fish parts to make broth, stock, curry, or soup	58 (47)	20 (53)	17 (40)	21 (50)
Fish preparation methods that reduce contaminant exposure, n (%)				
Grill or roast	109 (89)	31 (82)	38 (88)	40 (95)

[a]Group 1: No intervention components (control group).
[b]Group 2: Educational interventions only.
[c]Group 3: Self-affirmation and educational interventions.

Procedures

After screening, we randomized participants 1:1:1 to group 1 (no intervention), group 2 (educational messaging only), or group 3 (educational and motivational self-affirmation messaging). All participants completed a baseline REDCap survey. Within that survey, groups 2 and 3 completed the intervention components. After the interventions, all participants completed additional survey items in the same survey instrument. One month later, participants were sent a follow-up survey through REDCap. Each participant received $30 and $20 gift cards after completing the baseline survey and 1-month follow-up survey, respectively. This activity was reviewed by the Centers for Disease Control and Prevention (CDC), deemed not research, and conducted consistent with applicable federal law and CDC policy (45 CFR part 46.102(l)(2), 21 CFR part 56; 42 USC Sect 241(d); 5 USC Sect 552a; 44 USC Sect. 3501 et seq).

Intervention Components

Educational Messages: Groups 2 and 3 read health messages, including recommendations from the FDA, EPA, and Wisconsin DNR.[1-3,9] Participants read through infographics showing healthy fish serving sizes for children and adults and fish preparation methods to reduce chemical exposure. Graphics also showed fresh-caught and storebought fish species categorized as "up to 2 meals per week," "up to 1 meal per week," "up to 1 meal per month," and "do not eat." A final message included general advice for reducing contaminant exposure in fresh-caught fish (eg, "choose smaller, younger fish") (Appendices 1 and 2).

Self-Affirmation Messages: Immediately before they saw the educational messages, group 3 completed a self-affirmation exercise.

Table 2. Participant Fish Consumption Intentions, Consumption Behaviors, and Preparation Methods —Milwaukee, Wisconsin, June 7, 2023–February 24, 2023

	Group 1[a] (n = 38)		Group 2[b] (n = 43)		Group 3[c] (n = 42)	
Postintervention Intentions (Yes)	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
Eat 1 to 2 servings (but not more) of fish every week	N/Ad	N/Ad	33 (77)	Ref	33 (79)	1.11 (0.40–3.14)
Choose to eat types (species) of fish that are lower in chemicals, like mercury	N/A[d]	N/A[d]	39 (91)	Ref	39 (93)	1.33 (0.28–7.14)
Clean or cook fish using ways that may lower the amount of chemicals	N/A[d]	N/A[d]	40 (93)	Ref	39 (93)	0.98 (0.17–5.55)
Behaviors at 1-month follow-up	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Intention to follow educational messages (n: sometimes or more frequently)	N/Ad	N/Ad	33 (77)	Ref	32 (76)	0.97 (0.35–2.67)
Behavior changes in the past month (n: Yes)						
Eaten fewer fish meals	17 (45)	Ref	23 (53)	1.42 (0.59–3.44)	29 (69)	2.76 (1.12–7.03)
Eaten different types or species of fish	17 (45)	Ref	18 (42)	0.89 (0.47–2.15)	25 (60)	1.82 (0.75–4.47)
Avoided eating certain parts of fish (head, fat, belly, skin)	21 (55)	Ref	31 (72)	2.09 (0.84–5.37)	27 (64)	1.46 (0.59–3.61)
Avoided eating fish from some fishing locations	18 (47)	Ref	30 (70)	2.56 (1.04–6.51)	31 (74)	3.13 (1.25–8.22)
Specific fish consumption behaviors						
Consuming fish parts that contain more fat (n: sometimes or more frequently)						
Skin	27 (71)	Ref	26 (60)	0.69 (0.25–1.81)	22 (52)	0.54 (0.19–1.81)
Head	25 (66)	Ref	13 (30)	0.23 (0.09–0.59)	12 (29)	0.23 (0.08–0.60)
Guts, organs, or other innards	6 (16)	Ref	3 (7)	0.42 (0.08–1.73)	4 (10)	0.63 (0.15–2.40)
Belly fat	18 (47)	Ref	10 (23)	0.35 (0.13–0.91)	9 (21)	0.34 (0.12–0.89)
Fish preparation methods that might trap fat and increase contaminant exposure						
Use fish or fish parts to make broth, stock, curry, or soup (n: sometimes or more frequently)	22 (58)	Ref	11 (26)	0.26 (0.10–0.66)	12 (29)	0.32 (0.12–0.83)
Fish preparation method that might reduce contaminant exposure						
Grill or broil fish (n: sometimes or more frequently)	28 (74)	Ref	30 (70)	0.96 (0.34–2.74)	26 (62)	0.76 (0.27–2.13)

Abbreviation: OR, odds ratio.

[a]Group 1: No intervention components (control group).

[b]Group 2: Educational interventions only.

[c]Group 3: Self-affirmation and educational interventions.

[d]Group 1 was not asked items regarding postintervention intentions.

In self-affirmation interventions, participants are presented with reminders of their values to affirm a positive self-image. These reminders might increase perceived self-efficacy and willingness to adopt desired behaviors.[10] To remind participants of their values, we asked each participant to respond to a series of items about their motivations. Each participant selected from a list of statements that "best represents what is most important to you when deciding how and what you eat." Their selection prompted a nested list of new value statements related to their first choice. They selected a statement from this second list, then answered open-ended questions about why their chosen statement reflected their values (Appendices 1 and 2).

Survey Items

We collected demographic information and baseline fish consumption behaviors. A full list of survey items is available in Appendix 2. Immediately after the intervention, groups 2 and 3 reported whether they intended to make certain behavior changes (eg, "eat 1 to 2 servings [but not more] of fish every week") in the next 30 days.

One month after the initial survey and intervention, we reassessed how frequently participants had consumed local, fresh-caught, and storebought fish. Using the same items as the baseline survey, participants were asked how frequently they consumed certain fish parts and used different fish preparation methods. Participants reported whether they had made changes to their fish consumption habits in the past month. Groups 2 and 3 reported how frequently they intended to follow messages from the educational intervention.

Statistical Analysis

We calculated descriptive statistics of participant demographics, baseline fish consumption habits, and advisory awareness. We fit unadjusted logistic regression models to calculate odds ratios (OR) for differences among groups in postintervention intentions, reported behavior changes, fish consumption habits, and fish preparation methods at 1 month follow-up. For each model, the dependent variable was the 1-month survey item of interest, and the independent variable was the intervention group, with group 1 as the reference. For analysis, we focused on fish consumption habits and preparation methods mentioned in the educational materials as either increasing (ie, consuming the skin, head, guts, organs, innards, or belly fat or using fish to make broth, stock, curry, or soup) or decreasing (ie, grilling or broiling fish) contaminant exposure. To maximize sample size in each category, any item with a range of responses was dichotomized for analysis (eg, a 6-point scale from "1 time in the last month" to "2 or more times per day" was reduced to "<1 time

per week" vs "≥1 times per week"). We used R version 4.4.0 (R Core Team) for all analyses.

RESULTS

In total, 123 Asian women aged 20 to 50 years were survey participants. Thirty-eight participants were randomized to group 1, 43 to group 2, and 42 to group 3. Most participants were Hmong (n = 77, 63%), followed by Karen (n = 17, 14%), Chinese (n = 15, 12%), and Filipino (n = 14, 11%). Nearly all (n = 111, 90%) participants chose to complete the survey in English. Most participants had at least an associate degree (61%) (Table 1).

Most participants in the intervention groups reported intentions to follow educational messages. Immediately after the intervention, 77% of group 2 and 79% of group 3 reported they planned to "eat 1 to 2 servings (but not more) of fish every week." Likewise, 91% to 93% said they planned to "choose to eat types (species) of fish that are lower in chemicals, like mercury" and "clean or cook fish using ways that may lower the amount of chemicals." However, because group 1 did not answer these items, it is unclear whether the interventions improved participant intentions.

After 1 month, 77% of group 2 and 76% of group 3 reported they intended to follow the educational messages from the intervention (Table 2). Group 3 had higher odds than group 1 of reporting most behavior changes in the past 30 days, including "eating fewer fish meals" (OR 2.76; 95% CI, 1.12–7.03), "eating different types or species of fish" (OR 1.82; 95% CI, 0.75–4.47), and "avoided eating fish from some fishing locations" (OR 3.13; 95% CI, 1.25–8.22). Groups 2 and 3 reported eating the skin, head, guts, and belly fat of fish less often than group 1 (Table 2).

DISCUSSION

In this behavioral intervention of Asian WCBA in the Milwaukee area, we found motivational self-affirmation and educational messaging improved fish advisory awareness and safer fish consumption behaviors. Both groups 2 and 3 reported less frequent use of higher-contaminant fish preparation methods than group 1. These results are encouraging evidence that educational messaging might reduce these communities' contaminant exposure from fish consumption. Group 3 was more likely than group 1 to report behavior changes to avoid contaminants from fish, indicating self-affirmation interventions are also beneficial. In keeping with our previous findings, intervention components designed to increase both fish advisory knowledge and self-efficacy increased safe fish consumption behaviors.

Maternal exposure to mercury, PFAS, and PCB contamination may lead to adverse birth outcomes and impact cognitive and reproductive health in infants.[2] Our team's prior studies found that a sample of mostly White, mostly male Milwaukee-area anglers had elevated contaminant levels, and in Wisconsin, Asian people have higher incidence of severe maternal morbidity and low birthweight than comparator groups.[11,12] Although these poor outcomes are likely multifactorial, limiting contaminant exposure from eating fish in Asian WCBA in the Milwaukee area may improve maternal and child health and reduce these health disparities. Clinicians and public health practitioners can use these combined educational and self-affirmation materials to reduce contaminant exposure from fish consumption in this community.

Limitations

Our smaller-than-intended sample size (n = 201) limits inference. Second, surveys and intervention materials required internet access and fluency in written English, Hmong, Chinese, or Karen, which might have excluded some eligible persons. Third, responses were self-reported and subject to social desirability bias. Lastly, we followed participants for only 1 month, so durability of our findings is unknown.

CONCLUSIONS

This behavioral intervention was associated with increased safe fish consumption behaviors among Asian WCBA in the Milwaukee area. Self-affirmation paired with educational messaging might be a valuable tool to reduce contaminant exposure from fish in this population.

Funding/Support: None declared.

Financial Disclosures: None declared.

Acknowledgement: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Appendices: Available at www.wmjonline.org

REFERENCES

1. Advice about eating fish: For those who might become or are pregnant or breastfeeding and children ages 1-11 years. United States Food and Drug Administration; 2021. Accessed September 30, 2023. https://www.fda.gov/media/102331/download#:~:text=The%20Dietary%20Guidelines%20for%20Americans%20recommends%3A&text=At%20least%208%20ounces%20of,on%20a%202%2C000%20calorie%20diet.&text=Those%20who%20are%20pregnant%20or%20breastfeeding%20consume%20between%208%20and,that%20are%20lower%20in%20mercury.

2. Choose wisely: A health guide for eating fish in Wisconsin. Wisconsin Department of Natural Resources2024-2026. Accessed July 13, 2024. https://widnr.widen.net/s/s6mkcq6tmr/pub_fh_824_choosewisely

3. Advice for eating fish from the area: Milwaukee River Estuary from Estabrook Falls to Harbor Mouth Including Menomone and Kennickinnic Rivers. Wisconsin Department of Natural Resources. Accessed November 16, 2023. https://apps.dnr.wi.gov/fishconsumptionadvisoryquery/

4. Terry AL, Herrick KA, Afful J, Ahluwalia N. *Seafood consumption in the United States, 2013-2016*. NCHS Data Brief no. 321. National Center for Health Statistics, Centers for Disease Control and Prevention; 2018. Accessed July 13, 2024. https://www.cdc.gov/nchs/products/databriefs/db321.htm

5. Li A, Tang Q, Kearney KE, et al. Persistent and toxic chemical pollutants in fish consumed by Asians in Chicago, United States. *Sci Total Environ*. 2022;811:152214. doi: 10.1016/j.scitotenv.2021.152214

6. Shaw S, He X, Haban A, Tomasallo C, Meiman J. A focus group study of fish consumption behaviors among asian women in Milwaukee, Wisconsin. *Prev Med Rep*. 2023:36:102528. doi:10.1016/j.pmedr.2023.102528

7. Schinwald M, Polter E, Haban A, Meiman J, Tomasallo C. Fish consumption advisory awareness and behavior among Asian women of childbearing age — Milwaukee, Wisconsin, January 1, 2022–January 31, 2023. *WMJ*. 2024;123(6):521-527.

8. Cohen GL, Sherman DK. The psychology of change: self-affirmation and social psychological intervention. *Annu Rev Psychol*. 2014;65:333-371. doi:10.1146/annurev-psych-010213-115137

9. *Should I Eat the Fish I Catch? A guide to healthy eating of the fish you catch*. Office of Science and Technology, United States Environmental Protection Agency; 1997. Accessed April 16, 2024. https://www.epa.gov/sites/default/files/2019-05/documents/should-i-eat-fish-1997.pdf

10. Sherman DK, Cohen GL. The psychology of self-defense: Self-affirmation theory. In: Zann MP, ed. *Advances in Experimental Social Psychology.* Elsevier Academic Press; 2006(38):183-242. doi:10.1016/S0065-2601(06)38004-5

11. Gibson C, Rohan AM, Gillespie KH. Severe maternal morbidity during delivery hospitalizations. *WMJ*. 2017;116(5):215-220.

12. Birth Outcomes Dashboard. Wisconsin Department of Health Services, Division of Public Health, Office of Health Informatics. Updated February 26, 2024. Accessed August 30, 2024. https://www.dhs.wisconsin.gov/stats/births/birth-outcomes.htm

Vital Moments

Kristen Mahaffey

Artist Statement:

As an artist, my goal is to create whimsical art that doesn't take itself too seriously. I like to express the fun, happiness, and joy in mundane moments and mundane objects. Vital Moments depicts a typical doctor's office setting with a doctor checking vitals on her young patient who looks up at her with trusting eyes.

Gun Violence in Children: A Public Health Crisis and an Upstream Approach to Our Response

Kellie C. Snooks, DO, MPH; Michael Levas, MD, MS; Megan L. Schultz, MD, MA

For the past 6 decades, motor vehicle crashes have been the leading cause of death for American children and adolescents.[1] However, in 2020, guns overtook motor vehicles as the leading cause of death for all American youth.[2] We are now living in an age where guns kill more children than cancer or infection; we are living in a country where a child dies by a gun, on average, every 3.5 hours.[3] Every week, we lose 2 classrooms full of American children due to gun violence.

These dire statistics are also true for kids in Wisconsin: as of 2020, guns are the leading cause of death for Wisconsin children. From 2020 through 2022, guns claimed the lives of 130 Wisconsin children aged 0 to 17 years and 96 young adults aged 18 to 19 years.[4] As a comparison, these deaths represent a respective 23% and 99% increase from the years 2015 through 2018.[4] At Children's Wisconsin, we have seen a 3-fold increase in firearm injuries at our level I pediatric trauma center compared to prepandemic numbers: during 2016-2019, we treated 40 to 50 children per year for gunshot wounds, while in 2023, we saw more than 140 kids with gun shot wounds. We also have seen a sharp increase in firearm-related mortality at our hospital, peaking at 12 pediatric deaths in 2022.[5]

We are now living in an age where guns kill more children than cancer or infection; we are living in a country where a child dies by a gun, on average, every 3.5 hours. Every week, we lose 2 classrooms full of American children due to gun violence.

As we formulate our response to this national public health crisis, it is important to consider how guns impact children differently based on socioeconomic status, gender, age, and race. For example, children living in poverty are more likely to die from firearm injuries than their wealthier peers, and boys represent 85% of all pediatric gun deaths.[2] In children under 11 years of age, a significant percentage of firearm-related deaths are due to unintentional discharge (19%), while among adolescents, suicide represents an increased burden of firearm-related deaths (31%).[3] Across all ages, however, gun assaults remain the leading cause of firearm-related deaths, representing over two-thirds of all children who die by gun violence.[3]

Pediatric gun violence rates also vary widely – and tragically – by race, with Black children by far being the most affected: Black children are 6 times more likely to die by gun violence than White children.[6] Black children comprise just 14% of the US pediatric population, yet account for a staggering 48% of firearm-related pediatric deaths.[6] Gun violence has risen among other racial groups as well: from 2018 through 2022, Hispanic youth experienced a 73% increase in firearm deaths, and rates among American Indian and Alaska Native children nearly doubled.[3] White children, meanwhile, are disproportionately affected by gun suicide: in 2021, 78.4% of all pediatric firearm suicides were White children.[2]

The impact of gun violence continues far beyond hospital walls. Families, communities, health care workers, first responders, and educators carry long-lasting psychological burdens when a child is a victim of gun violence. Children who are injured by firearms have an increased risk of inpatient hospitalization, emergency department visits, mental health

Author Affiliations: Department of Pediatrics, Division of Critical Care, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Snooks); Department of Pediatrics, Division of Emergency Medicine, MCW, Milwaukee, Wisconsin (Levas, Schultz).

Corresponding Author: Kellie C. Snooks, DO, MPH, FAAP, Medical College of Wisconsin, Department of Pediatrics, Division of Pediatric Critical Care, 9000 W Wisconsin Ave, MS 681, Milwaukee, WI 53226; phone 414.266.3360; email ksnooks@mcw.edu; ORCID ID 0000-0001-8439-303X

Table. Effective Gun Violence Prevention Laws

Legislation	Parameters	Evidence
Child access prevention	Holds a gun owner liable if a child accesses a firearm. Degree of criminal liability varies based on state law.	The strictest child access prevention laws are associated with decreased pediatric firearm mortality.[15]
Universal background checks	Federal and local law enforcement checks of an individual purchasing a firearm.	In a 5-year analysis of gun laws and pediatric mortality rates, univeral background checks were associated with lower firearm mortality rates in children.[15]
Extreme risk protection, aka "Red Flag Laws"	Through a court order an individual who may be at imminent risk of injuring themselves or someone else may have their firearms temporarily removed and may be temporarily prohibited from purchasing a firearm.	Analyses following the implementation of Indiana and Connecticut Extreme Risk Protection Orders have shown decreases in suicide deaths in their states.[15,16]
Buyer regulations	Examples of buyer regulations include increasing the minimum age for purchasing certain types of firearms, requiring permits or licenses, and mandatory waiting periods.[15]	The mandatory 48 hour waiting period for purchasing a handgun in the state of Wisconsin was repealed in 2015. This repeal has been associated with increased suicide rates in the state.[17]

care utilization, substance use treatment, and health care costs in the year following their injury.[7,8] Research has shown that youth who simply witness gun violence, without being directly victimized, experience posttraumatic stress disorder, anxiety, and poor school performance.[3,9] Exposure to gun violence also affects first responders and health care providers: multiple studies have shown increasing rates of posttraumatic stress disorder among these groups specifically.[10,11] As the ripple effects of gun violence continue to traumatize so many Americans, we must enact change.

A Multifaceted Public Health Approach

An upstream, evidence-based public health approach to gun violence prevention is crucial to save the lives of children. We can look to successful public health injury prevention techniques in history for guidance: one particularly effective public health success story is decreasing injury and death due to motor vehicle crashes (MVC). Over the past 60 years, there have been steady financial, cultural, technological, and structural investments in our country to make automobiles safer, eventually leading to a 40% decrease in MVC-related injuries since 2000.[1] Seatbelts, airbags, and blind spot alerts represent examples of technological advancements that have made our cars safer, while drunk driving laws, driver's license age limits, and roadway reconfigurations are examples of legislative and environmental advancements that have made driving safer in general. There is also a federal agency that specifically oversees the safety of motor vehicles: the National Highway Traffic Safety Administration (NHTSA).[1] For decades, the NHTSA has maintained a database of the surrounding details for all MVC-related injuries and deaths, which has invaluably informed and shaped legislation, medical research, and publicly available data on automobile safety ratings in our country.

Now let's apply the lessons learned from this public health success story to guns: although guns are now the leading cause of death for American children, guns currently are not regulated by any federal agency. There is no federal database of gun shot wounds or firearm-related deaths. Gun manufacturers are exempt from civil prosecution,[12] and until 2019, medical research on gun violence prevention was restricted by federal law.[13] Meanwhile, the lethality of bullets, capacity of magazines, and firing rate of firearms all have increased dramatically during a time when legislation to address gun access and safety has relaxed nationwide.

A public health approach to preventing firearm injuries and deaths requires significant investment across public and private sectors. We need to prevent gun violence before it occurs with secure storage, evidence-based policy and legislation, and gun safety education. We need to mitigate the lethality of guns with industry regulations and technological advancements, and we need to improve outcomes for gun violence victims after an injury has occurred. Finally, it is essential we understand the etiology and disparities of gun violence with evidence-based research to target specific interventions and education at each level of care. Examples of a multifaceted upstream approach to gun violence include secure storage, community- and hospital-based violence intervention programs, and legislative measures and are detailed below.

Secure Storage

Secure firearm storage is a life-saving measure that can prevent deaths due to both suicide and unintentional shootings. The American Academy of Pediatrics (AAP) defines the secure storage of a firearm as unloaded, locked, with ammunition locked and stored separately from the firearm. Approximately 4.6 million children in the US live in a house with an improperly stored gun.[14] Notably, 85% of gun-related deaths in children under 12 occur at home.[15] The AAP emphasizes the need for pediatricians to provide anticipatory guidance on safe storage practices during all well child checks; ideally, this should be done for patients of any age to prevent gun-related suicides and homicides. There are a wide variety of secure storage devices that range in cost, from trigger locks to biometric safes; guidance on which device to choose should be tailored to each family's needs and locally available resources.

Community and Hospital Investments

Community violence intervention (CVI) programs and hospital-based violence intervention programs (+HVIP) are essential elements

of a comprehensive approach to gun violence. CVI programs focus on community level in fostering collaboration between hospital systems, trusted community members, community-based organizations, and government entities to reduce gun violence. This approach has been utilized in many major metropolitan areas with successful reductions in homicides. HVIPs identify youth who have experienced violent injuries and connect them with victim advocates. These advocates provide support throughout the healing process, with the goal of promoting recovery and reducing the risk of future violence. HVIPs have shown significant success in breaking cycles of violence and reinjury.[15] Investing in these programs is essential, as their preventive impact reduces both violence and the overall disease burden. Clinicians and health care systems must continue to invest in these lifesaving initiatives to ensure their long-term effectiveness.

Legislative Approaches

As health care providers, an understanding of how effective legislation at both the state and federal levels can save the lives of children is also essential. Child firearm access prevention laws, universal background checks, and extreme risk protection orders are all examples of legislation that work to prevent gun deaths and injuries.[15,16,18,19] The Table demonstrates examples of these type of evidence-based legislative solutions.

Conclusions

Guns are the leading cause of death for children across the US, including Wisconsin. Gun violence in youth is a public health crisis that requires a multifaceted upstream approach to overcome its current catastrophic trajectory. Approaching the crisis with such evidence-based public health methods as secure storage counseling, CVI and HVIP investments, and legislative action will mitigate gun deaths and injuries in children. We pediatricians are used to advocating for children's safety, from bike helmets to swimming lessons; it is now time for all health care providers, across the age spectrum, to advocate for gun violence prevention. It is time for us to look upstream and protect our country's and our state's children.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Lee LK, Douglas K, Hemenway D. Crossing lines - a change in the leading cause of death among U.S. children. *N Engl J Med.* 2022;386(16):1485-1487. doi:10.1056/NEJMp2200169

2. Roberts BK, Nofi CP, Cornell E, Kapoor S, Harrison L, Sathya C. Trends and disparities in firearm deaths among children. *Pediatrics*. 2023;152(3) e2023061296. doi:10.1542/peds.2023-061296

3. Panchal N. The Impact of Gun Violence on Children and Adolescents. KFF. Published February 22, 2024. Accessed November 26, 2024. https://www.kff.org/mental-health/issue-brief/the-impact-of-gun-violence-on-children-and-adolescents/#footnote-612901-1

4. WISH Query System: Injury-Related Mortality - 1999 -2022. Wisconsin Interactive Statistics on Health (WISH) Query System. Wisconsin Department of Health Services. Updated January 2024. Accessed November 26, 2024. https://www.dhs.wisconsin.gov/wish/index.htm

5. Children's Wisconsin Trauma Registry. Children's Wisconsin; 2024. Accessed November 26, 2024.

6. Recent increases in firearm deaths of children and adolescents have been driven by gun assaults, Black youths are disproportionally affected. News release. KFF. Feb. 22, 2024. Accessed November 26, 2024. https://www.kff.org/mental-health/press-release/recent-increases-in-firearm-deaths-of-children-and-adolescents-have-been-driven-by-gun-assaults-black-youths-are-disproportionally-affected/

7. Oddo ER, Simpson AN, Maldonado L, Hink AB, Andrews AL. Mental health care utilization among children and adolescents with a firearm injury. *JAMA Surg*. 2023;158(1):29-34. doi:10.1001/jamasurg.2022.5299

8. Gastineau KAB, Oddo ER, Maldonado LG, Simpson AN, Hink AB, Andrews AL. Health care utilization after nonfatal firearm injuries. *Pediatrics*. 2024;153(1): e2022059648. doi:10.1542/peds.2022-059648

9. Turner HA, Mitchell KJ, Jones LM, Hamby S, Wade R, Beseler CL. Gun violence exposure and posttraumatic symptoms among children and youth. *J Traum Stress*. 2019;32(6):881-889. doi:10.1002/jts.22466

10. Skogstad M, Skorstad M, Lie A, Conradi HS, Heir T, Weisaeth L. Work-related post-traumatic stress disorder. *Occup Med.* 2013;63(3):175-182. doi:10.1093/occmed/kqt003

11. Choi KR, Heilemann MV, Romero SA, et al. "The wild west:" nurse experiences of responding to the 2017 Las Vegas mass shooting. *Disaster Med Public Health Prep*. 2023;17: e492. doi:10.1017/dmp.2023.140

12. Vernick JS, Rutkow L, Salmon DA. Availability of litigation as a public health tool for firearm injury prevention: comparison of guns, vaccines, and motor vehicles. *Am J Public Health.* 2007;97(11):1991–1997. doi:10.2105/AJPH.2006.092544

13. Rostron A. The Dickey Amendment on federal funding for research on gun violence: a legal dissection. *Am J Public Health*. 2018;108:865-867. doi:10.2105/AJPH.2018.304450

14. Miller M, Azrael D. Firearm storage in US households with children: findings from the 2021 National Firearm Survey. *JAMA Netw Open.* 2022;5(2):e2148823. doi:10.1001/jamanetworkopen.2021.48823

15. Lee LK, Fleegler EW, Goyal MK, et al. Firearm-related injuries and deaths in children and youth. *Pediatrics*. 2022;150(6): e2022060071. doi:10.1542/peds.2022-060071

16. Kivisto AJ, Phalen PL. Effects of risk-based firearm seizure laws in Connecticut and Indiana on suicide rates, 1981-2015. *Psychiatr Serv*. 2018;69(8):855–862. doi:10.1176/appi.ps.201700250

17. Dunton ZR, Kohlbeck SA, Lasarev MR, Vear CR, Hargarten SW. The association between repealing the 48-hour mandatory waiting period on handgun purchases and suicide rates in Wisconsin. *Arch Suicide Res*. 2022;26(3):1327-1335. doi:10.1080/13811118.2021.1886209

18. Fleegler EW, Lee LK, Monuteaux MC, Hemenway D, Mannix R. Firearm legislation and firearm-related fatalities in the United States. *JAMA Intern Med*. 2013;173(9):732-740. doi:10.1001/jamainternmed.2013.1286

19. Goyal MK, Badolato GM, Patel SJ, Iqbal SF, Parikh K, McCarter R. State gun laws and pediatric firearm-Related Mortality. *Pediatrics*. 2019;144(2): e20183283. doi:10.1542/peds.2018-3283.

Outcomes Among Well-appearing Infants Initially Deferred Antibiotics for Fever

Emily Willey, PharmD; Tracy Zembles, PharmD, BCPS, BCIDP; Elizabeth Segar, MD; Evelyn Kuhn, PhD; Brianna Mayer, PharmD, BCPPS

ABSTRACT

Introduction: The 2021 American Academy of Pediatrics guideline on well-appearing febrile infants recommends deferral of lumbar puncture and/or initial antibiotics in certain patients 22 to 60 days old, along with shared decision-making with the patient's caregivers. This study sought to compare the incidence of invasive bacterial infection and/or need for escalation of care in febrile infants in this age group who did and did not receive initial empiric antibiotics before and after implementation of the guideline.

Methods: This was a single-center, retrospective cohort evaluation of admitted patients before and after guideline implementation. Well-appearing infants 22 to 60 days old who presented to the emergency department with fever and met guideline criteria were included. The primary outcome compares the incidence of invasive bacterial infections and escalation of care among patients who did and did not defer initial antibiotics. Secondary outcomes include rate of positive bacterial cultures, length of stay, and mortality. Patient demographics, antibiotic initiation, culture data, inflammatory markers, urinalysis, lumbar puncture and cerebrospinal fluid cell counts, readmission within 7 days of discharge, length of stay, and mortality within 30 days were collected and analyzed.

Results: Sixty-one patients were included: 21 in the pre-guideline group and 40 in the post-guideline group. There was no difference in the incidence of invasive bacterial infections or escalation of care between groups. There was no difference in rate of positive bacterial cultures, length of stay, or mortality. More patients in the pre-guideline group received a lumbar puncture compared to the post-guideline group.

Conclusions: Our results affirm guideline recommendations suggesting deferral of antibiotics in well-appearing infants meeting select criteria results in decreased antibiotic use and lumbar punctures without affecting the rate of invasive bacterial infections or need for escalation of care.

INTRODUCTION

Neonatal fever is common in the emergency department (ED) and a challenging presentation for infants less than 60 days old.[1] Clinical presentation cannot easily identify patients at high risk for invasive bacterial infection; fever is often the only clinical sign of an infection in these patients, which leads to many infants receiving lumbar punctures and empiric antibiotics.[2,3] Prompt initiation of antibiotics for infection leads to better outcomes.[1] Consensus recommendations support starting antibiotics within 1 hour of presentation for septic shock and 3 hours for all other infections.[1,4] However, unnecessary lumbar punctures, antibiotics, and hospital admissions are not without risks and can be costly, potentially harmful, and could lead to antimicrobial resistance and adverse effects.[5] Previous studies have developed criteria and algorithms for identifying patients at low risk for invasive bacterial infections.[1] Furthermore, advances in laboratory testing have led to more rapid identification of pathogens, and measurement of more specific inflammatory markers have improved the identification of infants at low risk for invasive bacterial infection.

Previously, a national guideline did not exist to guide treatment of febrile infants, and practice was largely based on expert opinion. In 2021, the American Academy of Pediatrics (AAP) released evidence-based guidelines to address evaluation and management of well-appearing, term infants 8 to 60 days old presenting with a fever and no evident source of infection.[5] The

• • •

Author Affiliations: Children's Wisconsin, Milwaukee, Wisconsin (Willey, Zembles, Kuhn, Mayer); Medical College of Wisconsin, Milwaukee, Wisconsin (Segar).

Corresponding Author: Emily Willey, PharmD; 8915 W Connell Ct, Milwaukee, WI 53226; email emilyrwilley@gmail.com; ORCID ID 0009-0000-2285-9674

guideline recommends deferral of lumbar puncture and/or initial antibiotics in certain patients 22 to 60 days old, along with shared decision-making with the patient's caregivers. This study sought to evaluate the impact of implementing the guideline by comparing the incidence of invasive bacterial infection and/or need for escalation of care in febrile infants 22 to 60 days old before and after guideline implementation who did and not receive antibiotics, respectively.

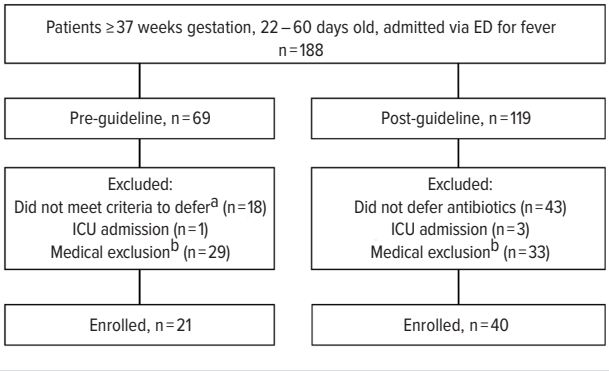
METHODS

This is a single-center, quasi-experimental study conducted at a 298-bed freestanding, academic children's hospital. Well-appearing patients 22 to 60 days old and at least 37 weeks gestation admitted through the ED for fever were included. An institutional guideline was created in 2021 that incorporated the AAP recommendations; well-appearing infants with no evident source of infection were candidates to be monitored without administration of antibiotics. We compared outcomes during a pre-guideline phase (January 1, 2020, through December 31, 2020) and a post-guideline phase (January 1, 2022, through December 31, 2022), with a washout period between when the guideline was being discussed and developed. Patients with confirmed or suspected herpes simplex virus infection, focal bacterial infection, clinical bronchiolitis, congenital or chromosomal abnormalities, or who were immunocompromised were excluded as outlined in the AAP guideline. Patients admitted to an intensive care unit (ICU) were excluded, as these patients were "ill-appearing" by guideline definition and did not qualify for antibiotic deferral. Infants who received antibiotics prior to admission also were excluded. Fever was defined as temperature ≥ 38 °C.

Patient demographics, laboratory, microbiologic, and clinical data were abstracted from the electronic health record. Patient demographics included age at admission, gestational age, and sex. Laboratory values collected included urinalysis, cerebrospinal fluid (CSF) analysis, and inflammatory markers (procalcitonin, C-reactive protein, absolute neutrophil count [ANC], and total white blood cell count). The urinalysis was considered positive if there were positive nitrites, leukocyte esterase, or greater than 5 white blood cells per high power field in the urine. Microbiologic data collected included blood, urine, and CSF cultures (if lumbar puncture was performed). Organisms considered contaminants by the medical team as documented in the electronic health record, such as coagulase negative *Staphylococci,* and urine cultures with less than 100 000 colony forming units were considered negative. Finally, antibiotic regimens, duration of therapy, length of hospital stay, readmission within 7 days of discharge with initiation of antibiotics for presumed or confirmed bacterial infection, and mortality within 30 days of admission also were reported through manual chart review.

Primary outcomes included (1) rate of invasive bacterial infections, defined as bacterial meningitis or bacteremia, and (2) need for escalation of care, defined as ICU admission, initiation of antibiotics after initial deferral, or readmission to the hospital or ED within 7 days of discharge for a bacterial infection. Secondary endpoints included rate of positive cultures, length of stay, and mortality within 30 days of discharge.

Figure. Consort Diagram



Abbreviations: ED, emergency department; ICU, intensive care unit.
[a]Criteria according to guidelines in accordance with the 2021 American Academy of Pediatric evaluation and management of well-appearing febrile infants 8–60 days old.
[b]Herpes simplex virus, focal bacterial infection, clinical bronchiolitis, congenital or chromosomal abnormalities, or immunocompromised.

The proportions of patients with various demographic or medical characteristics in the 2020 cohort versus the 2022 cohort were compared using chi-square tests or Fisher exact tests. Continuous/numeric variables (eg, age, antibiotic duration) were compared using *t* tests (not assuming equal variance). Statistical analysis was performed using IBM SPSS Statistics version 20.0 (IBM Corp, Armonk, New York). This study was reviewed by the Institutional Review Board and determined to be nonhuman subject research.

RESULTS

A total of 188 admitted patients from 22 to 60 days old were screened for inclusion; 21 met inclusion for deferral of antibiotics in the pre-guideline group and 40 in the post-guideline group (Figure). Baseline characteristics were similar between the groups (Table 1), except infants in the pre-guideline group were older than the post-guideline group (41 vs 33 days, $P = 0.031$).

Incidence of invasive bacterial infection was similar between the 2 groups (0 vs 1, $P = 1$) (Table 2). Likewise, need for escalation of care was similar ($P = 0.084$). Infants in the post-guideline group had fewer lumbar punctures performed compared to the pre-guideline group ($P < 0.001$). There were no deaths in either group. There was no difference in the number of positive cultures ($P = 0.541$). Length of stay was similar between groups ($P = 0.926$).

DISCUSSION

Our data suggest that deferring antibiotics in well-appearing febrile infants aged 22 to 60 days did not result in negative outcomes,

Table 1. Baseline Characteristics

	2020 Cohort (N = 21)	2022 Cohort (N = 40)	*P* value
Age (days), mean (SD)	40.76 (13.10)	33.13 (11.60)	0.031
22 – 28 days old, n (%)	8 (38.1)	23 (57.5)	0.150
29 – 60 days old, n (%)	13 (61.9)	17 (42.5)	
Gestational age (weeks), mean (SD)	38.38 (1.16)	38.58 (0.81)	0.500
Female, n (%)	10 (47.6)	15 (37.5)	0.445
Concomitant viral infection, n (%)	8 (38.1)	8 (20)	0.127
Maximum temperature, mean (SD)	38.26 (0.49)	38.35 (0.65)	0.576
White blood cell count, mean (SD)	9.94 (6.74)	9.49 (3.94)	0.781
Absolute neutrophil count, mean (SD)	4341.8 (4220.6)	3497.2 (2347.5)	0.403
Deferred initial antibiotics, n (%)	2 (9.5)	40 (100)	< 0.001

Table 2. Endpoints

	2020 Cohort (N = 21)	2022 Cohort (N = 40)	*P* value
Composite, escalation of care	0	7 (17.5)	0.084
ICU admission, n (%)	0	0	NA
ED or hospital within 7 days, n (%)	0	1 (2.5)	1.00
Initiation of antibiotics,[a] n (%)	0	6 (15.0)	1.00[b]
Lumbar puncture performed, n (%)	19 (90.5)	12 (30.0)	< 0.001
Invasive bacterial infection	0	1 (2.5)	1.00
Positive culture[c]	0	2	0.541
Blood, n (%)	0	0	NA
CSF or Biofire,[d] n (%) (n = 33)	0	1 (8.3)	0.364
Urine, n (%)	0	2 (5.0)	0.541
Length of stay (hours), mean (SD)	42.81 (11.99)	42.35 (26.68)	0.926
Mortality, n (%)	0	0	NA

Abbreviations: ICU, intensive care unit; ED, emergency department; CSF, cerebrospinal fluid.

[a]Among patients initially deferred antibiotics.

[b]Not applicable excluded.

[c]Contaminants excluded.

[d]Among patients with a lumbar puncture performed.

including invasive bacterial infections and need for escalation of care. Though not statistically significant, 6 patients in the post-guideline group had antibiotics initiated after initial deferral. One infant had an invasive bacterial infection with a positive CSF polymerase chain reaction (PCR) panel for *Haemophilus influenzae*, as well as a positive urine culture with *Escherichia coli*, which was subsequently treated with antibiotics. Another patient started antibiotics for an *Escherichia coli* urinary tract infection. Four patients who started antibiotics after initial deferral had no identified infection source and eventually stopped antibiotics within 48 hours. There was lack of documentation about the decision to start antibiotics in these patients; however, the AAP guideline includes shared decision-making with the patient's caretakers, so this may explain why antibiotics were initiated when they were initially deferred. Although there were no patients in the pre-guideline group who required escalation of care, most patients received antibiotics, which could explain why there were none admitted to the ICU or readmitted within 7 days.

Although patients were younger in the post-guideline cohort, the finding is not clinically relevant. The mean age for both populations falls within the 29- to 60-day-old algorithm per the guideline; therefore, both were assessed with the same criteria to defer initial antibiotics.

The use of inflammatory markers and urinalysis to determine risk stratification of febrile infants has been well described. Previous studies attempting to identify patients at highest risk of invasive bacterial infection were unsuccessful, but they were able to determine which patients were at low risk of infection.[5] Models such as the Boston, Philadelphia, and Rochester criteria as well as the step-by-step approach used clinical and laboratory data such as inflammatory markers and urinalysis to identify low risk patients; these risk stratifications have demonstrated high sensitivities and negative predictive values (>90%) with moderate specificity (20%-60%).[2,3,5] Urinary tract infection is the most common source of bacterial infection in patients with fever, and most will be identified by urinalysis.[2] Only 1 patient in the study who deferred initial antibiotics was identified as having an invasive bacterial infection, which supports the current risk stratification approach defined by the AAP guideline. At our institution, it is common practice for patients with a positive urinalysis in the ED to be started on antibiotics pending final identification and susceptibility results. Therefore, we excluded these patients because they did not defer initial antibiotics at admission.

Bacterial infection is a significant cause of infant morbidity and mortality and is preventable with timely initiation of antibiotics, but over half of patients without an invasive bacterial infection or urinary tract infection will receive unnecessary antibiotics.[1] The risks associated with antibiotics in infants include adverse drug reactions, intravenous line complications such as infection, disruption of the infant's gastrointestinal microbiome, and potential for antimicrobial resistance.[5] The risk-benefit discussion of initiating or deferring antibiotics must be assessed for each patient and further supports guideline recommendations.

There were more lumbar punctures performed in the pre-guideline group, but the ANC – an inflammatory marker used to determine if a patient qualifies for lumbar puncture and/or antibiotic deferral – was not different between groups. Lumbar punctures are invasive and painful procedures that can lead to complications, such as bleeding, infection, and respiratory compromise.[5,6] Our study supports the reduction in lumbar punctures performed based on inflammatory markers.

Although costs were not analyzed in this study, we suspect there was a cost savings due to the decreased number of lumbar punctures and antibiotics used, even with increased collection of procalcitonin. A previous study analyzed costs of incorporating procalcitonin in the evaluation of infants less than 60 days old and found an overall cost savings of about 10% when used to improve risk stratification practices.[7]

A strength of our study was inclusion of patients with COVID-19 and other positive viral PCRs as long as they did not have symptoms of bronchiolitis, which was determined by initiation of the bronchiolitis protocol and electronic heath record documentation. A study of 9841 febrile infants who tested positive for COVID-19 infection found the risk of bacterial co-infection to be low and were less likely to have a bacterial infection compared to those who tested negative for COVID-19.[8]

Limitations of this study include the retrospective design at a single center and including the timeframe of the COVID-19 pandemic. Patient volumes were lower during the COVID-19 pandemic and may have influenced the number of patients included in our study. Additionally, patients with suspected COVID-19 infection were placed in the hospital based on patient care and staffing needs, sometimes including ICU floors—even when not critically ill—thus excluding them from our data. Another limitation includes the small patient population; the estimated incidence of bacteremia and bacterial meningitis in infants is < 2% and < 0.5% respectively, so our study may not have been powered to detect a significant difference.[5] We did not include patients transferred from outside hospitals who otherwise may have qualified, as well as patients who were evaluated in the ED and discharged home; further studies would be needed to assess the impact on this patient population.

CONCLUSIONS

Our findings suggest that initial antibiotic deferral based on the 2021 AAP guideline criteria in well-appearing febrile infants is safe and the rate of invasive bacterial infection is low. Guideline implementation resulted in fewer lumbar punctures and antibiotic use without negatively affecting the incidence of invasive bacterial infections or escalation of care at our children's hospital. Future prospective, randomized controlled trials with a larger sample size are needed to fully investigate the impact of deferred antibiotics in this population.

Financial Disclosures: None declared.

Funding/Support: None declared.

REFERENCES

1. Yang J, Ong WJ, Piragasam R, Allen JC, Lee JH, Chong SL. Delays in time-to-antibiotics for young febrile infants with serious bacterial infections: a prospective single-center study. *Front Pediatr*. 2022;10:873043. doi:10.3389/fped.2022.873043

2. Aronson PL, Shabanova V, Shapiro ED, et al. A prediction model to identify febrile infants ≤60 days at low risk of invasive bacterial infection. *Pediatrics*. 2019;144(1):e20183604. doi:10.1542/peds.2018-3604

3. Kuppermann N, Dayan PS, Levine DA, et al. A clinical prediction rule to identify febrile infants 60 days and younger at low risk for serious bacterial infections. *JAMA Pediatr.* 2019;173(4):342-351. doi:10.1001/jamapediatrics.2018.5501

4. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Intensive Care Med*. 2020;46(suppl 1):10-67. doi:10.1007/s00134-019-05878-6

5. Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics*. 2021;148(2):e2021052228. doi:10.1542/peds.2021-052228

6. Aleem S, Greenberg RG. When to include a lumbar puncture in the evaluation for neonatal sepsis. *Neoreviews*. 2019;20(3):e124-e134. doi:10.1542/neo.20-3-e124

7. Dionisopoulos Z, Strumpf E, Anderson G, Guigui A, Burstein B. Cost modelling incorporating procalcitonin for the risk stratification of febrile infants ≤60 days old. *Paediatr Child Health*. 2022;28(2):84-90. doi:10.1093/pch/pxac083

8. Aronson PL, Louie JP, Kerns E, et al. Prevalence of urinary tract infection, bacteremia, and meningitis among febrile infants aged 8 to 60 days with SARS-CoV-2. *JAMA Netw Open*. 2023;6(5):e2313354. doi:10.1001/jamanetworkopen.2023.13354

Impact of a School-Based Mental Health Program on Academic Outcomes

David J. Cipriano, PhD; Samuel A. Maurice, PhD

ABSTRACT

Background: Academic achievement is an important indicator of a child's functioning and is inextricably linked with mental health. Prevalence rates of mental illness among children are alarmingly high, while relatively few receive treatment. Increasing accessibility to appropriate care is a major objective of school-based mental health programs. Providing mental health care in the schools should result in improved accessibility to care, decreased distress, and improved academic outcomes.

Methods: We followed 465 children in a large, urban school district who had been referred for school-based mental health services across 1 academic year. Outcomes including attendance, office disciplinary referrals, suspensions, and academic achievement were collected.

Results: Participation in school-based mental health was associated with lower rates of suspensions and higher math achievement scores. Dose-dependent relationships were found for attendance and suspensions.

Conclusions: School-based mental health care may improve access to treatment, thereby addressing health care inequities, and was associated with improvement in academic achievement and school-related behaviors.

BACKGROUND

Prevalence rates for mental health problems among US children range from 9.4% for anxiety in children and adolescents to 20.9% for major depression among adolescents.[1] These numbers have risen since the COVID-19 pandemic.[2] Yet, the number of children who receive mental health care is well below these prevalence estimates.[1] Socioeconomic disparities in mental health outcomes exist in the US indicating that these numbers are likely worse in impoverished communities.[3] Barriers to access to mental health care include stigma and lack of information for many families. Restricted access in impoverished communities is driven primarily by maldistribution of behavioral health providers.[4] Lack of transportation, scheduling difficulties, lack of health insurance and unresponsive providers further contribute to restricted access to care.[5] School-based mental health services are at the forefront of recommended actions to address access to care and treatment delays.[6]

School-based mental health care is believed to increase access to services.[7] Access is improved through less parental time off work, reduced childcare, decreased transportation needs, nonstigmatizing environment, and time and cost savings.[7,8] Students and their families may be more comfortable with mental health treatment as they see the provider as part of the school environment interacting with staff and other students. School-based health centers naturally improve access given that approximately 95% of youth ages 7 to 17 attend school every day.[9] In fact, some have acknowledged that our nation's schools are already the de facto provider of mental health services to our youth.[10]

Children living in impoverished or marginalized communities face barriers to academic achievement as well. Inequities by race, ethnicity, and income in educational achievement are well documented.[7] The significant opportunity gaps that exist between middle- and low-income children at school entry widen over time and contribute to differences in educational attainment and employment potential in the long term.[11] Placing mental health professionals in schools is thought to reduce these disparities.[7,10]

• • •

Author Affiliations: Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin (Cipriano); Milwaukee Public Schools, Milwaukee, Wisconsin (Maurice).

Corresponding Author: David J. Cipriano, PhD, Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226; phone 414.955.8954; email dcipriano@mcw.edu; ORCID ID 0000-0002-0165-0684

Children's psychological health is essential for their academic success.[12] However, academic outcomes are not always measured in studies of school-based mental health services, with some exceptions.[13-16] For example, Kase and colleagues were able to find only 36 articles from the previous 17 years that reported on the impact of school-based mental health on academic outcomes.[15] Academic outcomes include indices of classroom behavior in addition to achievement markers. Such behavioral outcomes include disciplinary actions and attendance. These are considered barriers to learning[14] and may be affected by psychosocial intervention.[17] The impact of school-based mental health on academic outcomes generally has been found positive though modest.[15]

Two research questions guided this study: (1) To what extent did students who participated in school-based mental health treatment evidence more adaptive levels of the behavior-based outcomes of attendance, office disciplinary referrals, and suspensions when compared to students who did not receive treatment (but who also were identified as having behavioral or emotional needs worthy of treatment)? and (2) To what extent did students who participated in school-based mental health treatment evidence higher levels of change over time on academic outcomes compared to students who did not receive treatment (but who also were identified as having behavioral or emotional needs worthy of treatment)?

Table 1. Sample Demographics Stratified by Intervention Condition

	Total	Treatment	Comparison	χ^2	*P* value
Gender %					
Female	32.7	32.5	33.9	0.071	.789
Male	67.3	67.5	66.1		
Ethnicity %					
American Indian	0.7	0.8	0.0		
Asian American	1.4	1.6	0.0		
Black	81.9	81.6	82.3	1.090	.297
Latin(x)	12.2	11.6	16.1		
White	2.7	3.1	1.6		
Multiracial	1.1	1.3	0.0		
Free and reduced lunch %					
Yes	94.4	93.7	96.8	1.537	.215
No	5.6	6.3	3.2		
English language learner %					
Yes	7.1	6.1	12.9	5.649	.017
No	92.8	93.7	87.1		
Unknown	0.1	0.1	0.0		
Special education %					
Yes	32.5	35.7	29.0	1.844	.175
No	67.5	64.3	71.0		

Note: Percentages are based off a total sample size 465 students, with 341 students in the treatment group and 124 students in the control group. Chi-square test for ethnicity and control/treatment group was only conducted for Black and Hispanic students due to low sample sizes.

METHODS

Participants

Students in Milwaukee Public Schools (MPS) who were referred to a school-based mental health program were the study participants. The MPS system has over 68 000 students: 14% are English-language learners and approximately 91% are students of color. The study participants are largely representative of these demographics. Typical criteria for identification included behavior problems exhibited in the school, student or parent complaint of psychological problems, and academic underachievement not otherwise explained by learning difficulties. Students were considered for services regardless of insurance coverage. The only exclusion criteria were parental refusal to consent for treatment or referral by the team to a more appropriate level of care not offered within the school. There were 22 schools participating in the program at the time of this study. Four of these were private "voucher" schools chartered by MPS and served the same constituency as MPS. However, these private schools did not provide data on school-related behavior or administer the STAR Reading and Math exams. Therefore, they were excluded from the final analyses.

There were 499 students referred for treatment; 34 declined the referral. A total of 341 students and their parent or guardian agreed with the referral, signed the consent form, and entered treatment. The remaining group of 124 children comprised the comparison group. This comparison group consisted of students who were referred for school-based mental health services, completed the consent process, but did not go on to start services. The reasons for this are varied and ultimately rested with the child and their parent or guardian (ie, they decided not to go through with treatment after initially consenting to do so). There is no anecdotal data that this group was more likely to be referred to a higher level of mental health care, which would obviously bias the results in favor of the treatment group. The two groups were similar on demographic characteristics such as gender, ethnicity, and economic status. We followed these 465 children who were referred during academic year 2016-2017.

Instrumentation

The STAR evaluation is a group-administered, school-wide measure of academic achievement (Renaissance Learning, Inc). It has widely accepted psychometric properties and is commonly used across the United States. This assessment tool is administered 3 times during the school year. For the purposes of our study, we analyzed the differences in the reading and math subject areas between the fall and spring administrations of the academic year. Scaled scores were used for the calculation of change, and a positive difference indicated growth in this area.

Indices of classroom behavior included office referrals for disciplinary actions (eg, for disruptive behavior or other relatively minor rule infractions), suspensions, and school absences. Such measures have high potential for bias when applied to children

Table 2. Estimates From Two-level Hierarchical Linear Models Predicting School Attendance

	Model 1	Model 2
Fixed effects		
Intercept	0.8643[a]	0.8685[a]
2014-2015 school attendance		0.4651[a]
Treatment		0.0126
Error variance		
Level 1	0.00974[a]	0.0088[a]
Level 2	0.00112	0.0005
Model fit		
Akaike Information Criterion (AIC)	-447.10	-385.90
Bayesian Information Criterion (BIC)	-444.40	-381.40

[a]Statistically significant, $P < .05$

Values based on SAS PROC MIXED. Lower AIC and BIC values represent stronger models.

Table 3. Estimates From Two-level Hierarchical Linear Models Predicting Office Disciplinary Referrals

	Model 1	Model 2
Fixed effects		
Intercept	4.4999[a]	5.2740[a]
2014-2015 office disciplinary referrals		0.7199[a]
Treatment		1.8358
Error variance		
Level 1	49.9002[a]	47.087[a]
Level 2	4.0649	1.1997
Model fit		
Akaike Information Criterion (AIC)	1787.40	1540.0
Bayesian Information Criterion (BIC)	1790.10	1543.5

[a]Statistically significant, $P < .05$

Values based on SAS PROC MIXED. Lower AIC and BIC values represent stronger models.

Table 4. Estimates From Two-level Hierarchical Linear Models Predicting School Suspensions

	Model 1	Model 2
Fixed effects		
Intercept	2.608[a]	2.197[a]
2014-2015 suspensions		0.663[a]
Treatment		-1.086
Error variance		
Level 1	14.7646[a]	15.144[a]
Level 2	2.1718	0.017
Model fit		
Akaike Information Criterion (AIC)	1474.50	1169.90
Bayesian Information Criterion (BIC)	1477.20	1173.50

[a]Statistically significant, $P < .05$

Values based on SAS PROC MIXED. Lower AIC and BIC values represent stronger models.

Table 5. Estimates from Two-level Hierarchical Linear Models Predicting Spring 2017 STAR Math Scores

	Model 1	Model 2
Fixed effects		
Intercept	541.14[a]	579.37[a]
Fall 2014 STAR math score		0.6275[a]
Treatment		30.12
Error variance		
Level 1	17829.0[a]	8265.57[a]
Level 2	5425.76	308.36
Model fit		
Akaike Information Criterion (AIC)	2733.20	1591.20
Bayesian Information Criterion (BIC)	2735.90	1595.10

[a]Statistically significant, $P < .05$

Values based on SAS PROC MIXED. Lower AIC and BIC values represent stronger models.

from minoritized and marginalized groups. The treatment and comparison groups do not differ significantly on ethnicity and poverty indicators, thus such bias is unlikely to affect the results of this study. These data were pulled by MPS Department of Research, Assessment and Data for each student in the treatment and comparison groups.

Procedure

School Community Partners for Mental Health (SCPMH), a public-private partnership in Milwaukee, Wisconsin, was developed to bring mental health services into the schools. At the time of this study, 4 community-based clinics were providing psychotherapy and consultation to MPS.

Students in need of mental health services – namely psychotherapy – were identified by an MPS student support staff member (eg, school social worker, school psychologist) in conjunction with teachers, administrators, and the community mental health provider (collectively known as the school-based team or "team"). All cases that were referred for mental health treatment by school personnel were tracked for successful entry into treatment.

Once the consent for treatment form was signed by the parent or guardian, psychotherapy sessions were conducted weekly, except in cases where scheduling did not allow or acuity did not necessitate. The majority of sessions were approximately 50 minutes long, and nearly all sessions were individual. The therapists regularly invited parents to sessions in the school and were otherwise reached out to by phone. Other services provided by SCPMH include teacher consultation, team planning meetings, and participation in school-based family activities.

The psychotherapists who saw children in this study used a cognitive-behavioral approach. Providers met monthly for didactics, case discussions, and peer review. The 18 therapists providing services were mostly masters level, licensed psychotherapists (either licensed clinical social worker or licensed professional counselor), though there were 2 doctoral level licensed psycholo-

gists. Approximately one third of these individuals were people of color.

Data Analysis

Hierarchical linear modeling (HLM) was used to answer the research questions. This choice was made to account for the hierarchical data clustering, which was judged to have the potential to impact the results – namely the individual characteristics of the child and the school the participant attended. Two levels of nesting were accounted for in the analyses: individual (student) and school. Analyses controlled for the previous year's functioning on the dependent variables (attendance, office disciplinary referrals, suspensions, and STAR exams). The predictor variable was treatment (involving 2 levels: yes, enrolled in school-based mental health treatment vs no, not enrolled for treatment, though identified as being a candidate for treatment). The intercepts were allowed to vary, but the slopes were fixed due to the fact that no group level predictors were used in building the models. All assumptions of HLM were checked and found to have been fulfilled. All analyses used the maximum likelihood method. Missing data were handled using list-wise deletion. Dose effect analyses were conducted on the behavioral measures. Chi square analyses were conducted for other group comparisons; this was chosen to help manage the large standard deviations seen in the data.

RESULTS

The subjects were 66% male; 82% were Black, 12% were Latin(x) and 3% were White. Most (94%) were living at or below the poverty level. Ninety-five percent were in the elementary grades (kindergarten through 8th grade), and the other 5% were in grades 9 through 12. See Table 1 for demographic data.

The treatment and comparison groups are quite comparable across gender, race/ethnicity, grade, and eligibility for Food Service (an indicator of low socioeconomic status). The comparison group did have significantly more English as a Second Language (ESL) students compared to the treatment group (Table 1). This raises the question of language being a prohibitive factor in this subgroup's decision to not enter treatment despite having been referred and having signed the consent form. SCPMH does have the consent form and the SDQ in Spanish language versions. It also has at its disposal a translation service. The mean number of sessions was 13.14 (SD = 9.81) with a range from 1 to 41 sessions. The median number of sessions attended was 11.00.

Over the course of the 2016-2017 school year, 499 children were referred by school personnel to mental health treatment; 341 entered treatment through the school-based mental health program. This number, representing 68% of those referred, is considerably higher than national estimates of 50% or less.[1,18] Incidentally, before the formation of SCPMH, MPS personnel calculated that approximately 5% of students referred to services started treatment. These findings demonstrate the utility of school-based mental health in increasing access to mental health care for children, perhaps especially those from marginalized or underserved communities who were the subject of this study.

Research Question 1

Do students receiving treatment have significantly better behavior-based outcomes, including attendance, office disciplinary referrals, and suspensions relative to students who do not receive treatment?

Attendance

Participants in the treatment group did not have significantly higher attendance rates in the 2016-2017 school year than those in the comparison group, $F(1, 193) = 0.73$, $P = .39$ (Table 2). Dose effect analyses were conducted. The number of therapy sessions did significantly predict attendance rate after controlling for the corresponding pre-outcome (ie, pretreatment) attendance. The full model predicting attendance percentage was significant, $F(2, 268) = 37.30$, $P < .0001$. The number of therapy sessions ($\beta = 0.0012$) was indeed a significant predictor of 2016-2017 attendance, $t(1) = 2.23$, $P < .05$, after controlling for the previous year's attendance, $t(1) = 8.25$, $P < .0001$. For each additional therapy session, student attendance percentage during the 2016-2017 school year was predicted to increase by approximately 0.1% percentage points after controlling for pretreatment attendance percentage. Practically speaking, this means that a student who attends 10 therapy sessions will be predicted to attend almost 2 more days of school each academic year (based on a 180-day academic calendar). The fact that children who have better attendance are more available for therapy sessions is a potential confounding variable in these analyses.

Office Disciplinary Referrals

Participants in the treatment group did not have significantly fewer office disciplinary referrals in the 2016-2017 school year than those in the comparison group, $F(1, 209) = 3.65$, $P = .0575$. There was no dose effect found for office disciplinary referrals (Table 3).

Suspensions

Participants in the treatment group had significantly fewer suspensions in the 2016-2017 school year than those in the comparison group, $F(1, 209) = 4.54$, $P = .034$ (Table 4). In addition, a dose effect was found for suspension rate. In terms of predicting 2016-2017 school suspensions, the full model was again significant, $F(2, 268) = 34.16$, $P < .0001$. The number of therapy sessions ($\beta = -0.067$) was a significant predictor of school suspensions, $t(1) = 3.01$, $P < .01$, after controlling for the previous year's school suspensions, $t(1) = 7.96$, $P < .0001$. For each additional therapy session, the number of school suspensions a student is predicted to accrue during the 2016-2017 school year was expected to decrease by approximately 0.067 after controlling for pretreatment school suspensions. In real terms, the model predicts that if a student attends 15 therapy sessions, they will be expected to have 1 fewer

day of school suspension even after controlling for pretreatment functioning.

Research Question 2

Do students in the treatment group have significantly greater academic outcomes than those in the comparison group? As would be hoped, all students (in both the treatment and comparison groups) showed improvement in these academic markers over the course of the study. In terms of the effect of treatment on academic outcomes, STAR Math and STAR Reading were analyzed.

STAR Math

Students (level 1) in the sample are nested within 18 schools (level 2), with an average of 11.89 students per school. The intraclass correlation was found to be 0.23, indicating that approximately 23% of the variability in STAR math scores can be accounted for by level 2 (school) group membership. After controlling for the previous fall STAR Math test, students in the treatment group did not have significantly higher scores on the spring 2017 STAR Math test than those in the comparison group, $F(1, 115) = 2.62$, $P = .11$. While students who received treatment ($M_{math} = 606.49$) scored higher than those in the comparison group ($M_{math} = 576.37$) this increase was modest relative to the large standard deviation seen in spring 2017 STAR Math scores ($SD = 151.23$). See Table 5.

The large standard deviations for STAR Math scores in both groups ($SD_{treatment} = 111.02$ and $SD_{comparison} = 101.56$) warranted a further look. After exploratory analysis, it was revealed that there were significant outliers in the treatment group in terms of STAR Math scores. Findings like these are not unusual in such a data set.[13] To account for this, students were categorized into 2 conditions for each academic year: growth or no growth. Students who demonstrated growth on STAR Math over the course of the study were put into the growth category; students who did not demonstrate growth (or who regressed) were put into the no growth category. Growth represented any nonzero positive change. The mean range of change was 135.91 for the treatment group and 92.38 for the comparison group.

A chi-square test of independence was performed to examine the relation between STAR Math growth and treatment. The relation between these variables was significant, $\chi^2([2]\ N = 171) = 14.22$, $P < .001$. Students who received therapy were more likely to show at least some growth on the STAR Math test (95%) than those who did not receive therapy (76%) over the course of the study.

STAR Reading

Students (level 1) in the sample are nested within 18 schools (level 2), with an average of 9.94 students per school. The intraclass correlation was found to be .134, indicating that approximately 13% of the variability in STAR Reading scores can be accounted for by level 2 (school) group membership. After controlling for the previous fall STAR Reading scores, students in the treatment group did not have significantly higher scores on the spring 2017 STAR Reading test than those in the comparison group, $F(1, 100) = 0.15$, $P = .70$. Large standard deviations were found again for both groups. However, analyses controlling for outliers—similar to those performed for the STAR Math tests—were performed without significant results.

DISCUSSION

Offering mental health services in schools to children from disadvantaged communities may improve access to care. Approximately 68% of students who were identified as having a mental health need ultimately were seen by a professional through this school-based mental health initiative. This is higher than rates found in previous studies.[5,18] Given that the present study involved a traditionally hard to reach and underserved population, our results contribute to the belief that school-based mental health has the potential to advance health equity.[7]

A major aim of this study was to show that the provision of mental health services at schools would benefit classroom performance. Students receiving psychotherapy through SCPMH had significantly lower numbers of suspensions than those in the comparison group. For those students receiving mental health care, there was a dose effect found for absence from school and suspensions: more therapy sessions predicted lower rates of these school-related behaviors. These behavioral variables have been conceptualized as potential barriers to academic achievement, and our findings suggest that mental health treatment may have a positive impact on them.[14,17] After statistically controlling for the wide variability in our sample (which is actually developmentally appropriate), we found school-based mental health treatment to be associated with more growth on a standardized math test over the course of the school year. This is in line with previous research and reinforces the notion that children's mental health is linked to their academic performance.[12,15]

Limitations

This study was hampered by the lack of a true control group and random assignment. We sought further statistical control by holding the previous year's functioning constant in the analyses. The large standard deviations in the academic data rendered standard analysis of variance approaches somewhat limited. We decided to use chi-square analysis, which manages such scatter. Nonetheless, we acknowledge that this weakens any conclusions to be made from the relationship between treatment and math achievement scores. We also did not control for multiple comparisons on variables that may have some degree of shared variance. It was our judgement at the time that the shared variance of the nesting variables (school building and the individual student) were more likely to have an impact on the results, hence the choice to use hierarchical linear modelling. Finally, we also did not have data on educational interventions or ancillary services that our subjects also

may have had at their disposal, raising the question of potential confounding variables at play.

Future Directions

Future research should address other mechanisms through which school-based mental health impacts children's functioning. For example, do the other roles that mental health professionals play in schools also affect change, such as consultation with teachers and administrators? Does this hoped-for partnership between educators and mental health professionals serve to decrease stigma surrounding mental health, which would facilitate the continuum of mental health promotion that Weist and colleagues spoke about?[19] Beyond mental health and academic outcomes, we should be studying systemic variables that may be related to children's functioning, such as connectedness to school.

CONCLUSIONS

School-based mental health care may improve access to treatment, thereby addressing health care inequities, and was associated with improvement in academic achievement and school-related behaviors in our study population.

For more information about school-based mental health in Wisconsin, visit the website for the Coalition for Expanding School-Based Mental Health at https://www.schoolmentalhealthwisconsin.org/ or the Wisconsin Association of Family and Children's Agencies at https://www.wafca.org/.

Funding/Support: This work received fuding support for statistical analysis from the Chucker Airing Fund.

Financial Disclosures: None declared.

Human Subjects Approval Statement: The study was approved by the Institutional Review Board of Children's Wisconsin, protocol 859525-3.

REFERENCES

1. Bitsko RH, Claussen AH, Lichstein J, et al. Mental health surveillance among children - United States, 2013-2019. *MMWR Suppl.* 2022;71(2):1-42. doi:10.15585/mmwr.su7102a1

2. Racine N, McArthur BA, Cooke JE, Eirich R, Zhu J, Madigan S. Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: a meta-analysis. *JAMA Pediatr*. 2021;175(11):1142-1150. doi:10.1001/jamapediatrics.2021.2482

3. Harden BJ, Slopen N. Inequitable experiences and outcomes in young children: addressing racial and social-economic disparities in physical and mental health. *Annu Rev Dev Psychol.* 2022;4:133-159. doi:10.1146/annurev-devpsych-121020-031515

4. Kepley HO, Streeter RA. Closing behavioral health workforce gaps: a HRSA program expanding direct mental health service access in underserved areas. *Am J Prev Med.* 2018;54(6 Suppl 3):S190-S191. doi:10.1016/j.amepre.2018.03.006

5. Atkins MS, Frazier SL, Birman D, et al. School-based mental health services for children living in high poverty urban communities. *Adm Policy Ment Health.* 2006;33(2):146-159. doi:10.1007/s10488-006-0031-9

6. Murphy JM, Abel MR, Hoover S, Jellinek M, Fazel M. Scope, scale, and dose of the world's largest school-based mental health programs. *Harv Rev Psychiatry.* 2017;25(5):218-228. doi:10.1097/HRP.0000000000000149

7. Knopf JA, Finnie RK, Peng Y, et al. School-based health centers to advance health equity: a community guide systematic review. *Am J Prev Med*. 2016;51(1):114-126. doi:10.1016/j.amepre.2016.01.009

8. Rohde P, Stice E, Shaw H, Brière FN. Indicated cognitive behavioral group depression prevention compared to bibliotherapy and brochure control: acute effects of an effectiveness trial with adolescents. *J Consult Clin Psychol.* 2014;82(1):65-74. doi:10.1037/a0034640

9. Brener N, Demissie Z. Counseling, psychological, and social services staffing: policies in U.S. school districts. *Am J Prev Med*. 2018;54(6 Suppl 3):S215-S219. doi:10.1016/j.amepre.2018.01.031

10. Connors EH, Stephan SH, Lever N, Ereshefsky S, Mosby A, Bohnenkamp J. A national initiative to advance school mental health performance measurement in the US. *Adv Sch Ment Health Promot.* 2016;9(1):50-69. doi:10.1080/1754730X.2015.1123639

11. Blair C, Raver CC. Poverty, stress, and brain development: new directions for prevention and intervention. *Acad Pediatr.* 2016;16(3 Suppl):S30-S36. doi:10.1016/j.acap.2016.01.010

12. Atkins MS, Cappella E, Shernoff ES, Mehta TG, Gustafson EL. Schooling and children's mental health: realigning resources to reduce disparities and advance public health. *Annu Rev Clin Psychol.* 2017;13:123-147. doi:10.1146/annurev-clinpsy-032816-045234

13. Baskin TW, Slaten CD, Sorenson C, Glover-Russell J, Merson DN. Does youth psychotherapy improve academically related outcomes? A meta-analysis. *J Couns Psychol.* 2010;57(3):290-296. doi:10.1037/a0019652

14. Iachini A, Brown EL, Ball A, Gibson JE, Lize S. School mental health early interventions and academic outcomes for at-risk high school students: a meta-analysis. *Adv Sch Ment Health Promot.* 2015;8(3):1-20. doi:10.1080/1754730X.2015.1044252

15. Kase C, Hoover S, Boyd G, et al. Educational outcomes associated with school behavioral health interventions: a review of the literature. *J Sch Healt*h. 2017;87(7):554-562. doi:10.1111/josh.12524

16. Sanchez AL, Cornacchio D, Poznanski B, Golik AM, Chou T, Comer JS. The effectiveness of school-based mental health services for elementary-aged children: a meta-analysis. *J Am Acad Child Adolesc Psychiatry*. 2018;57(3):153-165. doi:10.1016/j.jaac.2017.11.022

17. Becker KD, Brandt NE, Hoover SA, Chorpita BF. A review of educational outcomes in the children's mental health treatment literature. *Adv Sch Ment Health Promot.* 2014;7(1):5-23. doi:10.1080/1754730X.2013.851980

18. Merikangas KR, He JP, Brody D, Fisher PW, Bourdon K, Koretz DS. Prevalence and treatment of mental disorders among US children in the 2001-2004 NHANES. *Pediatrics*. 2010;125(1):75-81. doi:10.1542/peds.2008-2598

19. Weist MD, Mellin EA, Chambers KL, Lever NA, Haber D, Blaber C. Challenges to collaboration in school mental health and strategies for overcoming them. *J Sch Health.* 2012;82(2):97-105. doi:10.1111/j.1746-1561.2011.00672.x

Optimizing Pediatric Patients' Attainment of Outpatient Mental Health Services Following Emergency Department Care

Narmeen I. Khan, MD; Hayder Jaafar, MBChB; Sarah E. Wawrzyniak, APNP; Alexis Visotcky, MS; Jennifer A. Zaspel, MD; Erin P. O'Donnell, MD; Danny G. Thomas, MD, MPH

ABSTRACT

Introduction: Psychiatric emergency department (ED) visits among youth have risen in the United States in recent years. A major factor contributing to this increase is the lack of accessible inpatient and outpatient services, making the ED a safety net for mental and behavioral health emergencies. This study sought to assess outpatient mental and behavioral health care after ED discharge and understand barriers and facilitators that caregivers encounter when attaining outpatient care.

Methods: This was a mixed methods study conducted at a tertiary care pediatric ED. Patients ages 3 to 17 years seen for mental health concerns received a social work consult and were contacted 1 week after the ED visit by the mental and behavioral health navigator as part of ongoing quality improvement efforts. Descriptive data included types of outpatient care received, demographics, and repeat ED visit within 30 and 60 days. Results were analyzed via logistic regression. Patients' caregivers also were interviewed 4 weeks after the ED visit to explore barriers and facilitators to accessing outpatient care. Thematic content analysis was then performed.

Results: The navigator successfully reached 533 out of 720 (74%) patients. Most patients were unable to obtain follow-up mental and behavioral health care. Univariate regression analyses revealed that being White, having commercial insurance, or a positive suicide screen had higher odds of receiving intensive outpatient care. However, these variables were not statistically significant after multivariate analyses. Barriers to follow-up included long wait times and expense. Facilitators included support from ED staff and close relationships with primary care clinicians.

Conclusions: We found potential socioeconomic disparities that influence mental health care follow-up. Our findings highlight challenges patients face to receiving outpatient care, serving as a valuable guide for improving the transition from the ED to outpatient settings.

• • •

Author Affiliations: Department of Pediatrics (Emergency Medicine), Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Khan, Jaafar, Thomas); State of South Carolina Department of Psychiatry and WAW Mind and Body, Summerville, South Carolina (Wawrzyniak); Department of Biostatistics, MCW, Milwaukee, Wisconsin (Visotcky); Department of Psychiatry and Behavioral Medicine, MCW, Milwaukee, Wisconsin (Zaspel); TriHealth Primary Care Institute, Cincinnati, Ohio (O'Donnell).

Corresponding Author: Narmeen I. Khan, MD, Children's Corporate Center, Suite C550, 999 N 92nd St, PO Box 1997, Milwaukee, WI 53201-1997; phone 414.266.1601; email nikhan@mcw.edu; ORCID ID 0009-0002-0505-318X

INTRODUCTION

Prior to the COVID-19 pandemic, psychiatric emergency department (ED) visits among youth were rising in the United States.[1-3] During the pandemic, mental health-related pediatric ED visits increased by nearly 31% for ages 12 to 17 years.[4,5] A cross-sectional study of children ages 5 to 17 years with primary mental health diagnoses showed a 7% rise in visits for suicidal ideations and/or self-injury.[6]

A major factor contributing to the rise in ED mental and behavioral health (MBH) visits is the lack of accessible inpatient and outpatient services, making the ED a safety net for MBH emergencies.[7-13] Long ED wait times cause frustration and suboptimal care, with patients often boarding for hours or even days due to lack of available inpatient psychiatric beds.[14] Despite the urgent need for help, long waitlists for outpatient psychiatric interventions persist.[3]

Previous studies highlight the ED's essential role as a safety net for children experiencing MBH crises and advocate for a more systematic approach. This includes trauma-informed care, culturally appropriate interventions, and stronger collaboration with outpatient services. The literature stresses the importance of specialized training, incorporating mental health professionals in EDs, utilizing telehealth, and creating a safe environment for these patients. Recommendations focus on enhancing ED preparedness, improving management strategies, and ensuring effective follow-up care, while calling for further research to optimize resources and improve outcomes for pediatric MBH care.[15]

With increasing mental health-related ED visits, improving the transition of care from the ED to outpatient services for at-risk MBH patients is crucial.[16] The objectives of this project were to utilize our MBH navigator program to assess factors associated with obtaining outpatient MBH care after discharge from the ED and to conduct structured interviews with caregivers to understand barriers and facilitators encountered when seeking outpatient care.

MATERIALS AND METHODS

Setting

The study occurred at a large tertiary pediatric ED in an urban Midwestern city that has approximately 80 000 annual visits. ED clinicians are able to consult subspecialists, both in person and via phone, when providing care for their patients.

Design

This was a prospective cohort study with mixed methods incorporating both qualitative and quantitative components. Research was approved by the Medical College of Wisconsin Institutional Review Board (1829944-1).

Population

This study included patients from 3 to 17 years who presented to the ED with a mental health-related chief complaint, received a social work consult, and were discharged home. Exclusion criteria included involvement of child protective services or caregiver inability to participate in the interview (eg, if English was not their primary language). Further, patients with certain neurodevelopmental disorders such as autism spectrum disorder were excluded, as many have developmental delays that could preclude them from expressing their mental health concerns, potentially leading to inaccurate assumptions made by caregivers and clinicians.

Data Collection and Analysis

Quantitative Methods

At our tertiary-care pediatric hospital, ED visits for primary MBH concerns have surged to over 3000 children per year since 2018. Approximately 41% of these patients were considered high risk (an imminent threat to themselves or others, for instance) and required a social work consult for a more in-depth evaluation and resource provision. The treatment team assesses risk based on significant behavioral changes, safety concerns, and lack of existing mental health resources. When 1 or more of these concerns are present, a licensed social worker is consulted to formally evaluate the patient.

Our ED MBH navigator collaborates with our clinical and social work teams to support and coordinate mental health services after ED discharge. They engage closely with families to connect them to appropriate care settings, whether it is a behavioral health facility or community-based resources. The navigator is available for consultation to follow up with patients—even if their primary ED concern was not mental health-related—provided social work was involved and psychiatric needs were identified. After discharge, the navigator ensures follow-up care and coordinates treatment options with families via phone within 2 weeks of the ED visit.

Patients were recruited from August 2021 to June 2022. As part of ongoing quality assurance work, all patients ages 3 to 17 years who presented to our ED with MBH concerns such as depression and anxiety and received a social work consult were contacted 1 week after discharge via phone by the MBH navigator. During this call, the navigator provided a study-specific consent-to-contact script. The navigator made a maximum of 3 phone call attempts to the caregiver. The following data were collected at the index visit: age, sex, race, insurance status, nonpsychiatric and/or psychiatric history, and repeat ED visit within the last 30 and 60 days. These data were collected by the navigator and via chart review and then secured in a REDCap database.

Analyses were performed using SAS 9.4 software (SAS Institute, Cary, North Carolina). Univariate logistic regression models were used for the outcome variables of follow-up (scheduled, completed, ongoing, none, or attempted) with the primary care clinician, psychiatrist, therapist and/or psychologist, school counselor, and intensive outpatient care. Predictor variables included demographics, nonpsychiatric and psychiatric histories, and recent ED visit frequency. Statistically significant odds ratios were represented by $P < 0.05$.

Qualitative Methods

To explore barriers (obstacles or challenges when attaining outpatient care) and facilitators (support or resources when attaining outpatient care), subjects were screened for eligibility by trained research staff during their ED visit. After initial contact by a member of the care team, the research staff introduced the study to the patient and their caregiver. If eligible, research staff discussed the study with caregivers and obtained informed consent for enrollment. Approximately 4 weeks after the initial ED visit, the caregivers reconfirmed consent during a telephone interview. Patients were excluded if they returned to the ED within 4 weeks of their initial ED encounter, which was based on the MBH navigator's workflow. Participants received a $50 gift card after interview completion, delivered via mail or email.

A structured interview guide was used that incorporated open-ended questions evaluating experiences acquiring mental health care after the index ED encounter. The interviews were conducted by members of the research team, many of whom had prior experience conducting research-based interviews. Crisis resources were given to the caregivers during the telephone encounter, including the suicide prevention hotline and other local services. In addition to barriers and facilitators, caregivers were also asked to provide any recommendations for process improvement. Interviews were recorded, transcribed, and

entered into a secure REDCap database. Transcriptions were reviewed by 2 investigators using a grounded theory approach. In the open coding phase, they independently analyzed transcripts line by line, assigning codes to significant concepts. Investigators then convened to share codes generated and group them into broader categories during axial coding, where relationships between themes were identified and refined. Selective coding followed, focusing on developing a core theme that tied the analysis together. The process continued iteratively until theoretical saturation was reached, where no new themes or insights emerged from the data.

RESULTS

The MBH navigator successfully reached 533 out of 720 (74%) patients, representing 589 unique ED encounters. Most patients (83.3%) were 13 to 17 years old, with females comprising 72.6% of the population. The majority identified as White (58.5%), followed by Black (30.6%). Public insurance, including Medicaid, covered 55.0% of patients, while 45.0% had commercial insurance. Almost half (44.3%) were treated for both nonpsychiatric and MBH concerns. Around half (50.6%) had 2 or more psychiatric diagnoses, with 65.0% prescribed psychotropic medications, and 59.5% had 1 or more nonpsychiatric diagnoses. Few patients returned to the ED within 30 days (6.0%) or 60 days (9.4%).

Follow-up rates were low across various providers: 12.4% with primary care clinicians, 11.7% with psychiatrists, and only 3.9% with school counselors. Approximately one-third (33.7%) followed up with a therapist and/or psychologist, while over a quarter (28.5%) received intensive outpatient care.

Table 1. Primary Care Clinician Follow-up (n = 315) Comparing Outcome Variables: None/Attempted (n = 276) Versus Scheduled/Completed/Ongoing (n = 39)

Predictor Variable	Levels	OR	95% CI	*P* value
Age	13–17 years vs 3–12 years	0.715	0.307–1.666	0.4360
Sex	Female vs male	0.750	0.359–1.565	0.4421
Race	Black vs other	1.290	0.385–4.331	0.6789
	Black vs White	1.573	0.748–3.307	0.2313
	Other vs White	1.219	0.388–3.826	0.7338
Insurance	Commercial/self-pay vs public/government	1.291	0.657–2.536	0.4567
ED visit reason	MBH vs nonpsychiatric	0.523	0.182–1.503	0.2280
	MBH vs MBH and nonpsychiatric	0.740	0.351–1.557	0.4260
	Nonpsychiatric vs MBH and nonpsychiatric	1.414	0.519–3.857	0.4971
Home psychotropic medications	No vs Yes	1.280	0.632–2.592	0.4916
Psychiatric history	1 diagnosis vs 2+ diagnoses	1.570	0.745–3.309	0.2351
	1 diagnosis vs none	0.872	0.326–2.331	0.7844
	2+ diagnoses vs none	0.556	0.213–1.447	0.2280
Medical history	1+ diagnoses vs none	1.450	0.713–2.950	0.3040
ASQ	Negative vs positive	1.065	0.403–2.813	0.8986
ED visit within last 30 days	No vs yes	2.969	0.384–22.945	0.2959
ED visit within last 60 days	No vs yes	2.172	0.495–9.539	0.3031

Abbreviations: OR, odds ratio; ED, emergency department; MBH, mental and behavioral health; ASQ, Ask Suicide-Screening Questions.

Table 2. Psychiatrist Follow-up (n = 315) Comparing Outcome Variables: None/Attempted (n = 278) Versus Scheduled/Completed/Ongoing (n = 37)

Predictor Variable	Levels	OR	95% CI	*P* value
Age	13–17 years vs 3–12 years	0.467	0.210–1.040	0.0624
Sex	Female vs male	1.067	0.479–2.377	0.8734
Race	Black vs other	0.951	0.273–3.306	0.9364
	Black vs White	1.102	0.498–2.440	0.8097
	Other vs White	1.159	0.371–3.628	0.7988
Insurance	Commercial/self-pay vs public/government	0.600	0.296–1.217	0.1564
ED visit reason	MBH vs nonpsychiatric	1.241	0.390–3.949	0.7139
	MBH vs MBH and nonpsychiatric	1.687	0.807–3.526	0.1636
	Nonpsychiatric vs MBH and nonpsychiatric	1.360	0.415–4.450	0.6106
Home psychotropic medications	No vs yes	0.586	0.257–1.337	0.2034
Psychiatric history	1 diagnosis vs 2+ diagnoses	0.443	0.183–1.068	0.0696
	1 diagnosis vs none	0.696	0.191–2.532	0.5815
	2+ diagnoses vs none	1.573	0.513–4.820	0.4265
Medical history	1+ diagnoses vs none	0.899	0.448–1.802	0.76320
ASQ	Negative vs positive	0.342	0.077–1.523	0.1581
ED visit within last 30 days	No vs yes	0.504	0.158–1.605	0.2451
ED visit within last 60 days	No vs yes	0.632	0.225–1.775	0.3831

Abbreviations: OR, odds ratio; ED, emergency department; MBH, mental and behavioral health; ASQ, Ask Suicide-Screening Questions.

Univariate logistic regression analyses for follow-up with the primary care clinician, psychiatrist, therapist and/or psychologist, and intensive outpatient care are shown in Tables 1 through 4, respectively. Race, insurance, and Ask Suicide-Screening Questions (ASQ) score were significant predictors for intensive outpatient care, with White race, commercial insurance, and a positive ASQ score showing higher odds of receiving intensive outpatient care ($P < 0.05$). However, these variables did not retain significance after multivariate analysis (Table S1). No predictor variables were statistically significant for follow-up with primary care clinician, psychiatrist, or therapist and/or psychologist. Models for school counselor were not feasible due to limited data, with only 2.3%

of patients in the "scheduled/completed/ongoing" category.

Table 5 depicts caregiver quotes of negative and positive experiences when accessing outpatient mental health care, identified during interviews conducted 4 weeks after the initial ED visit. The sample size was determined based on achieving data saturation, which was reached after reviewing 13 interviews. Themes were categorized into facilitators, barriers, and solutions to outpatient MBH care.

Facilitators of follow-up care included supportive ED staff, such as social workers, and assistance from the hospital's MBH walk-in clinic. Close involvement of patients' primary care clinician, efficient scheduling, and providers accepting new mental health patients were also highlighted.

Limiting factors included personal (such as time and expense), systemic (waitlists and scarcity of MBH services), and familial concerns (relating to family members and legal resources). Caregivers mentioned long wait times, limited clinic hours, provider restrictions on insurance networks for new patients, and scheduling difficulties due to age or parental schedules as barriers to follow-up MBH care.

Our qualitative analysis, along with caregiver input, highlighted several areas for improvement in outpatient mental health care. These include establishing more school-based mental health support, offering more flexible clinic time slots (including evenings), and providing clearer ED discharge instructions (Table 5).

Table 3. Therapist and/or Psychologist Follow-up (n = 315) Comparing Outcome Variables: None/Attempted (n = 209) Versus Scheduled/Completed/Ongoing (n = 106)

Predictor Variable	Levels	OR	95% CI	*P* value
Age	13–17 years vs 3–12 years	0.678	0.366–1.257	0.2168
Sex	Female vs male	0.671	0.395–1.138	0.1385
Race	Black vs other	0.514	0.220–1.200	0.1235
	Black vs White	1.030	0.591–1.794	0.9176
	Other vs White	2.005	0.932–4.315	0.0751
Insurance	Commercial/self-pay vs public/government	0.937	0.586–1.498	0.7841
ED visit reason	MBH vs nonpsychiatric	0.774	0.349–1.715	0.5264
	MBH vs MBH and nonpsychiatric	1.158	0.703–1.908	0.5633
	Nonpsychiatric vs MBH and nonpsychiatric	1.497	0.681–3.287	0.3140
Home psychotropic medications	No vs Yes	1.169	0.706–1.935	0.5430
Psychiatric history	1 diagnosis vs 2+ diagnoses	0.925	0.546–1.568	0.7714
	1 diagnosis vs none	0.908	0.419–1.966	0.8052
	2+ diagnoses vs none	0.981	0.477–2.019	0.9588
Medical history	1+ diagnoses vs none	0.985	0.612–1.586	0.9510
ASQ	Negative vs positive	0.851	0.424–1.708	0.6477
ED visit within last 30 days	No vs yes	1.562	0.550–4.438	0.4015
ED visit within last 60 days	No vs yes	1.749	0.723–4.233	0.2143

Abbreviations: OR, odds ratio; ED, emergency department; MBH, mental and behavioral health; ASQ, Ask Suicide-Screening Questions.

Table 4. Intensive Outpatient Care Follow-up (n = 239) Comparing Outcome Variables: None/Attempted (n = 171) Versus Scheduled/Completed/Ongoing (n = 68)

Predictor Variable	Levels	OR	95% CI	*P* value
Age	13–17 years vs 3–12 years	1.284	0.546–3.021	0.5650
Sex	Female vs male	1.216	0.611–2.421	0.5753
Race	Black vs other	0.538	0.171–1.700	0.2899
	Black vs White	0.485	0.237–0.992	0.0474
	Other vs White	0.900	0.325–2.494	0.8388
Insurance	Commercial/self-pay vs public/government	1.964	1.107–3.485	0.0212
ED visit reason	MBH vs Nonpsychiatric	4.318	0.937–19.891	0.0604
	MBH vs MBH and nonpsychiatric	1.086	0.606–1.947	0.7814
	Nonpsychiatric vs MBH and nonpsychiatric	0.251	0.055–1.145	0.0741
Home psychotropic medications	No vs Yes	0.613	0.317–1.188	0.1463
Psychiatric history	1 diagnosis vs 2+ diagnoses	0.719	0.379–1.364	0.3108
	1 diagnosis vs none	1.163	0.430–3.146	0.7648
	2+ diagnoses vs none	1.618	0.643–4.073	0.3055
Medical history	1+ diagnoses vs none	0.673	0.380–1.191	0.1730
ASQ	Negative vs positive	0.376	0.145–0.970	0.0432
ED visit within last 30 days	No vs yes	1.538	0.489–4.842	0.4599
ED visit within last 60 days	No vs yes	1.764	0.634–4.911	0.2759

Abbreviations: OR, odds ratio; ED, emergency department; MBH, mental and behavioral health; ASQ, Ask Suicide-Screening Questions.

DISCUSSION

Racial and income disparities in outpatient mental health care were observed in our study, with White patients and those with commercial insurance having higher odds of receiving care than minoritized and publicly insured groups. However, these variables lost significance in the multivariate analyses, likely due to overlapping effects between race and insurance status. Similar disparities – particularly for Black patients and those with public insurance – have been reported in previous survey-based studies, but less so in prospective evaluations.[17] Our work highlights the need for closer, more frequent contact between the treatment team and non-White patients with public insurance, including considering inpatient psychiatric treatment or intensive outpatient care as potential interim solutions. Reflecting on our findings, race appears to serve as a proxy for the true barrier of health insurance. Intensive outpatient care may not be readily available

given transportation costs and parental job flexibility for those who have public insurance.

Our findings did not show associations between positive ASQ, past psychiatric history, and follow-up with primary care clinicians, psychiatrists, school counselors, or therapists/psychologists. We expected that individuals with current or previous psychiatric and/or nonpsychiatric conditions would be more likely to transition from ED to outpatient care, but our data did not support this.

While a significant portion did not follow up with primary care clinicians, about one-third followed up with therapists or psychologists. These results are particularly interesting when compared to our qualitative review of caregiver interview themes, where many caregivers mentioned the long wait times for therapy appointments. Our findings highlight the need for better communication—potentially initiated by the ED care team—and stronger engagement with primary care clinicians during the waiting period for outpatient mental health care. Close contact with primary care clinicians could provide critical resources that patients and caregivers often struggle to access while awaiting therapy appointments.

Table 5. Themes and Quotes From Caregiver Interviews Regarding Facilitators, Barriers, and Proposed Solutions for Outpatient Mental Health Support

Themes	Quotes
Facilitators	
Primary care clinician involvement	"And, you know, his doctor was involved the whole time…and I think they gave me some resources too"
Support from ED staff	"I think that everyone…should have to talk to a social worker before they leave. But we did and she was very helpful"
Support from MBH navigator	"I guess the call back was the one thing that maintained it"
Mental health walk-in clinic	"So to have the amount of support, you know, that you guys offer, especially knowing that you have [mental health walk-in clinic]"
Barriers	
Long wait times	"Because everybody had a 3- to 6-month waiting period, if not longer" "Being able to find someone who was available soon" "…Just it takes a very long time to see a psychiatrist" "Told it's gonna take a year to see somebody"
Having to reach out to multiple providers	"I think I called about seven places" "We had to call many providers…between emails and phone calls, probably 10"
Insurance concerns	"She was released after 3 weeks 'cause the insurance would not advocate for her to stay there, would not pay for her to stay there" "Not everyone takes our insurance and the long waiting list"
Proposed Solutions	
School-based MBH programs	"So, at his school, they do have a psychiatrist and then therapists. there's four of them"
Flexible time slots	"I guess later hours would be my biggest thing"
Clear ED discharge planning	"Just being able to have MyChart and you guys calling me"

Abbreviations: ED, emergency department; MBH, mental and behavioral health.

Caregivers reflected on the helpfulness of resources beyond the ED, including close contact with primary care clinicians and school counselors. Therefore, we advocate for increased school counselor availability and ensuring that they are well-trained, connected, and knowledgeable about MBH resources. Based on our qualitative analysis of caregiver interviews, the ED serves a critical role in acute care—particularly with access to social work and other resources—yet primarily functions as a safety net in its current capacity. The inability of the ED psychiatry providers to prescribe psychotropic medications highlights a limitation for long-term MBH care. Training ED or primary care clinicians (particularly the latter, who have closer patient contact and can thus monitor the effects of psychotropic medications) to initiate these prescriptions while patients await outpatient MBH care could be beneficial. Caregivers identified barriers that underscore the ongoing need for an improved transition from ED to outpatient mental health care.

Additionally, factors facilitating better transition included follow-up communication from staff, and advocacy for expanding the MBH navigator role beyond the ED to other clinical settings. Knowing that the ED is a safety net may allow utilization of resources, such as dialectic behavioral therapy tools, to combat MBH problems such as anxiety in the short term as patients seek outpatient care.[18]

Our study is limited by an inability to demonstrate causation due to primarily descriptive results. Unfortunately, we did not have the resources to translate the survey or conduct the qualitative interview in languages other than English, limiting the generalizability of our findings to non-English-speaking caregivers. Furthermore, for the qualitative portion of our study, we excluded patients who returned to the ED within 4 weeks of their initial visit. Future research should investigate the reasons for these patients' return to the ED. We also acknowledge that the qualitative questions in our mixed methods study were limited in scope, which may have contributed to premature thematic saturation.

Our findings highlight critical societal challenges in accessing outpatient mental health care in the community. This study offers valuable insights to inform future initiatives aimed at enhancing the transition of care from the ED to outpatient settings. Addressing these issues is essential for improving mental health care delivery and outcomes for pediatric patients.

Acknowledgements: The authors would like to acknowledge the Children's Research Institute Pilot Award Program for funding this research and would also like to thank Maya Guenther, medical student at Medical College of Wisconsin, for assisting with data collection.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Children's mental health: data and statistics on children's mental health. Centers for Disease Control and Prevention. Updated August 20, 2024. Accessed June 13, 2024. https://www.cdc.gov/children-mental-health/data-research/?CDC_AAref_Val=https://www.cdc.gov/childrensmentalhealth/data.html

2. Whitney DG, Peterson MD. US national and state-level prevalence of mental health disorders and disparities of mental health care use in children. *JAMA Pediatr.* 2019;173(4):389-391. doi:10.1001/jamapediatrics.2018.5399

3. Kalb LG, Stapp EK, Ballard ED, et al. Trends in psychiatric emergency department visits among youth and young adults in the US. *Pediatrics*. 2019;143(4):e20182192. doi:10.1542/peds.2018-2192

4. Mapelli E, Black T, Doan Q. Trends in pediatric emergency department utilization for mental health-related visits. *J Pediatr.* 2015;167(4):905-910. doi:10.1016/j.jpeds.2015.07.004

5. Simon AE, Schoendorf KC. Emergency department visits for mental health conditions among US children, 2001-2011. *Clin Pediatr.* 2014;53(14):1359-1366. doi:10.1177/0009922814541806

6. Shankar LG, Habich M, Rosenman M, et al. Mental health emergency department visits by children before and during the COVID-19 pandemic. *Acad Pediatr.* 2022;22(7):1127-1132. doi:10.1016/j.acap.2022.05.022

7. Krass P, Dalton E, Doupnik SK, et al. US pediatric emergency department visits for mental health conditions during the COVID-19 pandemic. *JAMA Netw Open*. 2021;4(4):e218533. doi:10.1001/jamanetworkopen.2021.8533

8. Cloutier P, Thibedeau N, Barrowman N, et al. Predictors of repeated visits to a pediatric emergency department crisis intervention program. *CJEM*. 2017;19(2):122-130. doi:10.1017/cem.2016.357

9. Leon SL, Polihronis C, Cloutier P, et al. Family factors and repeat pediatric emergency department visits for mental health: a retrospective cohort study. *J Can Acad Child Adolesc Psychiatry.* 2019;28(1):9-20.

10. O'Donnell EP, Yanek L, Reynolds E, Manning Ryan L, Ngo TL. Characteristics of mental health patients boarding for longer than 24 hours in a pediatric emergency department. *JAMA Pediatr.* 2020;174(12):1206-1208. doi:10.1001/jamapediatrics.2019.5991

11. Hoffmann JA, Stack AM, Samnaliev M, et al. Trends in visits and costs for mental health emergencies in a pediatric emergency department, 2010-2016. *Acad Pediatr.* 2019;19(4):386-393. doi:10.1016/j.acap.2019.02.006

12. Cutler GJ, Rodean J, Zima BT, et al. Trends in pediatric emergency department visits for mental health conditions and disposition by presence of a psychiatric unit. *Acad Pediatr.* 2019;19(8):948-955. doi:10.1016/j.acap.2019.05.132

13. Santiago LI, Tunik MG, Foltin GL, et al. Children requiring psychiatric consultation in the pediatric emergency department: epidemiology, resource utilization, and complications. *Pediatr Emerg Care*. 2006;22(2):85-89. doi:10.1097/01.pec.0000199568.94758.6e

14. Chun TH, Duffy SJ, Grupp-Phelan J. The increasing burden of psychiatric emergencies: a call to action. *Pediatrics*. 2019;143(4):e20190251. doi:10.1542/peds.2019-0251

15. Saidinejad M, Duffy S, Wallin D, et al. The management of children and youth with pediatric mental and behavioral health emergencies. *Pediatrics*. 2023;152(3):e2023063256. doi:10.1542/peds.2023-063256

16. Hansen AS, Telleus GK, Mohr-Jensen C, et al. Parent-perceived barriers to accessing services for their child's mental health problems. *Child Adolesc Psychiatry Ment Health.* 2021;15(1):4. doi:10.1186/s13034-021-00357-7

17. Whitney DG, Peterson MD. US national and state-level prevalence of mental health disorders and disparities of mental health care use in children. *JAMA Pediatr.* 2019;173(4):389-391. doi:10.1001/jamapediatrics.2018.5399

18. Linehan MM. Rationale for dialectical behavior therapy skills training. In: *DBT Skills Training Handouts and Worksheets*. 2nd ed. The Guilford Press; 2015:3-24.

Neurodevelopmental Screening Tests Outcomes of Children in Wisconsin With a Prenatal History of Travel to Zika Virus-Endemic Regions During 2015-2018: A Retrospective Case-Control Study

Sabrina A. Kavakov, OTD;* Rachel V. Spanton*; Elaina Razo; Erik Sanson; Christelle Cayton; Emmy Wanjiku; Jens Eickhoff, PhD; Karla K. Ausderau, OTR, PhD; Emma L. Mohr, MD, PhD

ABSTRACT

Background: Children with prenatal Zika virus exposure are at an increased risk of developing neurodevelopmental deficits in early childhood. Travel to Zika virus-endemic regions during pregnancy elevates the risk of offspring developing complications. This study examined developmental outcomes of children from Wisconsin with maternal or partner travel history to Zika virus-endemic regions during pregnancy compared to gestation and age-matched controls.

Methods: A retrospective chart review compared outcomes of cases (n = 181) with prenatal travel history to Zika virus-endemic regions to gestational and birth date-matched controls (n = 172) up to 7 years old. We reported Zika virus testing and travel, birth outcomes, standardized developmental screening tests, and specialist referral rates.

Results: There were no differences in referral rates and standardized developmental screening test outcomes, but cases tended to have more referrals for early intervention compared to the controls ($P = 0.059$). One Zika virus-positive case was identified with complications surrounding birth, and 2.2% of children had documentation in their health records noting potential Zika virus exposure. Regardless of groups, limited referrals were made at 9 (0%), 18 (60%), and 24 (40%) months based on Ages and Stages Questionnaire-version 3 (ASQ-3) recommendations.

Conclusions: This study found similar developmental screening outcomes and referral rates between groups. Longitudinal care of children whose mothers traveled to Zika virus-endemic regions could be improved with better documentation of prenatal Zika virus exposure in the child's medical record, use of standardized developmental screening tools at every recommended well-child visit, and referral when developmental screening test scores are low.

• • •

Author Affiliations: Department of Pediatrics, University of Wisconsin (UW) School of Medicine and Public Health (SMPH), Madison, Wisconsin (Kabakov, Spanton, Razo, Sanson, Cayton, Wanjiku, Mohr); Department of Kinesiology, Occupational Therapy Program, UW–Madison, Madison, Wisconsin (Kabakov, Ausderau); Department of Biostatistics and Medical Informatics, UW SMPH, Madison, Wisconsin (Eickhoff); Waisman Center, UW–Madison, Madison, Wisconsin (Ausderau); Department of Medical Microbiology and Immunology, UW SMPH, Madison, Wisconsin (Mohr). **Denotes co-first authors.*

Corresponding Author: Emma Mohr, 600 Highland Ave, Madison WI 53792, phone 608.265.5107, email emohr2@wisc.edu, ORCID ID 0000-0003-0742-305X

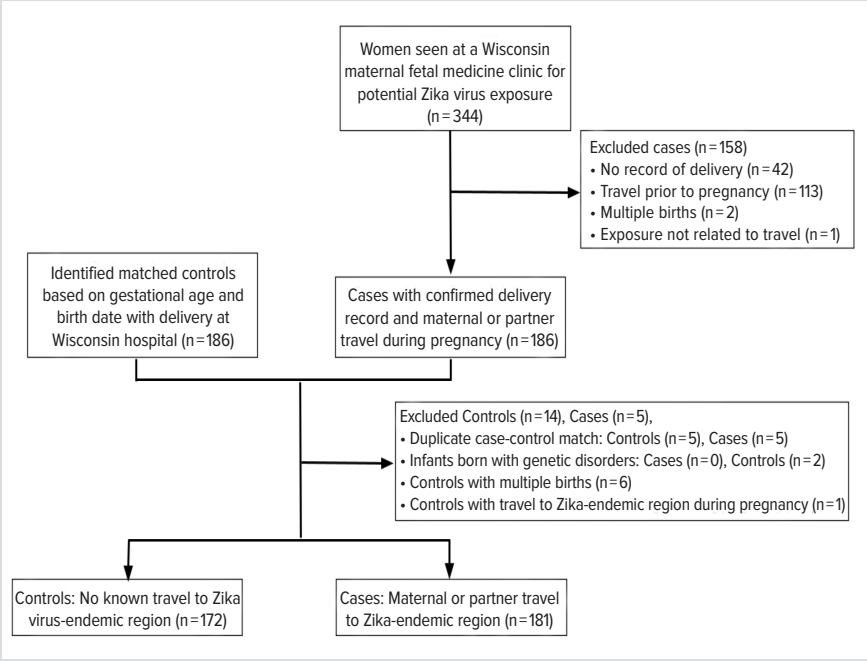
BACKGROUND

Zika virus was declared a public health emergency in 2016 when prenatal Zika virus exposure was linked to congenital defects in newborns, including microcephaly and visual and hearing deficits.[1,2] Approximately 5% of children with laboratory-confirmed Zika virus exposure in the United States are born with congenital defects.[3] An additional 30% of children who are born without congenital deficits manifest neurodevelopmental deficits in early childhood, with language development being the most affected.[4] As cohorts of children with Zika virus exposure during the 2015-2018 epidemic are now entering school age, recent research has identified neurodevelopmental deficits in preschool age.[5,6] Additional research is necessary to define how potential prenatal Zika virus exposure affects developmental outcomes in childhood, especially in pregnancies where exposure to mosquitoes occurred but no testing for Zika virus was performed.

Most developmental research on Zika virus has focused on cohorts in countries with high prevalence and incidence of Zika virus or on congenital defects. Zika virus has multiple modes of transmission, including (1) transmission from mosquito to human, (2) sexual transmission, and (3) vertical transmission from mother to child.[7] The Centers for Disease Control and Prevention (CDC) recommends caution when traveling to areas with reported Zika virus infections (both past and current), which are countries where there is a high prevalence of *Aedes aegypti* mosquitos.[8] Travel to a Zika virus-endemic area(s) during pregnancy increases the risk of congenital defects or late-onset

neurodevelopmental deficits compared to pregnancies with no travel history to endemic regions.[9,10] Zika virus infection is often asymptomatic, even during pregnancy, suggesting that pregnant persons who travel to endemic regions may have no knowledge of a Zika virus infection. Fetuses remain at risk for developing deficits independent of the presence of acute Zika virus infection symptoms.[3] Current CDC testing guidelines recommend testing only for symptomatic pregnant women after travel to a country with a past or current Zika virus outbreak.[11] Asymptomatic pregnant women do not meet the testing criteria despite their fetuses remaining at risk for deficits. Defining the incidence of neurodevelopmental deficits in this unique group of children is important for developing travel and testing recommendations during pregnancy and specifying which children should receive early intervention.

Figure 1. Exclusion and Inclusion Criteria



This study aimed to investigate the developmental screening outcomes of children with a prenatal travel history to Zika virus-endemic regions during the height of the Zika virus epidemic in 2015-2018, within a Wisconsin hospital health care system. This study utilized electronic health records (EHR) to define maternal Zika virus information, developmental screening outcomes, and specialist referrals.

METHODS

A retrospective chart review was conducted to determine how travel exposure to a Zika virus-endemic region(s) during pregnancy affected developmental screening outcomes. Maternal records were obtained from women seen at a Wisconsin maternal-fetal medicine clinic to evaluate for Zika virus from January 1, 2015, through December 31, 2018. Cases were defined as children with prenatal maternal or partner travel history to a Zika virus-endemic region during 2015-2018, based on the CDC classification.[8] Cases were removed from the study based on the following exclusion criteria: (1) no record of delivery in the same Wisconsin health system, (2) travel history prior to pregnancy, (3) multiple births, and (4) potential Zika virus exposure unrelated to travel (Figure 1). We identified matched-control offspring based on gestational age (+/- 1 week) and birth date (+/- 1 birth month) using PeriData.Net, a comprehensive birth registry that provides birth-level data (Ancilla Partners, Inc, Milwaukee, Wisconsin). After matching, cases and controls were excluded based on the following criteria: (1) duplicate assignments in the case/control group, (2) children with diagnosed genetic disorders, (3) controls with multiple births, (4) controls with maternal or partner travel history to a Zika virus-endemic region. After all exclusion criteria were considered (Figure 1), 181 cases and 172 controls were available for study. This chart review was approved by the UnityPoint Health Meriter Institutional Review Board (#2019-024). Data from children's EHRs were extracted from birth until 7 years of age or April 1, 2023.

The EHR provided demographic and socioeconomic information, Zika virus testing, travel history, and birth and developmental outcomes. Paper records from the maternal-fetal medicine clinic provided supplemental travel information, including travel continent, potential paternal travel, any acute Zika virus symptoms, estimated trimester of exposure, and confirmed test results. The University of Wisconsin-Madison Clinical and Health Informatics Institute was used to identify maternal demographic information, type of delivery, and birth measurements. ZIP codes were obtained from the maternal EHR in January 2024 (due to the absence of maternal ZIP codes in the delivery records). The distribution of health services across urban and rural areas is known to affect health outcomes.[12] To account for the impact of socioeconomic status on developmental outcomes, maternal ZIP codes were assigned a rural or urban status using the Health Innovation Program's Zip Code Toolkit.[13]

Multiple variables were obtained to compare birth and developmental outcomes between groups. These included delivery type, sex, gestational age at birth, Apgar scores, birth measurements, documentation of potential Zika virus exposure, specialist referrals, and developmental screeners including the Ages and Stages Questionnaire-version 3[14] (ASQ-3) and Modified

Checklist for Autism in Toddlers-Revised[15] (MCHAT-R). The ASQ-3 is a screening tool to measure developmental milestone attainment, and MCHAT-R is a screening tool for identifying the risk of autism spectrum disorder. ASQ-3 outcomes were documented at 9, 18, and 24 months across 5 areas of development (communication, fine motor, gross motor, personal social, and problem-solving). They were interpreted as on schedule (within 1 SD), monitor (between 1 and 2 SD), or further assessment needed (>2 SD) per ASQ-3 guidelines. The MCHAT-R was documented at 2 time points (16-21 months and 22-30 months of age), with total scores categorized as no further action (0-2 score), additional screening needed (3-7 score), or refer to specialists (8-20 score).

We evaluated referrals to multiple pediatric subspecialties, therapies, and early intervention (Wisconsin Birth to 3 Program[16]) because diagnoses related to developmental deficits or complications from congenital Zika virus infection may be evaluated by all of these specialties. Referrals to dentists, dermatologists, rheumatologists, and allergists were excluded as these specialties were not determined to help evaluate or manage developmental outcomes. Specialists also were excluded if the frequency was reported less than 5 times across both cases and controls. Search terms to identify the frequency of specialists were "consult" or "referral" in the chart. Before calculating the referral rate, charts with EHR visits documented after birth hospitalization were included, indicating they were still engaged in the health care system.

Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted by the UW-Madison School of Medicine and Public Health.[17,18] All data were verified for accuracy by the co-first authors. Statistical analyses were conducted using SAS software, version 9.4 (SAS Institute; Cary, North Carolina). Demographic characteristics were compared between cases and controls using chi-square analysis for categorical characteristics or the nonparametric Wilcoxon rank sum test for characteristics measured on a quantitative scale. Referral rates by specialists were compared between cases and controls using a chi-square or Fisher exact test. Analogously, the MCHAT-R and ASQ-3 categories were compared using a chi-square test or Fisher exact test for each area of development and time point. All reported P values are 2-sided, and $P < 0.05$ was used to define statistical significance.

RESULTS

We investigated both maternal and partner travel (due to sexual transmission of Zika virus) because paper records did not explicitly outline who traveled. Solely partner travel was indicated in 11 paper charts (6.07%). Partner travel was included in the country of travel but was excluded from the travel duration and trimester of travel (Table 1). Most prenatal Zika virus-endemic travel history occurred within North America followed by South America, with specific countries outlined in Supplemental Table 1. The mean maternal travel duration was 39.5 days (median = 8 days), which was skewed since 13.5% of maternal travel had periods of ≥ 30 days. The majority of reported travel was during the first trimester (81.8%), followed by the second (27.1%) and third trimesters (9.4%); 11.6% reported travel occurred across multiple trimesters. Records did not include activities during travel, so it is unclear what mosquito exposures were encountered. In total, 56.4% of maternal cases received Zika virus testing. Just over half of the pregnant women had Zika virus IgM testing, and fewer were tested by polymerase chain reaction (PCR) or plaque reduction neutralization test (PRNT). Only 10.5% of maternal cases reported symptoms consistent with acute Zika virus infection, including rash, acute conjunctivitis, headache, arthralgia, myalgia, and fever. Of the symptomatic maternal cases, 63.2% received testing. One maternal case had a positive Zika virus result, and the infant born had multiple comorbidities at birth (including imperforate anus, congenital rectovaginal fistula, and caudal regression syndrome); however, no infant medical records after birth were available.

Comparison of the maternal cases and matched controls demonstrates similarity in variables, such as maternal age and rural/urban location (Table 1). More cases than controls had an ethnicity or race defined as "Other" ($P = 0.002$) or reported "Hispanic or Latino" ($P = 0.001$) in the maternal health record. Immediate delivery and birth outcomes, including delivery type, infant sex, gestational age, Apgar scores, and measurements, did not differ between cases and controls. Only 4 of the 181 child cases had potential Zika virus exposure included in their problem list.

Developmental screening test results were evaluated to define whether prenatal travel history increases the likelihood of poor performance on standardized screening tests. Results from the MCHAT-R were reported in 45.3% to 56.4% of cases and 41.3% to 41.9% of controls across all timepoints (Supplemental Table 2). At the 16- to 21-month timepoint, more cases (11%) scored in the "additional screening needed" category compared to controls (0%, $P = 0.0038$) (Supplementary Table 4). However, at 22 to 30 months administration, there were no significant differences between the MCHAT-R assessment results for cases and controls (Figure 2). Overall, the majority of children scored in the "no further action" category in both groups and time points. The ASQ-3 was reported in 34.8% to 39.8% of cases and 35.4% to 39.5% controls (Supplemental Table 2) across all timepoints. There were limited significant differences between the cases and controls in ASQ-3 scores across 9, 18, and 24 months (Figure 2, Supplemental Table 3). The only significant ASQ-3 difference was in the 18-month problem-solving domain, with more cases (6.3%) performing in the monitor zone compared to the controls (0%, $P = 0.045$). Overall, the ASQ-3 (24 months) and MCHAT-R (22-30 months) at the latest timepoint revealed that the majority of children, regardless of prenatal travel history, perform within the expected range (Figure 2).

Table. Maternal and Infant Demographic and Exposure Information

	Controls (n = 172)	Cases (n = 181)	*P* value
Travel and Exposure Information			
Travel continent,[a] n (%)			
North America	–	152 (84.0)	–
South America	–	20 (11.0)	–
Europe	–	0 (0)	–
Africa	–	4 (2.2)	–
Asia	–	11 (6.1)	–
Oceania	–	2 (1.1)	–
Travel durations,[b] no. days			
Mean (SD)	–	39.5 (145.6)	–
Median	–	8	–
Trimester with travel history recorded,[c] no. days			
1st trimester	–	139 (81.8)	–
2nd trimester	–	46 (27.1)	–
3rd trimester	–	16 (9.4)	–
Maternal Zika symptoms, n (%)			
Any reported symptom(s)[d]	–	19 (10.5)	–
Rash	–	3 (1.7)	–
Acute conjunctivitis	–	2 (1.1)	–
Headache	–	6 (3.3)	–
Arthralgia	–	7 (3.9)	–
Myalgia	–	9 (5.0)	–
Fever	–	7 (3.9)	–
Zika virus testing performed[e]/symptomatic mothers	–	12/19 (63.2)	–
Tests performed, n (%)			
Zika virus testing performed[e]		102 (56.4)	
IgM	–	99 (54.7)	–
PCR	–	29 (16)	–
PRNT	–	1 (0.6)	–
Maternal Zika symptomatic, n (%)			
Unknown	–	5 (2.8)	–
Zika positive test, n	–	1[f]	–

	Controls (n = 172)	Cases (n = 181)	*P* value
Maternal Demographics			
Maternal race and ethnicity, n (%)			
White	120 (69.8)	125 (69.1)	0.972
Black (African American)	12 (7.0)	7 (3.9)	0.290
Asian	21 (12.2)	12 (6.6)	0.106
Other	13 (7.6)	35 (19.3)	0.002
Hispanic or Latino	14 (8.1)	44 (24.3)	< 0.001
Unknown or not reported	5 (3.0)	1 (0.6)	0.113
Maternal age at birth, mean (SD)			
Years	30.7 (5.0)	31.6 (5.7)	0.175
Maternal socioeconomic status, n (%)			
Rural	32 (19.3)	30 (16.9)	0.559
Urban	134 (80.7)	148 (83.1)	
Birth Outcomes			
Delivery type, n (%)			
Vaginal	131 (76.2)	128 (70.7)	0.247
Cesarean birth	41 (23.8)	53 (29.3)	
Infant sex, n (%)			
Male	84 (48.8)	87 (48.1)	0.561
Female	88 (51.2)	94 (51.9)	
Gestational age at birth, mean (SD)			
Weeks	39.16 (8.2)	39.24 (10.6)	0.175
Apgar scores, mean (SD)			
1-minute	8.2 (1.3)	8.0 (1.7)	0.643
5-minute	8.8 (0.6)	8.7 (1.1)	0.232
Birth measurements, mean (SD)			
Head circumference (cm)	34.6 (4.7)	34.2 (2.0)	0.643
Length (cm)	50.8 (3.5)	51.3 (2.6)	0.250
Weight (kg)	3.4 (0.5)	3.4 (0.5)	0.310
Infant Record Information			
Problem list includes prenatal history of potential Zika virus exposure, n (%)			
"Zika virus exposure" or "potential Zika" virus exposure"	–	4 (2.5)	–

Abbreviations: IgM, immunoglobulin M; PCR, polymerase chain reaction; PRNT, plaque reduction neutralization tests.

[a]Some women disclosed travel to multiple countries, so the sum of all women at each travel location does not equal the sample size. Partner travel was included in the travel destination. We were unable to differentiate travel from immigration status using medical records.

[b]Travel duration includes time in the country by maternal travel dates. Unable to capture travel duration for 26 records and charts solely with partner travel were additionally excluded from the calculation. The final sample size was 143.

[c]Some women reported travel across multiple trimesters, so the sum of all women with travel does not equal the sample size. Charts solely with partner travel were excluded from the calculation (n = 170).

[d]Number of women with 1 or more symptoms consistent with acute Zika virus infection.

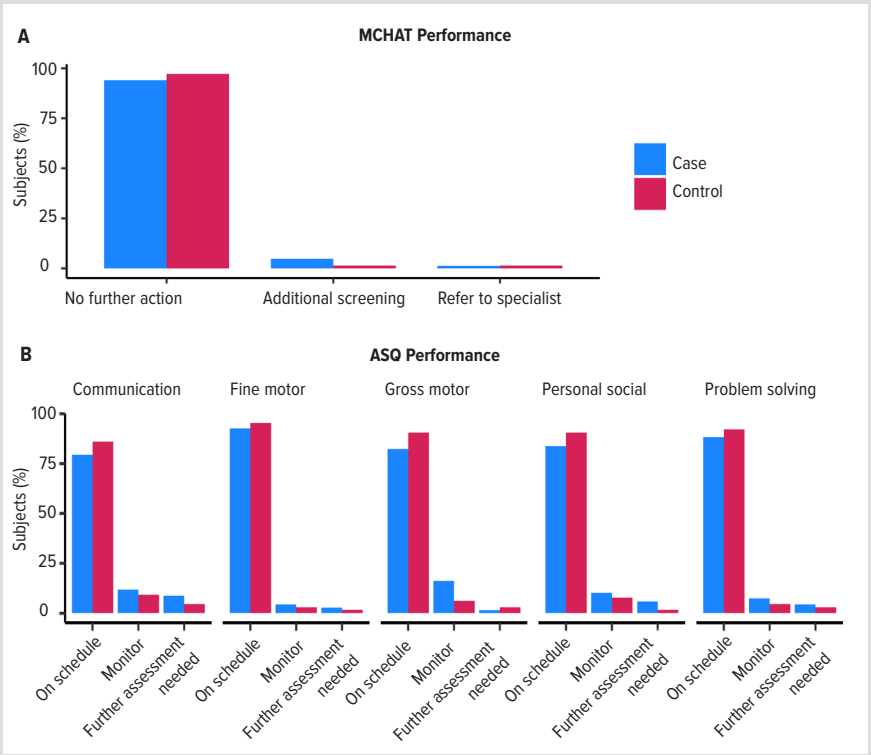
[e]The number of women with any Zika virus test (IgM, PCR, PRNT, and/or unknown) performed.

[f]Zika positive case (n = 1) by IgM enzyme-linked immunoassay and PRNT.

Rates of referrals to specialists were evaluated as a proxy marker of clinician or parental concern for additional specialized evaluation. The number of children included in this "specialist referral rate" evaluation is smaller because fewer children in both groups had medical visits documented after the birth hospitalization (Figure 3A). Overall, 48.1% of cases and 49.0% of controls were referred to at least 1 specialist. There were no significant differences between cases and controls in the referral rate to multiple specialists (Figure 3). However, there was a trend for more cases (20%) than controls (12%) having referrals to the Wisconsin Birth to 3 Program ($P = 0.058$). We also evaluated whether children were referred appropriately after receiving scoring in the "further assessment needed" category on the ASQ-3. There were similar referral rates for both the cases and controls. Combining cases and controls, zero referrals were made at 9 months and only 40% to 60% of children received a referral at 18 months ($P < 0.001$) or 24 months ($P = 0.003$) when a referral was recommended by ASQ-3 screening (Supplemental

Table 5). In summary, there were no differences in referrals to pediatric subspecialties and therapies, but many children were not referred appropriately to specialists after receiving a score indicating further assessment needed on the ASQ-3 developmental screening test.

Figure 2. Standardized Developmental Screening Tests



A) Modified Checklist in Toddlers-Revised (MCHAT-R) at 22–30 months (sample size: 71 controls, 84 cases).
B) Ages and Stages Questionnaire-version 3 (ASQ-3) at 24 months (sample size: 64 controls, 68 cases).

DISCUSSION

This retrospective case-control study identified children in Wisconsin who had maternal or partner travel during pregnancy to Zika virus-endemic areas during 2015-2018. This study found that 56.4% of maternal cases received Zika virus testing during pregnancy, and only 1 pregnant woman tested positive. We found similar developmental screening and referral outcomes between the travel-exposed cases and matched controls.

We found no differences in developmental screening outcomes between the cases and controls up to 30 months of age. However, our evaluation of developmental screening tests is limited because there are no standardized developmental screening tests for school-age children during their well-child visits.[19] Current American Academy of Pediatrics (AAP) guidelines recommend screening at 9, 18, and 24 or 30 months during well-child visits.[20,21] Because new deficits emerge–specifically in executive function and emotional regulation–in school-age children with prenatal Zika virus exposure,[5,6] our finding that developmental screening results were similar between cases and controls only applies to up to 30 months of age. Families and clinicians should obtain specific developmental evaluations if there are concerns during the preschool and elementary school years.

We also found that more cases than controls tended to receive referrals for early intervention services (Birth to 3 Program). While not statistically significant, the trend is meaningful because it suggests that early intervention services may be needed more commonly by children with potential prenatal Zika virus exposure. We also found that many children are still not referred when developmental concerns are identified.[22] None of the infants in either group were appropriately referred to specialists at 9 months of age when they received a low developmental screening score, and only half were appropriately referred at a later age. For successful intervention, it is crucial that children are referred for specialty care after scoring low on screening tests. This may reflect the physicians and caregivers opting to use a "wait and see" approach, disregarding AAP recommendations that all children be referred after a low score.[20]

Accurately diagnosing maternal Zika virus infection is challenging, and better diagnostics need to be developed. Only 1 pregnant woman had a positive Zika virus test in our chart review. This may reflect the true maternal infection rate or could reflect the inaccuracy of tests done outside of the targeted test range.[11,23] Developing better tests to diagnose maternal Zika virus infection is critical as children remain at equal risk for developmental deficits whether maternal cases are symptomatic or asymptomatic.[3]

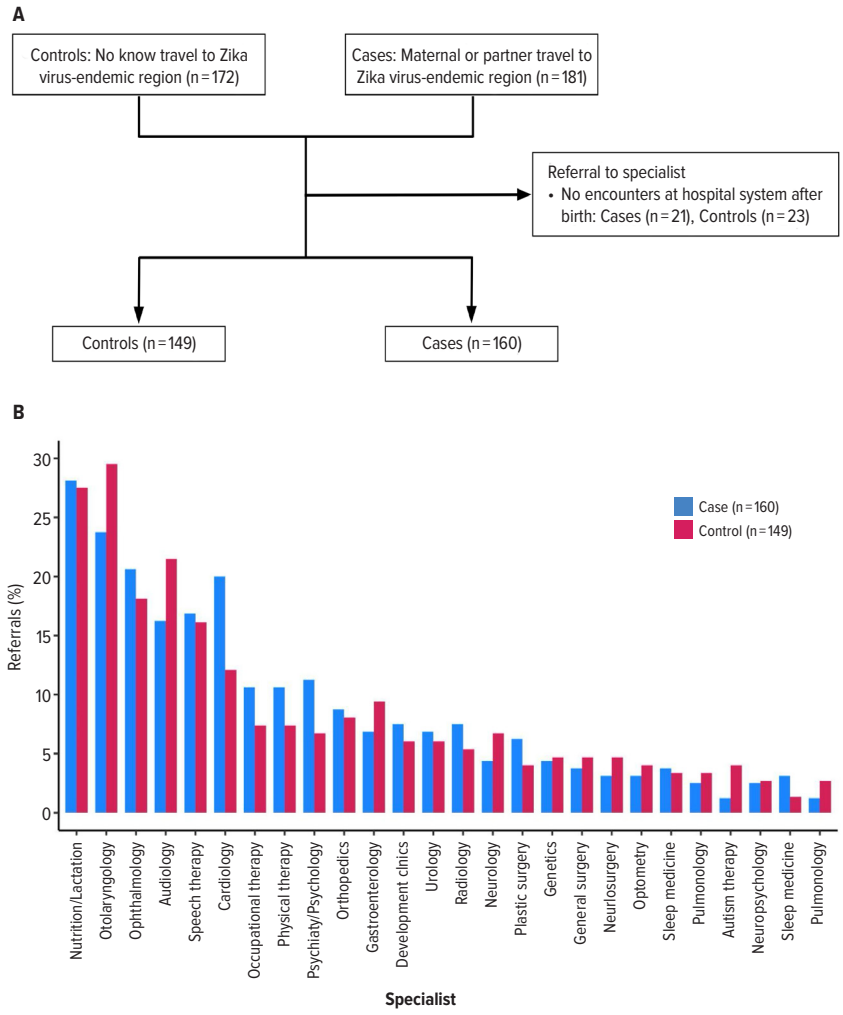
There was inadequate documentation in the EHR stating that a child was exposed to Zika virus. Our study identified only 4 children's charts with "potential Zika virus exposure" listed. This may be the result of the lack of an appropriate ICD-10 (*International Classification of Diseases, 10th Edition*) code at this date.[24] Improving documentation within the EHR is one approach to alert all future medical providers that a child is at risk for developmental deficits. Creating better documentation of prenatal travel history in the child's EHR can support the identification of children who could benefit from appropriate referrals so that early referral rather than a "wait and see" approach is used.

Limitations

Even though there were limited differences, there are multiple limitations that may have prevented early identification of children with developmental deficits in this chart review. The main limitation is that we could not determine whether any of these

infants were exposed to Zika virus prenatally because (1) travel does not inherently equate to Zika virus exposure, (2) different travel activities may have different risk (eg, cruises and high altitudes), and (3) there are lower rates of Zika virus transmission by sexual contact compared to mosquito exposure. Additionally, we could not determine whether the testing was performed within the targeted test range (within 3 weeks of exposure for the Zika virus PCR and 3 months of exposure for Zika virus IgM) given the lack of specific dates available in this chart review. If done within the targeted time period, serology testing has a sensitivity of approximately 75% to 90% depending on the test provided, with PRNT being the most sensitive and IgM being the least sensitive.[25] Another limitation of our developmental screening test evaluation is that results were not available for many children at later time points, perhaps because screening tests were delayed or canceled during the COVID pandemic As a result, children with possible prenatal exposure may still be at a high risk of developmental deficits and there is a need for better referrals and documentation in health record systems.

Figure 3. Referral Rate by Specialist



A) Final sample of children that had medical visits after the birth hospitalization and were included in the count for specialist referrals.

B) Percent referrals were calculated using the total number of referrals per group divided by the denominator for cases (n = 160) and for controls (n = 149), ordered from the most common to least common.

CONCLUSIONS

Zika virus is likely to reemerge and cause future epidemics.[26] Although we found no screening test differences between the children born to mothers with and without a travel history, there is a need to continue to monitor children born after prenatal Zika virus exposure. Monitoring children can be achieved with better documentation of prenatal Zika virus exposure in the child's medical record, use of standardized developmental screening tools at every recommended well-child visit, and referral when developmental screening test scores are low rather than waiting to see if the problem improves. The increased rate of referrals to the Wisconsin Birth to 3 Program seen in the children with prenatal travel history is interesting and warrants further evaluation to see the program was more heavily utilized following the Zika virus pandemic.

Acknowledgments: The authors wish to thank Donovin Widmann, a medical student who supported the data acquisition of this chart review; the members of Dr Mohr and Dr Ausderau's lab for supporting this work; Dr. Kathleen Antony, a maternal-fetal medicine specialist, who provided them with the paper records; and Ancilla Partners, Inc for its comprehensive birth registry data of PeriData.net.

Funding/Support: This work was supported by departmental funding to Dr Mohr, National Institutes of Health (NIH) funding (K08AI139341) to Dr Mohr, and the UW School of Medicine and Public Health Shapiro Summer Research Program. The UW–Madison Clinical and Health Informatics Institute was supported by the Clinical and Translational Science Award (CTSA) program, through the NIH National Center for Advancing Translational Sciences (NCATS) grant UL1TR002373.

Financial Disclosures: None declared.

REFERENCES

1. de Araújo TVB, Ximenes RA de A, Miranda-Filho D de B, et al. Association between microcephaly, Zika virus infection, and other risk factors in Brazil: final report of a case-

control study. *Lancet Infect Dis.* 2018;18(3):328-336. doi:10.1016/S1473-3099(17)30727-2

2. Krow-Lucal ER, de Andrade MR, Cananéa JNA, et al. Association and birth prevalence of microcephaly attributable to Zika virus infection among infants in Paraíba, Brazil, in 2015–16: a case-control study. *Lancet Child Adolesc Health.* 2018;2(3):205-213. doi:10.1016/S2352-4642(18)30020-8

3. Roth NM, Reynolds MR, Lewis EL, et al. Zika-associated birth defects reported in pregnancies with laboratory evidence of confirmed or possible Zika virus infection — U.S. Zika Pregnancy and Infant Registry, December 1, 2015–March 31, 2018. *MMWR Morb Mortal Wkly Rep*. 2022;71(3):73-79. doi:10.15585/mmwr.mm7103a1

4. Marbán-Castro E, Vazquez Guillamet LJ, Pantoja PE, et al. Neurodevelopment in normocephalic children exposed to zika virus in utero with no observable defects at birth: a systematic review with meta-analysis. *Int J Environ Res Public Health.* 2022;19(12):7319. doi:10.3390/ijerph19127319

5. Mulkey SB, Peyton C, Ansusinha E, et al. Preschool neurodevelopment in Zika virus-exposed children without congenital Zika syndrome. *Pediatr Res.* 2023;94(1):178-184. doi:10.1038/s41390-022-02373-5

6. Mulkey SB, Corn E, Williams ME, et al. Neurodevelopmental outcomes of normocephalic Colombian children with antenatal Zika virus exposure at school entry. *Pathogens*. 2024;13(2):170. doi:10.3390/pathogens13020170

7. Holtzman M, Golden WC, Sheffield JS. Zika virus infection in the pregnant woman. *Clin Obstet Gynecol*. 2018;61(1):177-185. doi:10.1097/GRF.0000000000000343

8. Zika virus: recommendations for travelers and people living abroad. Centers for Disease Control and Prevention. May 30, 2024. Accessed July 14, 2024. https://www.cdc.gov/zika/travel/index.html

9. Marbán-Castro E, Goncé A, Fumadó V, et al. Zika virus infection in pregnant travellers and impact on childhood neurodevelopment in the first two years of life: a prospective observational study. *Travel Med Infect Dis*. 2021;40:101985. doi:10.1016/j.tmaid.2021.101985

10. Vouga M, Chiu YC, Pomar L, et al. Dengue, Zika and chikungunya during pregnancy: pre- and post-travel advice and clinical management. *J Travel Med.* 2019;26(8):taz077. doi:10.1093/jtm/taz077

11. Zika virus: testing for Zika. Centers for Disease Control and Prevention. May 15, 2024. Accessed July 14, 2024. https://www.cdc.gov/zika/testing/?CDC_AAref_Val=https://www.cdc.gov/zika/symptoms/diagnosis.html

12. Blumenthal SJ, Kagen J. MSJAMA. The effects of socioeconomic status on health in rural and urban America. *JAMA*. 2002;287(1):109. doi:10.1001/jama.287.1.109-JMS0102-3-1

13. ZIP Codes by Rural and Urban Groupings Toolkit (Model 2b). University of Wisconsin-Madison Health Innovation Program; 2024. Accessed July 14, 2024. https://hipxchange.org/toolkit/ruralurbangroups/

14. Squires J, Twombly E, Bricker D, Potter L. *The ASQ-3 Users Guide*. 3rd ed. Paul H. Brookes Publishing; 2009.

15. Robins DL, Casagrande K, Barton M, Chen CM, Dumont-Mathieu T, Fein D. Validation of the modified checklist for autism in toddlers, revised with follow-up (M-CHAT-R/F). *Pediatrics*. 2014;133(1):37-45. doi:10.1542/peds.2013-1813

16. Birth to 3 Program. Wisconsin Department of Health Services. Accessed December 11, 2024. https://www.dhs.wisconsin.gov/birthto3/index.htm

17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

18. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform.* 2019;95:103208. doi:10.1016/j.jbi.2019.103208

19. Lipkin PH, Macias MM; Council on Children with Disabilities, Section on Developmental and Behavioral Pediatrics. Promoting optimal development: identifying infants and young children with developmental disorders through developmental surveillance and screening. *Pediatrics*. 2020;145(1):e20193449. doi:10.1542/peds.2019-3449

20. Council on Children with Disabilities, Section on Developmental Behavioral Pediatrics, Bright Futures Steering Committee, Medical Home Initiatives for Children with Special Needs Project Advisory Committee. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. *Pediatrics*. 2006;118(1):405-420. doi:10.1542/peds.2006-1231

21. Hyman SL, Levy SE, Myers SM, et al. Executive summary: identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*. 2020;145(1):e20193448. doi:10.1542/peds.2019-3448

22. Lipkin PH, Macias MM, Baer Chen B, et al. Trends in pediatricians' developmental screening: 2002–2016. *Pediatrics*. 2020;145(4):e20190851. doi:10.1542/peds.2019-0851

23. Jorge FA, Thomazella MV, de Castro Moreira D, Lopes LDG, Teixeira JJV, Bertolini DA. Evolutions and upcoming on Zika virus diagnosis through an outbreak: a systematic review. *Rev Med Virol.* 2020;30(3):e2105. doi:10.1002/rmv.2105

24. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines.* World Health Organization; 1992.

25. Medialdea-Carrera R, Levy F, Castanha P, et al. A systematic evaluation of IgM and IgG antibody assay accuracy in diagnosing acute Zika virus infection in Brazil: lessons relevant to emerging infections. *J Clin Microbiol.* 2021;59(12):e0289320. doi:10.1128/JCM.02893-20

26. Van Wyk H, Eisenberg JNS, Brouwer AF. Long-term projections of the impacts of warming temperatures on Zika and dengue risk in four Brazilian cities using a temperature-dependent basic reproduction number. *PLoS Negl Trop Dis.* 2023;17(4):e0010839. doi:10.1371/journal.pntd.0010839

Association Between Lead Poisoning and Academic Performance of Third-Grade Children in Milwaukee

Ronald Anguzu, MD, MPH, PhD; Lisa E. Rein, MS; Sergey Tarima, PhD; Melanie Stewart, PhD; Constance Kostelac, PhD; Catherine Carter, MPH; John R. Meurer, MD, MBA; Laura D. Cassidy, MS, PhD

ABSTRACT

Introduction: Lead-poisoned children with blood lead levels (BLL) of > 5 µg/dL among those tested in Milwaukee, Wisconsin, increased from 8.6% to 10.4% between 2014 and 2016. We examined the association between lead poisoning and academic performance of third-grade children in Milwaukee.

Methods: Data from Milwaukee Public Schools, birth certificates, and the City of Milwaukee Health Department on third-grade students from 2010 through 2015 were analyzed. The outcome was academic performance measured as standardized math and reading scores. The key independent variable was elevated BLL ≥ 5 µg/dL. Standardized reading and math test scores were modeled using mixed effects linear regression, including a school-specific random intercept and repeated effects for school trimesters using an autoregressive correlation structure of first order. The association of reading scores with lead exposure was explored after adjusting for school year, trimester, child, and maternal characteristics.

Results: Of 18 213 children with available lead testing data, the median maximum BLL was 4.0 µg/dL (interquartile range 34.0-6.1). Nearly 60% (58.3%) had maximum BLLs < 5 µg/dL, 27.7% had maximum BLLs of 5-9 µg/dL, 11.0% had maximum BLLs of 10-19 µg/dL, and 3.0% had maximum BLL ≥20 µg/dL. After controlling for potential confounders, children with BLLs ≥20 µg/dL, 10-19 µg/dL, and 5-9 µg/dL, respectively, had lower standardized math and reading scores when compared to children with BLLs <5 µg/dL at $P < 0.001$.

Conclusions: Even at low levels, childhood lead poisoning persists in Milwaukee and is associated with lower third-grade academic performance in standardized reading and math tests. Parent education, childhood lead testing, and home lead abatement are critical strategies to improve children's educational performance.

• • •

Author Affiliations: Division of Epidemiology and Social Sciences, Institute for Health and Equity, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Anguzu, Kostelac, Carter, Cassidy); Division of Biostatistics, Institute for Health and Equity, MCW, Milwaukee, Wisconsin (Rein, Tarima); Department of Research, Assessment, and Data, Milwaukee Public Schools, Milwaukee, Wisconsin (Stewart); Division of Community Health, Institute for Health and Equity, MCW, Milwaukee, Wisconsin (Meurer).

Corresponding Author: Ronald Anguzu, Institute for Health and Equity, Medical College of Wisconsin, 2153 N Martin Luther King Jr Dr, Milwaukee, WI 53212; email ranguzu@mcw.edu; ORCID ID 0000-0002-7924-7182

INTRODUCTION

Lead is an environmental neurotoxicant of public health importance that may result in lead poisoning.[1] Lead poisoning remains a public health priority that has harmful effects on the brain development of children and adults.[2] Lead exposure also has demonstrated adverse effects, such as neurobehavioral deficits;[3] cardiovascular, immune, and behavioral development;[4] and adverse birth outcomes.[5] Although the Centers for Disease Control and Prevention (CDC) set a reference blood lead level (BLL) cutoff of ≥ 3.5 µg/dL to indicate lead poisoning, no BLLs are safe.[6] In Wisconsin, children under 6 years of age are considered lead poisoned at a capillary or venous BLL ≥ 5 µg/dL.[7] Studies consistently show an association between low BLL, such as 10 µg/dL or less, and impaired cognitive function in children.[8] The effects of childhood lead exposure can persist throughout a lifetime and result in negative long-term consequences in adulthood, such as cognitive decline, aggressive behavior, sociobehavioral problems,[9] and communication and language difficulties.[10] Lead-based paint is the main source of childhood lead exposure, especially in older houses.[11] Other lead poisoning sources include manufacturing products, such as children's toys containing lead, mining waste, lead dust,[12] and leaded water service lines/pipes,[13] as well as leaded gasoline phased out by the Environmental Protection Agency (EPA).[14]

Reporting blood lead test results to Wisconsin public health officials is mandatory.[15] From 2014 through 2017, 6.9% of children under 6 years of age in Milwaukee had a BLL above

Table 1. Summary of Child/Maternal Variables by Maximum Blood Lead Test Result

	BLL Not Tested N = 2720	Max BLL <5 µg/dL N = 10 618	Max BLL ≥5 µg/dL N = 7595	*P* value
School year, n (%)				<0.001
2010 – 2011	588 (13.87)	1759 (41.49)	1893 (44.65)	
2011 – 2012	521 (12.78)	1970 (48.31)	1587 (38.92)	
2012 – 2013	553 (13.18)	2163 (51.55)	1480 (35.27)	
2013 – 2014	528 (13.07)	2186 (54.11)	1326 (32.82)	
2014 – 2015	530 (12.10)	2540 (58.00)	1309 (29.89)	
Gender, n (%)				<0.001
Male	1350 (12.62)	5303 (49.56)	4047 (37.82)	
Female	1370 (13.39)	5315 (51.94)	3548 (34.67)	
Race, n (%)				<0.001
African American/Black	1425 (11.67)	5707 (46.72)	5083 (41.61)	
White	650 (22.53)	1702 (58.99)	533 (18.47)	
Hispanic	441 (9.25)	2586 (54.23)	1742 (36.53)	
Other	204 (19.17)	623 (58.55)	237 (22.27)	
Area deprivation index				<0.001
Mean (SD)	124.52 (21.45)	127.62 (21.28)	136.55 (19.40)	
Median (Q1, Q3)	126.82 (107.48, 140.62)	131.06 (111.17, 142.40)	139.39 (126.60, 151.46)	
Minimum, maximum	62.53, 169.26	40.19, 169.26	65.56, 169.26	
Missing	149	845	663	
Food service indicator, n (%)				<0.001
No	654 (20.38)	1989 (61.98)	566 (17.64)	
Yes	2066 (11.66)	8629 (48.69)	7029 (39.66)	
Special education, n (%)				<0.001
No	2327 (13.53)	9023 (52.47)	5847 (34.00)	
Yes	393 (10.52)	1595 (42.69)	1748 (46.79)	
English language learner n (%)				<0.001
No	2557 (13.54)	9576 (50.70)	6753 (35.76)	
Yes	163 (7.96)	1042 (50.90)	842 (41.13)	
Attendance days				<0.001
Mean (SD)	145.99 (28.06)	148.79 (23.23)	146.48 (26.02)	
Median (Q1, Q3)	155.00 (144.00, 159.00)	155.00 (146.50, 159.00)	154.00 (143.00, 159.00)	
Minimum, maximum	1.00, 187.00	2.00, 204.00	3.00, 195.00	
Missing	1332	5015	4339	
Gestational age (weeks), n (%)				0.002
23 – 25	5 (8.06)	32 (51.61)	25 (40.32)	
26 – 32	56 (11.79)	218 (45.89)	201 (42.32)	
33 – 34	42 (9.50)	205 (46.38)	195 (44.12)	
35 – 37	388 (12.73)	1536 (50.41)	1123 (36.86)	
38 – 43	2229 (13.18)	8627 (51.03)	6050 (35.79)	
Missing	0	0	1	
Small for gestational age, n (%)				0.017
No	2657 (13.03)	10 364 (50.84)	7365 (36.13)	
Yes	63 (11.58)	252 (46.32)	229 (42.10)	
Missing	0	2	1	
1-minute Apgar, n (%)				0.062
0 – 3	50 (12.25)	189 (46.32)	169 (41.42)	
4 – 6	135 (11.96)	555 (49.16)	439 (38.88)	
7 – 10	2519 (13.05)	9834 (50.95)	6947 (35.99)	
Missing	16	40	40	
5-minute Apgar, n (%)				0.598
0 – 3	3 (12.50)	13 (54.17)	8 (33.33)	
4 – 6	10 (9.43)	50 (47.17)	46 (43.40)	
7 – 10	2591 (12.92)	10 158 (50.64)	7312 (36.45)	
Missing	116	397	229	

Abbreviations: BLL, blood lead level; max, maximum; Q, quarter.

continued on next page

5 µg/dL, decreasing to 6.3% from 2018 through 2021.[15] During 2010 to 2015, the lead poisoning threshold for children under 6 was set at 10 µg/dL by the Wisconsin Department of Health Services (DHS), aligning with CDC guidelines at that time.[16] In 2012, after the CDC lowered this level to 5 µg/dL to improve detection of elevated BLLs, DHS adopted the same threshold.[17]

Average childhood BLLs are disproportionately higher among children in predominantly minority populations who are living in socioeconomically disadvantaged communities[18] in racially segregated neighborhoods.[18] The State of Wisconsin addresses childhood lead poisoning prevention efforts through CDC funding to ensure blood lead testing and reporting, to enhance BLL surveillance, to improve linkage to support services, and to support case management and environmental investigations by local health departments.[20]

Primary prevention of childhood lead exposure is essential to mitigating the negative effects of BLL on children. This includes increasing awareness among parents and caregivers of all children – especially those exposed to lead. Secondary prevention approaches include appropriate provider lead testing, case management, surveillance reporting and referral to and through appropriate service providers,[21] (ie, community outreach[22]) and environmental investigations provided by local health departments. In Wisconsin, children's lead testing typically occurs at pediatricians' offices, Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) clinics, and public health departments – particularly during well-child visits or in high-risk areas.[23] However, data on the percentage of children with a primary care provider or consistent well-child visits for lead testing between ages 1 and 5 years are limited. One-third (35.2%) of Medicaid enrolled children were not tested for lead, suggesting that all children were not receiving appropriate testing for BLL.[24]

This highlights the challenge of childhood BLLs, which may be undetected as this recent evidence suggests.

Studies consistently have demonstrated the association between higher BLLs and poorer academic achievement in standardized reading and math tests among school-aged children.[25,26] However, a need exists to inform childhood lead prevention efforts implemented by the City of Milwaukee Health Department (MHD) and health care centers on the magnitude and significance of lead effects on academic performance. Since academic performance is mostly determined by other (non-lead) factors, the objective of this study was to examine the association between lead exposure and the academic performance of third-grade children in Milwaukee while controlling for the effects of confounding variables.

METHODS

Study Setting and Data Sources

In 2016, Milwaukee County had the highest prevalence of elevated BLLs (≥5 µg/dL) at 10.8% among children under 6 years of age who were tested for lead versus levels statewide of 5.0% and those of 9 other counties with local health department jurisdictions ranging from 5.1% to 8.4%.[27] Similarly, during 2018 to 2021, 6.3% of children under 6 years in Milwaukee County were poisoned with a BLL ≥5 µg/dL when compared to 3.6% in Wisconsin overall.[28] Therefore, we analyzed existing data on 20 933 third-grade students who attended Milwaukee Public Schools (MPS) during 2010 to 2015 and who had individual health-related data collected through the MHD in Milwaukee, Wisconsin.

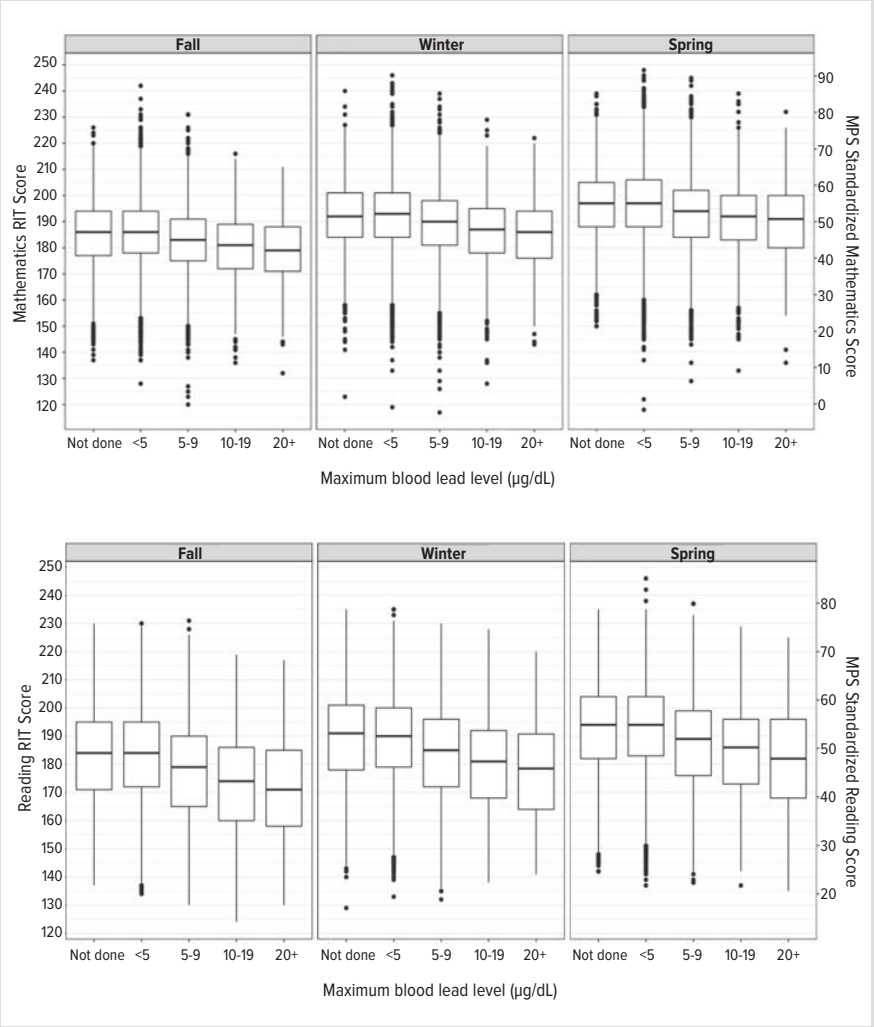
The MHD dataset contains blood lead testing data reported to the Wisconsin Childhood Lead Poisoning Prevention Program of a child's most recent confirmatory (venous) test, which follows an elevated screening (capillary) test. If no confirmatory test for the child is available, the most recent screening test result is reported. We included data that did not have blood lead

Table 1 continued. Summary of Child/Maternal Variables by Maximum Blood Lead Test Result

	BLL Not Tested N = 2720	Max BLL <5 µg/dL N = 10 618	Max BLL ≥5 µg/dL N = 7595	*P* value
Mother's age at birth, n (%)				< 0.001
12 – 18	277 (9.13)	1333 (43.92)	1425 (46.95)	
19 – 34	2176 (13.36)	8416 (51.69)	5690 (34.95)	
35+	267 (16.52)	869 (53.77)	480 (29.70)	
First trimester	2036 (13.06)	8240 (52.86)	5313 (34.08)	
No prenatal care	41 (12.93)	133 (41.96)	143 (45.11)	
Second trimester	523 (12.54)	1897 (45.48)	1751 (41.98)	
Third trimester	109 (14.16)	296 (38.44)	365 (47.4)	
Missing	11	52	23	
Number of prenatal visits				< 0.001
Mean (SD)	10.80 (4.04)	10.88 (3.85)	9.95 (4.07)	
Median [Q1, Q3]	12.00 (9.00, 13.00)	11.00 (9.00, 13.00)	10.00 (7.00, 12.00)	
Min, Max	0.00, 40.00	0.00, 50.00	0.00, 50.00	
Missing		65	29	

Abbreviations: BLL, blood lead level; max, maximum.

Figure. Box Plots of Math and Reading Test Scores by Lead Exposure for Each Season



Abbreviations: RIT, Rasch UnIT scale; MPS, Milwaukee Public Schools.

Table 2. Regression for Math and Reading Standardized Scores

	Standardized Scores			
	Math – Model I		Reading – Model II	
	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value
Maximum blood lead level (µg/dL)		< 0.001		< 0.001
< 5	Reference		Reference	
Not done	-0.70 (-1.01 to -0.38)		-0.62 (-0.94 to -0.31)	
5 – 9	-0.65 (-0.91 to -0.40)		-0.94 (-1.19 to -0.68)	
10 – 19	-0.84 (-1.21 to -0.48)		-1.64 (-2.01 to -1.27)	
20+	-1.29 (-1.93 to -0.64)		-2.26 (-2.91 to -1.62)	
School year	< 0.001			< 0.001
2010 – 2011	Reference		Reference	
2011 – 2012	-0.49 (-0.81 to -0.17)		-0.4 (-0.72 to -0.08)	
2012 – 2013	-0.36 (-0.68 to -0.04)		-0.11 (-0.43 to 0.21)	
2013 – 2014	-0.63 (-0.96 to -0.31)		-0.72 (-1.05 to -0.39)	
2014 – 2015	-0.78 (-1.13 to -0.44)		-0.92 (-1.26 to -0.57)	
Test administration period		< 0.001		< 0.001
Fall	Reference		Reference	
Winter	4.64 (4.57 to 4.72)		3.59 (3.51 to 3.67)	
Spring	7.88 (7.77 to 7.98)		5.81 (5.70 to 5.91)	
Gender		< 0.001		< 0.001
Male	Reference		Reference	
Female	-0.72 (-0.93 to -0.52)		1.04 (0.83 to 1.24)	
Race				
Black or African American	Reference	< 0.001	Reference	< 0.001
White	4.46 (4.06 to 4.85)		3.29 (2.89 to 3.69)	
Hispanic	2.71 (2.31 to 3.10)		1.83 (1.44 to 2.22)	
Other	3.66 (3.10 to 4.22)		2.75 (2.19 to 3.32)	
Gestational age in weeks		< 0.001		< 0.001
38+	Reference		Reference	
23 to 25	-2.65 (-4.61 to -0.68)		-0.63 (-2.58 to 1.33)	
26 – 32	-2.16 (-2.84 to -1.47)		-1.43 (-2.12 to -0.74)	
33 – 34	-0.66 (-1.35 to 0.04)		-0.31 (-1.01 to 0.39)	
35 – 37	-0.33 (-0.61 to -0.05)		-0.32 (-0.6 to -0.03)	
1-minute Apgar		0.941		0.468
7 – 10	Reference		Reference	
0 – 3	-0.12 (-0.85 to 0.61)		0.37 (-0.36 to 1.09)	
4 – 6	-0.03 (-0.48 to 0.42)		0.19 (-0.27 to 0.64)	
Mother's age at birth		< 0.001		< 0.001
19 – 34	Reference		Reference	
12 – 18	-0.66 (-0.95 to -0.37)		-0.66 (-0.96 to -0.37)	
35+	0.27 (-0.12 to 0.66)		0.69 (0.30 to 1.07)	
Mother's number of prenatal visits (continuous)	0.06 (0.03 to 0.08)	< 0.001	0.06 (0.03 to 0.08)	< 0.001
Mother cigarette use during pregnancy		< 0.001		< 0.001
No	Reference		Reference	
Yes	-0.52 (-0.81 to -0.22)		-0.91 (-1.21 to -0.62)	
Food service indicator		< 0.001		< 0.001
No	Reference		Reference	
Yes	-2.64 (-2.98 to -2.31)		-2.62 (-2.96 to -2.29)	
Special education indicator		< 0.001		< 0.001
No	Reference		Reference	
Yes	-6.34 (-6.61 to -6.07)		-8.91 (-9.19 to -8.64)	
English language learner		0.998		< 0.001
No	Reference		Reference	
Yes	0.001 (-0.44 to 0.44)		-2.92 (-3.36 to -2.48)	
Attendance days (continuous) among available	0.03 (0.03 to 0.04)	< 0.001	0.03 (0.02 to 0.03)	< 0.001

continued on next page

results in our analyses.[29] We first merged data from the MHD birth certificate files and lead exposure files, then merged these data with MPS standardized math and reading scores. Math and reading scores for each third-grade student were linked to their corresponding BLL and birth certificate data. Measures of Academic Progress (MAP) tests are purposely designed to be comparable from year to year in order to track children's academic performance over time.[29]

This research obtained ethical approval from the Medical College of Wisconsin Human Research Review Board. Both MPS and MHD data were obtained from DataShare, a secure, integrated data system that links and deidentifies data across multiple sectors to support research and analysis in public health, public safety, education, and related areas.[30] DataShare was established as a collaboration across multiple partner agencies to enhance the use of data to inform decisions to improve the health and safety of individuals and the community.

Study Measures

Student characteristics included in our analyses were as follows: gender (female or male), race (African American, White, Hispanic, Other), gestational age categorized into week groups (23 – 25, 26 – 32, 33 – 34, 35 – 37, 38 – 43), birth weight, small for gestational age designation (no, yes), 1-minute and 5-minute Apgar scores (score categories 0 – 3, 4 – 6, and 7 – 10), food service indicator measured as yes/no to receipt of free/reduced lunch, special education status (no, yes), and English language learner status (no, yes). Our continuous variables were the number of third-grade attendance days and the number of prenatal visits attended by the mother during pregnancy. Other parental characteristics included mother's age at birth (12 – 18, 19 – 34, or 35+ years). To account for the neighborhood effect, area deprivation indices were calculated for the census tracts at each student address whose computation is described in prior literature.[31]

Lead testing data were obtained from the MHD, including dates and results for all tests on record from birth to third grade. Students were grouped into lead exposure categories based on the highest observed BLL: <5, 5–9, 10–19, and ≥20 µg/dL; students without any blood lead testing information on record were grouped into a separate category.

Table 2 continued. Regression for Math and Reading Standardized Scores

	Standardized Scores			
	Math – Model I		Reading – Model II	
	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value
Attendance data availability		<0.001	<0.001	
Available	Reference		Reference	
Unavailable	3.74 (2.76 to 4.73)		2.79 (1.81 to 3.78)	
ADI (continuous) among available	-0.02 (-0.02 to -0.01)	<0.001	-0.02 (-0.03 to -0.02)	<0.001
ADI availability	<0.001	<0.001		
Available	Ref		Ref	
Unavailable	-2.75 (-3.64 to -1.85)		-3.03 (-3.93 to -2.13)	

Abbreviations: ADI, area deprivation index.
Models I and II are adjusted linear regression models that controlled for potential confounders in Table 2.

Statistical Analysis

Student academic performance outcomes included reading and math Rasch UnIT scale (RIT) test scores taken during the fall, winter, and spring trimesters of third grade. All test scores were standardized to a mean of 50 and standard deviation (SD) of 10 prior to analysis. All study variables were described using the mean, SD, median, and range for continuous variables and frequency and percentage for categorical variables. The frequency of missing values was reported for each variable. Variables were summarized both overall and stratified by lead exposure groups. Child and parental characteristics were compared between lead exposure categories using ANOVA for continuous variables and chi-square tests for categorical variables. Standardized reading and math test scores were modeled using mixed effects linear regression including a school-specific random intercept and a repeated effect for school trimester (fall, winter, spring) within student using an autoregressive correlation structure of first order. Model covariates were selected a priori based on clinical expertise and data availability. The global models were presented without subsequent model selection procedures. The regression models were fitted for each reading outcome separately and included multiple predictors: lead exposure group, school year, trimester, and all child and maternal characteristics. All statistical analyses were performed using R software version 3.6.0 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria). All *P* values were two-sided, and those <0.05 were considered statistically significant. No adjustments were made for multiple testing.

RESULTS

Table 1 describes the characteristics of children and their mothers stratified by BLL. A slightly higher proportion of males (37.8%) show elevated BLL (≥5 µg/dL) compared to females (34.7%). Conversely, more females (51.5%) had BLLs below 5 µg/dL compared to males (49.6%). In terms of availability of BLL test results, a higher percentage of females (13.4%) had no BLL test results, compared to 12.6% of males. Mothers' mean number of prenatal care visits were higher when children's BLL was <5 µg/dL (mean 10.8, SD ± 3.9) and BLL was not tested (mean 10.7, SD ± 4.1) versus children with BLL ≥5 µg/dL (mean 9.9, SD ± 4.1) at *P*<0.001

From 2010 to 2015, the proportion of children with BLLs below 5 µg/dL increased from 41.5% to 58.0%, while the proportion of children with BLLs of 5 µg/dL or higher decreased from 44.7% to 29.9% over the same period. In addition, from 2010 to 2015, the percentage of children with no BLL test results declined slightly from 13.9% in 2010-2011 to 12.1% in 2014-2015.

As shown in the Figure, the children's math test scores changed by different lead exposure levels and over the 3 school-year seasons. On average, third-grade math scores increased over the course of the school year from the fall to winter and winter to spring trimesters. In all 3 seasons, the highest median math RIT scores were observed consistently in children with the lowest lead levels (<5 µg/dL) and children whose BLLs were not tested. This was followed by lower median math RIT scores at 5-9 µg/dL and 10-19 µg/dL BLLs, respectively. The lowest median math RIT scores were seen in children with the highest (≥20 µg/dL) lead levels in the fall, winter, and spring seasons. Similar trends were observed for reading scores in the Figure.

Results of the adjusted linear regression model for the independent association between math standardized score and maximum BLL while controlling for potential confounding factors are shown in Table 2. Among children with a maximum BLL ≥20 µg/dL, each unit increase in BLL is associated with a 1.29 decrease in standardized math scores. This association was statistically significant (*P*<0.001) when compared to the decrease in standardized math scores among children with a maximum BLL <5 µg/dL. Similarly, among children with a maximum BLL of 10-19 µg/dL, each unit increase in BLL is associated with a 0.84 decrease in standardized math scores, and among those with a BLL of 5-9 µg/dL, each unit increase is associated with a 0.65 decrease in standardized math scores – all with statistical significance (*P*<0.001) when compared to the decrease in standardized math scores among children with a maximum BLL <5 µg/dL after adjusting for potential confounders.

Table 2 also shows the adjusted linear regression model for the independent association between standardized reading scores and maximum BLL while controlling potential confounders. Among children with a maximum BLL ≥20 µg/dL, each unit increase

in BLL is associated with a 2.26 decrease in standardized reading scores. This association was statistically significant ($P < 0.001$) when compared to the decrease in standardized reading scores among children with a maximum BLL < 5 µg/dL. Similarly, among children with a maximum BLL level of 10-19 µg/dL, each unit increase in BLL is associated with a 1.64 decrease in standardized reading scores, and among those with BLLs of 5-9 µg/dL, each unit increase is associated with a 0.94 decrease in standardized reading scores—all with statistical significance ($P < 0.001$) when compared to the decrease in standardized reading scores among children with a maximum BLL < 5 µg/dL after adjusting for potential confounders.

DISCUSSION

This study revealed 2 main findings. First, most children (58.3%) in third grade had a maximum BLL < 5 µg/dL, while 3.0% had a maximum BLL of 20 µg/dL or higher. Second, our results suggest that having a BLL ≥ 20 µg/dL was a significant independent risk factor for lower math and reading scores compared to children with a BLL < 5 µg/dL after controlling for potential confounding factors.

Although most children in Milwaukee had a recorded BLL < 5 µg/dL, there are still children who are exposed to very high BLLs (> 20 µg/dL). These finding align with a prior Wisconsin CDC report showing that 5% of children tested had lead poisoning at the CDC cutoff of ≥ 5 µg/dL.[27] DHS surveillance reports showed an increase in children tested for lead, with lead poisoning rates rising slightly from 4.4% to 5.0% between 2014 and 2016.[27] The ongoing childhood lead poisoning crisis disproportionately affects communities in Milwaukee due to socioeconomic and racial inequities.[32,33] For example, a previous study found that Milwaukee students had equal proportions of lead-exposed and nonexposed individuals, whereas in Racine, three quarters of students had no lead exposure.[26]

Lead poisoning remains an environmental justice issue that perpetuates disparities in health outcomes, even at low BLLs.[34] Communities most affected by lead exposure usually consist of minority populations, with children in low-income households and often residing in rental properties within economically disadvantaged ZIP codes.[35,36] For example, in our study, the majority of children (66.9%) with BLLs above 5 µg/dL were African American, food insecure, and their mothers were in their late third trimester (38-40 weeks) at birth. Multiple factors are implicated in lead poisoning in Milwaukee; however, age of housing is one of the most important factors linked to the risk of elevated BLL. Before 2006, nearly all incident cases of lead poisoning in Milwaukee were among children who lived in houses constructed prior to 1950. Older houses are associated with the use of lead-based paints, dust, and old water lateral supplies, which increases predisposition of children to lead and their harmful effects. Children living in socioeconomically disadvantaged neighborhoods are more likely to have greater exposure to lead, hence lead poisoning.[37] This finding highlights the importance and need to strengthen community-based lead prevention strategies targeting older homes with children at-risk for childhood lead exposure in Milwaukee.

The second key finding showed a significant association between BLL and both math and reading scores in third-grade students in Milwaukee. These findings are in line with prior literature that demonstrated an inverse relationship in between BLL and end-of-grade examination and standardized intelligence scores of school-going children.[26,38] A recent study showed that although BLL had a detrimental effect on both fourth-grade reading and math scores, racial residential segregation specifically augmented the negative effect of elevated BLLs on reading test scores among non-Hispanic Black children compared to non-Hispanic White children.[39] This implies that environmental lead exposure may result in high BLLs, which has detrimental cognitive effects on children. It is worth noting that the timing (early childhood) and dosage of lead exposure may be related to long-term mental health effects, such as cognition and intellectual impairment in adulthood.[40] This suggests a potential longer susceptibility period to environmental lead exposure.

Study Implications

No lead levels are safe; therefore, building a lead-safe environment for all children requires deliberate and decisive policy action that addresses the sources of lead exposure. In Milwaukee, paint and dust remain the primary sources of lead exposure, followed by lead in drinking water. Recently, the Wisconsin Department of Natural Resources estimated that replacing the current 229 000 private laterals containing or galvanized with lead would cost from $620 million to $966 million.[41] A new proposed rule by EPA, the Lead and Copper Rule Improvements (LCRI), would accelerate the rate at which existing lead pipes will be replaced to 2037.[42] Policy efforts to address this challenge included $30 million in funding through the federal bipartisan infrastructure law to replace lead service lines and eliminate lead pipe replacement costs to residential property owners.[43]

From a clinical perspective, DHS recommendations in 2000 of universal childhood lead testing[44] for all children in Milwaukee and Racine and universal testing for all children in Wisconsin in 2024 could address the missingness of BLL in our data, which may allow for better estimation of lead exposure and its impact on school-going children in the MPS system. More complete data containing BLLs for MPS, Medicaid, and non-Medicaid students may better inform state strategies to educate affected populations, which is key to lowering lead poisoning's burden. These findings guide community-based interventions like educating individuals and highlight the importance of ongoing lead surveillance and reducing primary sources of lead exposure.

Lead prevention interventions that need strengthening, such

as the lead outreach program in primary care health centers, can be a potential source of referrals and education while the state-funded Lead Safe Homes program[45] may increase environmental investigations and abatement to partner organizations. It is worth noting that ongoing lead prevention programs in Wisconsin are implementing door-to-door home visits to conduct educational sessions on lead exposure reduction, such as distributing water filters, faucet replacement, home-based lead testing, and follow-up of lead poisoned children.

The CDC currently recommends routine BLL testing for all young children—particularly those at higher risk—to prevent and mitigate the effects of lead exposure.[46] Public health agencies, such as the WDHS, advocate for universal lead testing in high-risk areas like Milwaukee to identify elevated BLLs early.[44] Research increasingly shows that even low BLLs negatively affect cognitive development and academic performance, especially in reading and math.[26,39] To further address lead exposure risks, the EPA's recent LCRI proposal[47] mandates replacement of all lead service lines within 10 years, lowering the lead action level from 15 µg/dL to 10 µg/dL, enhancing tap water sampling protocols, and requiring public transparency on lead service line locations. These initiatives align with our research findings and underscore the urgent need for lead-safe environments to support children's academic success and overall well-being.[34]

For research, leveraging multi-institutional datasets to inform childhood lead prevention activities has been underscored. Our findings have highlighted the potential to prospectively examine long-term effects of childhood lead exposure to inform prevention efforts in Milwaukee and other communities. Our key study strength was the robustness of our analysis, using longitudinal data merged from MPS and MHD datasets and analyzing data on over 20 000 third-grade students. Additionally, our findings are generalizable to urban communities; however, it is likely for lead poisoning to be a public and environmental issue in rural settings too.

Standardized testing as a measure of academic performance has faced criticism for its inherent limitations and potential biases, especially in diverse and underresourced districts like MPS. Studies indicate that standardized tests may disadvantage English language learners, students with individualized education plans or Section 504 protections for persons with learning disabilities, and students from various socioeconomic backgrounds due to cultural bias and language barriers.[48] Additionally, standardized tests may not fully capture a student's academic progress or abilities, overlooking essential factors such as progression through grades, high school matriculation rates, or support needs, which are often more indicative of long-term success. These limitations are particularly pronounced in Milwaukee, where schools face funding shortages and high needs across certain ZIP codes, amplifying disparities in test preparation and performance.[49]

Our study findings should be interpreted in light of some limitations. First, it is possible that unavailable variables in our dataset could be correlated with both lead exposure levels and academic performance, such as prenatal cocaine or other drug exposures, neighborhood violence exposure, parental IQ, and secondhand smoke exposure during childhood. This study also identifies covariates as intervention targets that pediatricians or primary care providers should be more alert about as potential risk factors for high BLL. Such factors to target include late prenatal care, young maternal age, children in special education, and food insecurity. Parental health education is needed to improve prevention and early abatement efforts prior to lead testing.

Second, selection bias may have occurred. Our data may not be representative of third graders in the MPS system during 2010-2015 due to the following: (a) the data being a convenience sample, (b) the population being limited to individuals with health-related data with the MHD, (c) pediatric BLL testing among the Medicaid population may be low in Wisconsin[24] despite CDC mandatory universal lead testing requirements, (d) no recommendations during 2010-2015 for pediatric universal lead testing for the non-Medicaid children in Milwaukee, and (e) approximately 20% of our final study population did not have test results. Additionally, measurement error may have occurred, although standardized tests taken during 2010- 2015 are intended to be comparable. Finally, this study did not examine the impact of high- versus low-performing schools on standardized testing as a potential modifying or interacting factor.

The missing test results for 20% of our study population likely arise from health care access barriers, affecting data completeness and possibly underestimating lead exposure's effects. This gap adds some uncertainty to our findings, so conclusions require cautious interpretation. This untested group may face a uniquely high risk of elevated lead levels due to socioeconomic and environmental factors and are more likely to lack health care access, as shown by their higher deprivation and food insecurity levels (Table 1). Wisconsin's universal testing policies in Milwaukee and now statewide aim to close this gap, enhancing data accuracy and the assessment of the impact of lead exposure on Milwaukee children.

CONCLUSIONS

Although most children had BLLs below 5µg/dL, some had very high BLLs. Higher BLLs were associated with lower math and reading scores among children in Milwaukee. The implications of surveillance to detect blood lead in children are significant and timely for policy action to strengthen childhood lead prevention strategies in Milwaukee amd other urban and rural settings

Funding/Support: The Medical College of Wisconsin's Advancing a Healthier Wisconsin endowment Research and Education Program Fund funded this study. The funder had no role in the design and conduct of the study.

Financial Disclosures: None declared.

Acknowledgments: The authors would like to thank the City of Milwaukee Health Department and Milwaukee Public Schools for their support through sharing data files for this study analysis.

REFERENCES

1. Centers for Disease Control and Prevention. Implementation of the Lead Contamination Control Act of 1988. *MMWR Morb Mortal Wkly Rep*. 1992;41(17):288-290. Accessed January 14, 2025. https://www.cdc.gov/mmwr/preview/mmwrhtml/00016599.htm

2. NTP Monograph on Health Effects of Low-Level Lead. US Dept of Health and Human Services, National Institutes of Health, National Institute of Environmental Health Sciences, National Toxicology Program, Office of Health Assessment and Translation; June 2012. Accessed January 14, 2025. https://ntp.niehs.nih.gov/whatwestudy/assessments/noncancer/completed/lead

3. Canfield RL, Kreher DA, Cornwell C, Henderson CR Jr. Low-level lead exposure, executive functioning, and learning in early childhood. *Child Neuropsychol*. 2003;9(1):35-53. doi:10.1076/chin.9.1.35.14496

4. Kennedy DA, Woodland C, Koren G. Lead exposure, gestational hypertension and pre-eclampsia: a systematic review of cause and effect. *J Obstet Gynaecol*. 2012;32(6):512-517. doi:10.3109/01443615.2012.693987

5. Jelliffe-Pawlowski LL, Miles SQ, Courtney JG, Materna B, Charlton V. Effect of magnitude and timing of maternal pregnancy blood lead (Pb) levels on birth outcomes. *J Perinatol*. 2006;26(3):154-162. doi:10.1038/sj.jp.7211453

6. Childhood lead poisoning prevention. Centers for Disease Control and Prevention. Updated May 23, 2024. Accessed January 14, 2025. https://www.cdc.gov/lead-prevention

7. Environmental public health tracking: data details. Wisconsin Department of Health Services. Updated April 12, 2024. Accessed November 27, 2023. https://www.dhs.wisconsin.gov/epht/data-details.htm

8. Min MO, Singer LT, Kirchner HL, et al. Cognitive development and low-level lead exposure in poly-drug exposed children. *Neurotoxicol Teratol*. 2009;31(4):225-231. doi:10.1016/j.ntt.2009.03.002

9. Amato MS, Magzamen S, Imm P, et al. Early lead exposure (<3 years old) prospectively predicts fourth grade school suspension in Milwaukee, Wisconsin (USA). *Environ Res*. 2013;126:60-65. doi:10.1016/j.envres.2013.07.008

10. Min MO, Lewis BA, Minnes S, Gonzalez-Pons KM, Kim JY, Singer LT. Preschool blood lead levels, language competency, and substance use in adolescence. *Environ Res*. 2022;206:112273. doi:10.1016/j.envres.2021.112273

11. LaFlash S, Joosse-Coons M, Havlena J, Anderson HA. Wisconsin children at risk for lead poisoning. *WMJ*. 2000;99(8):18-22.

12. Braun JM, Yolton K, Newman N, Jacobs DE, Taylor M, Lanphear BP. Residential dust lead levels and the risk of childhood lead poisoning in United States children. *Pediatr Res*. 2021;90(4):896-902. doi:10.1038/s41390-020-1091-3

13. Balza J. Hidden toxins: bathtubs as a potential source of lead exposure in children. *J Toxicol Environ Health A*. 2022;85(9):376-380. doi:10.1080/15287394.2021.2022053

14. EPA takes final step in phaseout of leaded gasoline. Press release. US Environmental Protection Agency. January 29, 1996. Accessed January 14, 2025. https://www.epa.gov/archive/epa/aboutepa/epa-takes-final-step-phaseout-leaded-gasoline.html

15. City of Milwaukee childhood lead poisoning data and reports. Milwaukee Health Department. Updated 2016. Accessed March 21, 2022. https://dhsgis.wi.gov/dhs/clpde/

16. Binns HJ, Campbell C, Brown MJ; Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning Prevention. Interpreting and managing blood lead levels of less than 10 microg/dL in children and reducing childhood exposure to lead: recommendations of the Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning Prevention. *Pediatrics*. 2007;120(5):e1285-e1298. doi:10.1542/peds.2005-1770

17. Advisory Committee on Childhood Lead Poisoning Prevention. Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention. Centers for Disease Control and Prevention; January 4, 2012. Accessed January 14, 2025. https://stacks.cdc.gov/view/cdc/11859

18. Perron T, Hartt K, McCann D, McGowan R, Segers N. Lead poisoning in populations with low-socio-economic status in the United States. *Br J Sch Nurs*. 2018;13(7):332-336. doi:10.12968/bjsn.2018.13.7.332

19. Morrell E, Blackwell D. Spatialized intersectionality: gendered and racialized residential segregation and the Milwaukee lead crisis. *Environ Justice*. 2022;15(1):31-38. doi:10.1089/env.2021.0015

20. Childhood Lead Poisoning Prevention: Wisconsin. Centers for Disease Control and Prevention. Updated February 15, 2024. Accessed March 20, 2022. https://www.cdc.gov/lead-prevention/success-stories-by-state/wisconsin.html?CDC_AAref_Val=https://www.cdc.gov/nceh/lead/programs/wi.htm

21. Bruce SA, Christensen KY, Coons MJ, Havlena JA, Meiman JG, Walsh RO. Using Medicaid data to improve childhood lead poisoning prevention program outcomes and blood lead surveillance. *J Public Health Manag Pract*. 2019;25(suppl 1):S51-S57. doi:10.1097/PHH.0000000000000931

22. Schlenker TL, Baxmann R, McAvoy P, Bartkowski J, Murphy A. Primary prevention of childhood lead poisoning through community outreach. *WMJ*. 2001;100(8):48-54.

23. Lead-safe Wisconsin. Wisconsin Department of Health Services. Updated October 28, 2024. Accessed November 4, 2024. https://www.dhs.wisconsin.gov/lead/index.htm

24. Christensen K, Coons MJ, Walsh RO, Meiman JG, Neary E. Childhood lead poisoning in Wisconsin. *WMJ*. 2019;118(1):16-20.

25. Evens A, Hryhorczuk D, Lanphear BP, et al. The impact of low-level lead toxicity on school performance among children in the Chicago Public Schools: a population-based retrospective cohort study. *Environ Health*. 2015;14:21. doi:10.1186/s12940-015-0008-9

26. Magzamen S, Imm P, Amato MS, et al. Moderate lead exposure and elementary school end-of-grade examination performance. *Ann Epidemiol*. 2013;23(11):700-707. doi:10.1016/j.annepidem.2013.08.007

27. 2016 Report on Childhood Lead Poisoning in Wisconsin. Wisconsin Dept of Health Services; October 2017. Accessed January 14, 2025. https://www.dhs.wisconsin.gov/publications/p01202-16.pdf

28. Childhood lead poisoning data explorer: percent poisoned, 2018-2021. Wisconsin Department of Health Services. Accessed January 23, 2024. https://dhsgis.wi.gov/dhs/clpde/

29. Historical assessments: history of assessments in Wisconsin. Wisconsin Department of Public Instruction. Accessed November 1, 2024. https://dpi.wi.gov/assessment/historical

30. DataShare, Milwaukee Public Schools, Student, Attendance and Assessment Data. 2020: Provided by DataShare, through the Medical College of Wisconsin.

31. Shour AR, Hamberger LK, Meurer J, Kostelac C, Cassidy L. Context matters: assessing the association between area deprivation and the severity of injury and types of domestic violence victimization among women. *J Interpers Violence*. 2022;37(23-24):NP22352-NP22374. doi:10.1177/08862605211072209

32. Lynch EE, Meier HCS. The intersectional effect of poverty, home ownership, and racial/ethnic composition on mean childhood blood lead levels in Milwaukee County neighborhoods. *PLoS One*. 2020;15(6):e0234995. doi:10.1371/journal.pone.0234995

33. Kodros JK, Carter E, Oke O, Wilson A, Jathar SH, Magzamen S. Cumulative exposures to environmental and socioeconomic risk factors in Milwaukee County, Wisconsin. *Geohealth*. 2024;8(5):e2023GH000927. doi:10.1029/2023GH000927

34. Landrigan PJ, Rauh VA, Galvez MP. Environmental justice and the health of children. *Mt Sinai J Med*. 2010;77(2):178-187. doi:10.1002/msj.20173

35. Benfer EA. Contaminated childhood: how the United States failed to prevent the chronic lead poisoning of low-income children and communities of color. *Harv Environ Law Rev*. 2017; 41(2):493-561. https://ssrn.com/abstract=2977465

36. Miller T, Balza J, Kellis J, Paradis H, Meurer J, Nelson D. Lead poisoning in Milwaukee: a medical and public health update. *WMJ*. 2024;123(4):267-271.

37. Aizer A, Currie J, Simon P, Vivier P. Do low levels of blood lead reduce children's future test scores? *Am Econ J Appl Econ*. 2018;10(1):307-341. doi:10.1257/app.20160404

38. Miranda ML, Kim D, Galeano MA, Paul CJ, Hull AP, Morgan SP. The relationship between early childhood blood lead levels and performance on end-of-grade tests. *Environ Health Perspect*. 2007;115(8):1242-1247. doi:10.1289/ehp.9994

39. Bravo MA, Zephyr D, Kowal D, Ensor K, Miranda ML. Racial residential segregation shapes the relationship between early childhood lead exposure and fourth-grade standardized test scores. *Proc Natl Acad Sci U S A*. 2022;119(34):e2117868119. doi:10.1073/pnas.2117868119

40. Reuben A, Schaefer JD, Moffitt TE, et al. Association of childhood lead exposure with adult personality traits and lifelong mental health. *JAMA Psychiatry*. 2019;76(4):418-425. doi:10.1001/jamapsychiatry.2018.4192

41. Kaeding D. Wisconsin faces up to nearly $1B in costs to replace private lead lines.

Wisconsin Public Radio. December 15, 2023. Accessed January 14, 2025. https://www.wpr.org/economy/wisconsin-faces-nearly-1b-costs-replace-private-lead-lines

42. Schulte L, Dirr A. New rule would require Wisconsin to replace all lead pipes by 2037. *Milwaukee Journal Sentinel*. December 2, 2023:A1. Accessed December 17, 2023. https://www.jsonline.com/story/news/local/milwaukee/2023/12/01/new-federal-plan-would-require-replacement-of-all-lead-pipes-by-2037/71753820007/

43. Dirr A. Milwaukee is making it easier, cheaper to replace your lead water pipes. *Milwaukee Journal Sentinel*. December 18, 2023:A3. Accessed January 14, 2025. https://www.jsonline.com/story/news/politics/2023/12/18/milwaukee-makes-replacing-lead-water-pipes-easier-cheaper/71742611007/

44. Volpenhein S. Lead testing is now recommended for all Wisconsin children, as lead testing levels lag behind pre-pandemic levels. *Milwaukee Journal Sentinel*. January 20, 2024:A1. Accessed January 22, 2024. https://www.jsonline.com/story/news/health/2024/01/19/lead-testing-now-recommended-for-all-wisconsin-children-dhs-says/72269869007/

45. Lead-Safe Wisconsin: The Lead-Safe Homes Program. Wisconsin Department of Health Services. Accessed December 11, 2024. https://www.dhs.wisconsin.gov/lead/lshp.htm

46. Preventing childhood lead poisoning. Centers for Disease Prevention and Control. Updated June 12, 2024. Accessed January 14, 2025. https://www.cdc.gov/lead-prevention/prevention/index.html

47. Lead and copper rule improvements. US Environmental Protection Agency. Updated December 2, 2024. Accessed January 14, 2025. https://www.epa.gov/ground-water-and-drinking-water/lead-and-copper-rule-improvements

48. Au W. *Unequal by Design: High-Stakes Testing and the Standardization of Inequality*. 2nd ed. Routledge; 2022.

49. Milner HR IV. Policy reforms and de-professionalization of teaching. National Education Policy Center. February 2013. Accessed January 14, 2025. https://nepc.colorado.edu/publication/policy-reforms-deprofessionalization

Systematic Review of Studies Measuring Social Media Use and Depression, Anxiety, and Psychological Distress in Adolescents: 2018-2020

Quinlan D. Alfredson, BS; Amrutha Garimella, BS; Bradley Kerr, MS; Megan A. Moreno, MD, MSEd, MPH

ABSTRACT

Introduction: Previous systematic reviews have examined social media use and adolescent mental health. The current literature has yet to examine study characteristics that may influence these associations.

Objective: This systematic review examined research on the association between adolescent social media use and mental health, focusing on depression, anxiety, and psychological distress, with particular attention to demographic differences and reporting quality.

Methods: PubMed, Embase, PsycINFO, Cumulative Index to Nursing and Allied Health, and Social Sciences Citation Index were searched for studies that included measures of social media use and mental health concerns with adolescent participants from 2018 through June 2020. We identified and described: (1) social media use measures used, (2) associations between use and depression, anxiety, and psychological distress, (3) differences in associations by demographic characteristics, and (4) quality of reporting.

Results: Of the 3131 studies identified, 19 were included. Seven studies (36.8%) used frequency-based measures of social media use (eg, time spent, frequency checking), 10 (52.6%) used risk-based measures (eg, social media addiction or disorder, Facebook intrusion, etc), and 2 (10.5%) used both frequency and risk-based measures. Most studies (n = 12, 63%) reported positive association(s) between social media use and mental health concerns. Many studies reported that the results differed by gender (n = 11, 58%) with positive associations more common among females. Quality of report scores ranged from 32 to 43 total points (44 maximum).

Conclusions: Future studies should consider both frequency and risk-based social media measures to develop a balanced understanding of adolescent social media use.

INTRODUCTION

Mood disorders, specifically depression and anxiety, are the most prevalent mental illnesses among adolescents. By 14 years of age, half of all mental health conditions have already manifested in symptoms.[1] Among adolescents who are 10 to 14 years of age, 1.4% experience symptoms of depression and 4.4% experience symptoms of anxiety.[2] Among adolescents who are 15 to 19 years of age, these illnesses are more prevalent, with 2.8% of adolescents experiencing depression and 4.6% experiencing anxiety.[2] These mental health conditions can lead to severe consequences, such as suicide—the second leading cause of death for adolescents in the United States.[3] It is crucial to understand the influences of adolescent mental health conditions in order to guide prevention.

Social media use is one of several hypotheses that may explain the observed uptick in prevalence of depression and anxiety in adolescents.[4] About 45% of teens report going online nearly constantly.[5] Prior systematic reviews have reported that for adolescents, social media use correlates with harmful psychiatric outcomes, specifically with increasing symptoms of depression and anxiety.[6,7] In addition to the research on social media use posing a negative influence on mental health, research also supports associations between social media use and mental health benefits.[8-10] For example, 1 study found that people with mental illnesses benefited from using social media through greater social connectedness, providing personal empowerment and hope.[10]

• • •

Author Affiliations: Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Alfredson, Garimella, Kerr, Moreno).

Corresponding Author: Quinlan D. Alfredson, Research Intern, Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, 2870 University Ave, Suite 200, Mailcode 9010, Madison, WI 53705; email qalfredson@wisc.edu; ORCID ID 0000-0002-1020-5507

To better understand the relationship between social media use and adolescent mental health, systematic reviews have been completed to summarize findings.[11-13] One review of studies examining social media use and depression in adolescents reported that 2 randomized control studies provided evidence to support a causal relationship between young adults reducing their social media use and declines in depression scores.[6] In contrast, a review on digital technology (eg, online communication and social media use) and adolescent mental health observed that the associations between digital technology use and adolescents' mental health were inconsistent and that additional studies are needed to support cause and effect conclusions.[14] The inconsistency between reviews shows that the impact of social media use on adolescent mental health remains unclear.

To gain a more comprehensive understanding of the relationship between social media and mental health, researchers have included a focus on broader conditions, like psychological distress. Although several studies and analyses have focused on specific Diagnostic and Statistical Manual of Mental Disorders (DSM-5) conditions like anxiety and depression, others have taken a more comprehensive approach by incorporating psychological distress.[15-19] This term refers to temporary and treatable mood disturbances, including anxiety and depression.[20] Therefore, exploring both clinically defined mental disorders such as anxiety and depression, as well at the broader concept of psychological distress, is crucial.

A review by Keles et al[11] explored diagnostic criteria for depression and anxiety as well as the broader construct of psychological distress. This study aimed to review studies observing the relationship between social media use and depression, anxiety, or psychological distress among adolescents. The Keles review assessed studies through 2018. However, since the review, social media users worldwide increased 9% to 3.484 billion in 2019.[21] This increase may impact the relationship between social media use and mental health. Therefore, this study aimed to reexamine this relationship.

In addition to the gap in systematic reviews since 2019, previous reviews have yet to evaluate how demographic variables, such as gender, race, and socioeconomic status, may affect this association. Social media use may have unique effects on the mental health of different subgroups of adolescents. A past systematic review on demographic characteristics and mental health found inconsistent results regarding the important roles of demographics in mental health.[22] Thus, investigating the demographics across studies focused on mental health and social media can shed light on the multiplicative effects of gender, race, and socioeconomic status. The moderation of demographic variables may explain the inconclusive associations between social media use and adolescent mental health and can help to guide future interventions. The purpose of this study was to examine the characteristics of recent studies of social media use and depression, anxiety, and psychological distress in adolescents, including the way in which social media use, association, and demographic characteristics (such as gender, race, and socioeconomic status) are reported.

METHODS

This systematic review followed the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[23] The protocol for this review was registered with the International Prospective Register of Systematic Reviews (Prospero; CRD42021237729). This study was exempt from institutional review board approval because no human subjects were involved.

Eligibility Criteria

Eligibility criteria were based on the previous systematic review by Keles et al to further investigate and build upon their findings.[11] Eligible studies included participants with mean age of 13 to 18 years old; an exposure variable that measured social media use (studies solely measuring exposure to the internet more generally, cyberbullying or cyber-victimization, or non-social media internet activities were excluded); and an outcome variable of depression, anxiety, or psychological distress assessed by validated instruments. (Outcomes of substance misuse, eating disorders, well-being, life satisfaction, self-esteem, body image problems, externalizing, loneliness or stress were excluded.) Eligible studies were also empirical, observational, and published from 2018 through June 2020 in peer-reviewed journals with full text available in English. If longitudinal papers reported on 2 or more groups of participants, only the results of the group that met eligibility criteria were examined.

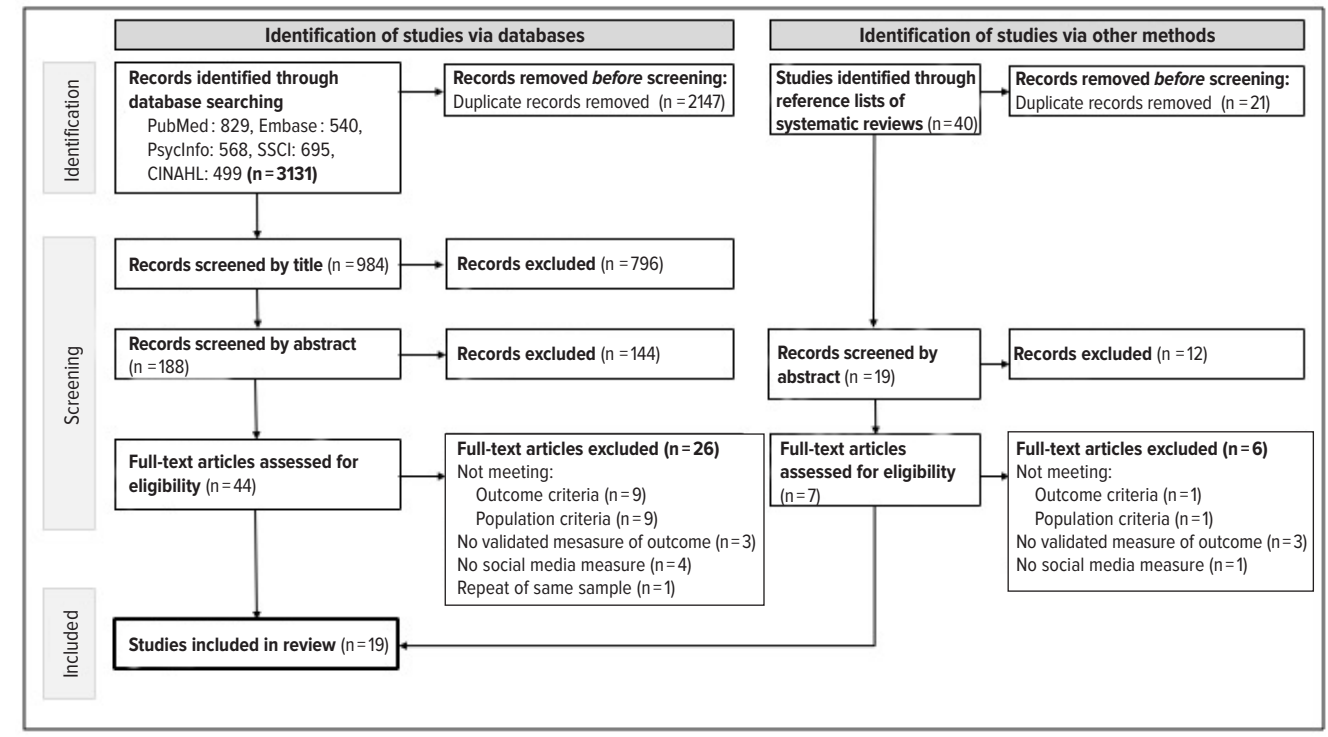
Search Strategy

The databases PubMed (via NCBI), Embase (via Elsevier), PsycINFO (via OVID), Cumulative Index to Nursing and Allied Health (CINAHL via EBSCO) and Social Sciences Citation Index (SSCI via Web of Science) were systematically searched on June 30, 2020. Filters applied to the search results included publication 2018 through June 2020 with full text available in English. The following search terms were used to describe adolescents: adolescent, teen, youth, young, juvenile, high school student, secondary school student, middle school student. The following terms were used to describe the exposure social media variable: social media, social network, Facebook, Instagram, Twitter, Snapchat, TikTok, YouTube. The following terms were used to describe the mental health outcome variable: mental health, mental disorder, mood disorder, affective disorder, depression, depressive, anxiety, anxious, psychological stress, psychological wellbeing, psychological well-being, psychological distress, bipolar, neurotic, agoraphobia, cyclothymic, dysthymia. Additionally, reference lists of systematic reviews were hand-searched to identify additional papers. (See Appendix for search strategies by database.)

Screening

All papers from the automated database searches were collated

Figure. PRISMA Flow Diagram



using the EndNote Online reference management software (Clarivate, Philadelphia, Pennsylvania). After duplicates were deleted, 3 reviewers (QA, AJ, MS) independently completed a screening conducted by reviewing title and abstract using the aforementioned eligibility criteria, documenting reasons for exclusion. To ensure accurate inclusion or exclusion of articles, QA and AJ, or MS and AJ, compared excluded articles to confirm agreement. Finally, 2 reviewers (QA, AJ) independently screened the remaining papers by reviewing full text and again documented exclusion reason and compared to confirm agreement. Article eligibility discrepancies were resolved by an additional reviewer (MM). The background and training of the reviewers are as follows: AJ, a research specialist, trained QA and MS (undergraduate students) on how to screen data. MM is the lab principal investigator.

Data Extraction

Key information relevant to the research question was systematically extracted by 2 reviewers (QA, AJ), and discrepancies were resolved by an additional reviewer (MM). Descriptive data variables extracted included citation, study design, country where study took place, total participants, age of participants. Key study variables extracted included measurement of social media use, measurement of outcome variable, associations between variables, and demographic information. Measure of social media use included measures of both quantity and quality. Measurement of outcome variable indicated the validated measurement tool used to measure depression, anxiety, or psychological distress. Association indicated whether social media usage had a positive, negative, mixed, or null association with symptoms of mental health outcome variable. Demographic information included socioeconomic status, race, gender, and gender report format (binary vs full gender spectrum). Acceptable proxies to measure socioeconomic status included family income, ZIP code, education, and access to internet.

Quality Review

Our quality review tool was derived from the Strengthening the Report of Observation Studies in Epidemiology (STROBE) tool.[24] The quality review tool consists of 22 items assessing the quality of study design, data collection, and analysis of each study. A study could score a maximum of 2 points for each item if the criteria were completely met, 1 point if the criteria were partially met, and 0 points if criteria were not met. There were 44 total possible points. Two investigators scored each article, and discrepancies were resolved by consensus.

RESULTS

The literature search yielded 3131 articles from 5 databases. After 2147 duplicates were removed, screening on title excluded 796 of the 984 unique papers. The remaining 188 articles were screened on abstract, with 144 removed, leaving 44 papers. Additionally, hand-searching the references of 14 systematic reviews on social

media and mental health identified another 40 papers, of which 21 were duplicates. Next, 12 of these articles were eliminated based on abstract, and 7 were retained for full-text screening. Thus, a total of 51 articles were retained for full-text screening. Full text-screening excluded 32 more articles, for a total sample of 19. The PRISMA flowchart (Figure) provides further detail on search results and reasons for exclusion.

Study Characteristics

This systematic review resulted in 19 studies that met inclusion criteria. Table 1 provides data extracted from each study in the final sample. Included studies had sample sizes ranging from 249 to 154981 participants. Most studies used a cross-sectional design (n = 13, 68.4%). The most common outcome variable measured was depression (n = 13, 68.4%).

Measurement of Social Media

The most used measures for social media use were time spent on social media (n = 7, 36.8%), the Bergen Social Media Addiction Scale (n = 4, 21.1%), and the Facebook Intrusion Questionnaire (n = 2, 10.1%). Other methods of measuring social media use included intense social media use,[15] Bergen Facebook Addiction scale,[25] frequency of use,[19] screen-based sedentary behavior,[26] social media aggression and victimization,[27] and social media disorder scale.[28] In summary, 7 studies (36.8%) used frequency-based measures of social media use (eg, time spent, frequency checking), 10 (52.6%) studies used risk-based measures (eg, social media addiction or disorder, problematic or maladaptive social media use, Facebook intrusion, etc), and 2 studies (10.5%) used both frequency and risk-based measures.

Time spent on social media was the most prevalent single social media measure and was used by 7 of the 19 studies to measure social media use. This method of measurement involved time-use diaries,[29] self-report,[18,30,31] Likert scales,[32,33] and by indicating time spent on Facebook versus highly visual media (platforms focused on sharing visual content, such as Instagram and Snapchat).[17]

In addition to frequency-based measures of social media, risk-based measures also were used. For example, the Bergen Social Media Addiction Scale (BSMAS) was used by 4 of the 19 studies to measure social media use. The BSMAS is a self-reported 6-item survey used to measure at-risk social media addiction. One example survey question is: "You spend a lot of time thinking about social media or planning how to use it.[34]

In addition, the Facebook Intrusion Questionnaire (FIQ) was used by 2 of the 19 studies to measure social media use. For example, the first item is "I often think about Facebook when I am not using it."[35] The FIQ includes 8 items to be rated on a 7-point scale—where 1 is strongly disagree and 7 is strongly agree. The higher the FIQ score, the higher Facebook intrusion. High Facebook intrusion is "characterized by an excessive attachment to Facebook, which interferes with day-to-day activities and with relationship functioning."[35]

Associations

Of the 19 included studies, 12 reported finding a positive association between social media use and the outcome variable (depression, anxiety, or psychological distress). Of studies measuring depression, 58.3% reported positive association, and of studies measuring psychological distress, 60.0% reported positive association. The 1 study that measured anxiety reported a positive association.[25] Additionally, the only included study to measure both depression and anxiety reported a positive association for both variables.[27] For example, 1 study analyzed both between-person and within-person social media use and found a positive correlation between time spent on social media and depressive symptoms for both.[30] Additionally, initial social media use levels, increased problematic social media use (PSMU), and social networking site addiction were positively associated with depressive symptoms.[36,37] Furthermore, when comparing use reported by adolescents versus their use as reported by their parents, reporting of social media aggression from both sources was correlated with anxiety and depressive symptoms.[27]

Of the 19 included studies, 6 studies reported mixed findings regarding associations between social media use and the outcome variable. For example, when measuring multiple types of social media use, 1 study found that time spent on social media and maladaptive social media use were positively associated with depressive symptoms; however, the intensity of social media use had no significant association with depressive symptoms.[33] Moreover, highly visual social media users, such as users of Snapchat and Instagram, reported greater internalizing symptoms of depression and anxiety compared to nonusers; however, there were no significant associations between Facebook users and nonusers.[17] Participants in a longitudinal study with a higher initial PSMU had significantly higher depressive symptoms, and the path from initial depressive symptoms to the change in PSMU was significant.[36] However, the intercept of PSMU predicted the trajectory of depressive symptoms—indicating participants with greater initial PSMU had no greater increase in depressive symptoms across time compared to those with a lower baseline PSMU.[36]

Notably, 1 study reported results in a different manner that was neither positive nor negative while using an exposure variable of social media and an outcome variable of psychological distress—meeting inclusion criteria. The study used latent profile analysis to identify psychopathological risk in various adolescent age groups.[38] None of the studies in this systematic review reported a negative association between social media use and the outcome variable.

Associations also were observed for the 3 most common social media use measurements. First, out of the 7 studies that used time spent to measure social media use, 4 found results with a positive association. For example, it was reported that time spent on social media was significantly associated with depressive symp-

Table 1. Characteristics and Findings of Studies Examining the Relationship Between Social Media Use and Mental Health Conditions

Citation	Study Design	Country	Sample Size	Social Media	Outcome	Association	Conclusions
Anjum et al, 2019[26]	Cross-sectional	Bangladesh	311	Yes/no to use of social media, SBSB	PHQ-9 measured depression	Mixed	Use of social media and >2 hours of screen-based sedentary behaviors daily were significantly associated with depressive symptoms
Barry et al, 2019[27]	Cross-sectional	United States	428	Social media aggression and victimization	DSM-5 checklist measured anxiety and depression	Positive	Adolescent- and parent-reported social media aggression were correlated with anxiety and depressive symptoms
Barthorpe et al, 2020[29]	Cross-sectional	United Kingdom	4032	Time spent on social media	SMFQ measured depression	Mixed	In females, time spent on social media was associated with depressive symptoms, little evidence for an association in males
Boer et al, 2020[15]	Cross-sectional	29 countries	154 981	Intense social media usage and PSMU	4-item subscale from the HBSC symptom checklist measured psychological distress	Mixed	In some countries, intense users reported more frequent psychological complaints than nonintense users. In all countries, problematic social media users reported more psychological complaints
Boers et al, 2019[30]	Longitudinal	Canada	3826	Time spent on social media	BSI measured depression	Positive	Time spent on social media was associated with depressive symptoms
Cerniglia et al, 2019[38]	Cross-sectional	Italy	643	BSMAS	Symptom Checklist-90-R measured depression, anxiety, and psychopathology symptoms	N/A	Profile that differed in psychological risk showed similar scores in technology-based addictions
Coyne et al, 2019[32]	Longitudinal	United States	457	Time spent on social media	CES-D measured depression	Positive	Users with low social media use that increased quickly and then returned to baseline levels and low social media use that increased gradually were associated with higher levels of depressive symptoms than users with steady social media use over time
Fabris et al, 2020[16]	Cross-sectional	Italy	472	BSMAS	Emotional symptoms subscale of SDQ measured emotional symptoms	Positive	Social media addiction was associated with emotional symptoms
Hawes et al, 2020[33]	Cross-sectional	Australia	763	Time spent on social media, intensity of social media use, and maladaptive social media use	SMFQ measured depression	Mixed	Time spent on social media and maladaptive social media use were associated with depressive symptoms. Intensity of social media use was not associated with depressive symptoms
Kelly et al, 2018[31]	Cross-sectional	United Kingdom	10 904	Time spent on social media	SMFQ measured depression	Positive	Time spent on social media was associated with higher depressive symptoms scores
Louragli et al, 2019[25]	Cross-sectional	Morocco	541	BFAS	GAD-7 measured anxiety	Positive	High Facebook addiction was linked with a state of severe anxiety
Marengo et al, 2018[17]	Cross-sectional	Italy	523	Time spent on social media	Italian self-rated version of SDQ measured internalizing symptoms	Mixed	Users who spent more than 2 hours/day on highly visual social media were associated with higher internalizing symptoms scores vs nonusers. There were no significant differences between FB users and nonusers
Przepiorka and Blachnio, 2020[40]	Cross-sectional	Poland	426	FIQ	CES-D measured depression	Positive	Depression was a positive predictor of FB intrusion
Raudsepp, 2019[39]	Longitudinal	Estonia	249	BSMAS	CES-D measured depression	Positive	Initial PSMU predicted change in depressive symptoms. Increase in PSMU was associated with increase in depressive symptoms
Raudsepp and Kais, 2019[36]	Longitudinal	Estonia	397	BSMAS	CES-D measured depression	Mixed	Baseline PMSU was associated with baseline depressive symptoms. Changes in PMSU were related to changes in depressive symptoms. Baseline PMSU did not predict depressive symptom changes longitudinally
Riehm et al, 2019[18]	Longitudinal	United States	6595	Time spent on social media	GAIN-SS measured internalizing symptoms	Positive	Use of social media for >3 hours per day vs no use was associated with internalizing problems

continued on next page

Table 1 continued. Characteristics and Findings of Studies Examining the Relationship Between Social Media Use and Mental Health Conditions

Citation	Study Design	Country	Sample Size	Social Media	Outcome	Association	Conclusions
Viner et al, 2019[19]	Longitudinal	England	12 866	Frequency of checking social media accounts	GHQ measured psychological distress	Positive	Frequent social media use was associated with psychological distress
Wartberg et al, 2018[28]	Cross-sectional	Germany	1001	SMDS	DesTeen measured depression	Positive	More PSMU was associated with depressive symptoms
Wang et al, 2018[37]	Cross-sectional	China	365	Adapted FIQ	CES-D measured depression	Positive	Social networking sites addiction was associated with depressive symptoms

Abbreviations: SBSB, Screen Based Sedentary Behavior; PHQ-9, Patient Health Questionnaire-9; DSM-5, Diagnostic and Statistical Mental Disorders; SMFQ, Short Mood and Feelings Questionnaire; PSMU, problematic social media use; HBSC, Heath Behavior in School-aged Children; BSI, Brief Symptoms Inventory; BSMAS, Bergan Social Media Addiction Scale; CES-D, Center for Epidemiologic Studies Depression Scale; SDQ, Strength and Difficulties Questionnaire; BFAS, Bergen Facebook Addiction Scale; GAD-7, Generalized Anxiety Disorder-7; FB, Facebook; FIQ, Facebook Intrusion Questionnaire; GAIN-SS, Global Appraisal of Individual Needs Short Screener, GHQ, General Health Questionnaire; SMDS, Social Media Disorder Scale; DesTeen, Validated Depression Screener for Teenagers.

toms.[33] The other 3 studies that used time spent on social media as a method of measurement found mixed results with a combination of positive and null results – no studies found a negative association. Second, out of the 4 studies that used the BSMAS to measure social media use, 2 studies found a positive association between the BSMAS score and depression or psychological distress.[16,39] An additional study reported a mixed association between social media use measured with the BSMAS and depression.[36] Lastly, both studies that used the FIQ to measure social media use reported that social media addiction (measured using the FIQ) was positively associated with depression.[19,40]

Demographics

All 19 studies included in this systematic review measured gender; 11 studies presented results stratified by gender. All studies reported gender as a categorical variable, reporting gender as female, male, or chose not to say. Of the 11 studies that reported results stratified by gender, 3 studies found no statistically significant differences between genders,[18,25,32] and 5 studies found evidence for positive associations between adolescent females' social media use and depression, anxiety, or psychological distress. For example, in 1 study, increased time spent on social media was associated with a greater number of depressive symptoms for females, but an association was not found for males.[29] For females, greater daily hours of social media use were associated with an increase in depressive symptom scores and in clinically relevant symptoms. However, for males, higher depressive symptoms scores were found only when 3 or more hours of daily social media use were reported.[31] When the study only included a sample of adolescent females, there was a positive association for social media use and depressive symptoms.[36]

Of the 19 included studies, 6 measured race. Race was most often reported as a descriptive result. For example, a study included a descriptive result stating the percentage of participants that were White and the percentage that were non-White.[29] Other studies included percentages of participants that were White, Black, Asian, Hispanic, Native American, and an option for "other."[27] Of the 6 studies that measured race, none stratified by race. However, 2 of the six 6 measuring race reported that race was controlled for.[18,31] In addition, 1 study conducted in Italy reported that race was the same among all participants.[38]

Of the 19 included studies, 9 reported details regarding socioeconomic status. Of those 9 studies, 2 included analyses involved socioeconomic status as a predictor. In 1 study, those who reported lower socioeconomic status showed more severe symptoms of depression. However, the relationship between socioeconomic status and social media use was not observed.[30] In another study, adolescents living in lower income and 1-parent households were more likely to use social media for 5 or more hours daily,[31] but the study did not assess the association between social media use and depression, anxiety, or psychological distress. No studies stratified results by socioeconomic status.

Quality Review

Study designs included cross-sectional (n = 13, 68.4%) and longitudinal (n = 6, 31.6%). The quality review scores for each study ranged from 32 to 43 total points out of a possible 44 points. The average quality review score was 37.79 (SD = 2.22) total points. See Table 2 for quality review results.

The quality review criterion met most frequently (19 studies fully met these criteria) included explaining the background and rationale, stating study objectives, clearly defining all variables, and discussing the generalizability. The quality review criterion met least frequently was describing efforts to address sources of bias (11 studies fully met this criterion). Additionally, reporting numbers of participants at each stage with reason for nonparticipation (14 studies partially met this criterion, 5 studies fully met this criterion) and giving characteristics of study participants (10 studies partially met this criterion, 7 studies fully met this criterion) were items that occurred less frequently than the other items.

Table 2. Studies by Quality Review Scoring

Item	Studies by Quality Review Scoring (Source)			Total Score[a]
	0	1	2	
Study designed with a commonly used term in the title or abstract and informative summary of study in abstract		Barry 2019, Fabris 2020, Hawes 2020, Marengo 2018, Przepiorka and Blachino 2019	Anjum 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Kelly 2019, Louragli 2019, Raudsepp and Kais 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	33
Explain background and rationale			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
State specific objectives and hypotheses			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Present key elements of study design	Barry 2019, Fabris 2020, Hawes 2020, Przepiorka and Blanchino 2019	Barthorpe 2020, Boer 2020, Coyne 2019, Viner 2019	Anjum 2019, Boers 2019, Cerniglia 2019, Kelly 2019, Louragli 2019, Marengo 2018, Raudsepp and Kais 2019	26
Describe setting, location, and relevant dates		Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Przepiorka and Blachino 2019	Boers 2019, Cerniglia 2019, Louragli 2019, Marengo 2018, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	29
Report participant eligibility criteria and sources of selected participants		Barthorpe 2020, Cerniglia 2019, Fabris, 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp 2019, Viner 2019, Wang 2018, Wartberg 2018	Anjum 2019, Bary 2019, Boer 2020, Boers 2019, Coyne 2019, Raudsepp and Kais 2019, Riehm 2019	26
Define all outcomes, exposures, predictors, confounders, and effect modifiers			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Give source of data and details of assessment for each variable		Anjum 2019, Barthorpe 2020, Boers 2019, Riehm 2019, Viner 2019	Barry 2019, Boer 2020, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Wang 2018, Wartberg 2018	33
Describe efforts to address sources of bias	Boer 2020, Cerniglia 2019, Fabris 2020, Hawes 2020, Louragli 2019, Przepiorka and Blachino 2019, Raudsepp 2019, Wartberg 2018		Anjum 2019, Barry 2019, Barthorpe 2020, Boers 2019, Coyne 2019, Kelly 2019, Marengo 2018, Raudsepp and Kais 2019, Riehm 2019, Viner 2019, Wang 2018	22
Explain how study size was arrived at		Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Kelly 2019, Louragli 2019, Przepiorka and Blachino 2019, Viner 2019, Wang 2018, Wartberg 2018	Anjum 2019, Barry 2019, Hawes 2020, Marengo 2018, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019	26
Explain how quantitative variables were handled			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Describe all statistical methods			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38

continued on next page

Table 2 continued. Studies by Quality Review Scoring

	Studies by Quality Review Scoring (Source)			
Item	**0**	**1**	**2**	**Total score**
Report numbers of participants at each stage, give reason of nonparticipation		Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Przepiorka and Blachino 2019, Viner 2019, Wang 2018, Wartberg 2018	Anjum 2019, Marengo 2018, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019	24
Give characteristics of study participants	Cerniglia 2019, Fabris 2020	Barthorpe 2020, Boers 2019, Coyne 2019, Hawes 2020, Kelly 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Viner 2019	Anjum 2019, Barry 2019, Boer 2020, Louragli 2019, Riehm 2019, Wang 2018, Wartberg 2018	24
Report numbers of outcome events or summary measures			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Give unadjusted estimates and report category boundaries			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Report other analyses done			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Summarize key results with reference to the study objectives			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Discuss limitation, taking into account sources of bias and their magnitude and direction	Louragli 2019	Anjum 2019, Barry 2019, Boer 2020, Boers 2019, Cerniglia 2019, Fabris 2020, Raudsepp 2019	Barthorpe 2020, Coyne 2019, Hawes 2020, Kelly 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	29
Give a cautious overall interpretation of results			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Discuss generalizability of study results			Anjum 2019, Barry 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Louragli 2019, Marengo 2018, Przepiorka and Blachino 2019, Raudsepp and Kais 2019, Raudsepp 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	38
Give the source of funding	Barry 2019, Louragli 2019, Marengo 2018, Raudsepp and Kais 2019, Raudsepp 2019		Anjum 2019, Barthorpe 2020, Boer 2020, Boers 2019, Cerniglia 2019, Coyne 2019, Fabris 2020, Hawes 2020, Kelly 2019, Przepiorka and Blachino 2019, Riehm 2019, Viner 2019, Wang 2018, Wartberg 2018	28

[a]Total score out of 38 maximum points.
Note: Citations for studies are listed in Table 1.

DISCUSSION

This systematic review examined the characteristics of recent studies that reported associations between social media use and outcome variables of depression, anxiety, and psychological distress. Of the studies included, most reported a positive association between social media use and depression, anxiety, or psychological distress. This review shows that few studies have examined a relationship between social media use and mental health across demographic groups.

Our first finding was that many measures of social media use were used and associations between use and mental health outcomes tended to differ based on type of measure. Although only 2 studies used the FIQ, which measures excessive attachment to social media (Facebook), they both found positive associations.[37,40] In contrast, the 7 studies using participants' time spent on social media—a more general measurement of use—found both mixed[17,29,33] and positive[18,30,31] associations. These findings suggest

that characteristics of risk-based social media use measures may be more associated with mental health symptoms compared to frequency-based measures.

Our second finding was that measurements of social media use reflected a trend toward understanding risky use, with over half of the studies measuring solely risk-based use. For example, the BSMAS is designed to measure social media addiction.[34] Other examples of social media measures in this review that measured risk-based use include social media aggression,[27] maladaptive social media use,[33] and a social media use disorder scale.[28] It is important to consider that none of the social media use measurements utilized by studies in this systematic review were measuring positive social media use or healthy social media use. For example, studies utilizing methods that measure a benefit to mental health, such as peer interaction on social media, may show associations with better mental health outcomes.[10] This is a possible explanation for why none of the included studies reported a negative association between social media use and depression, anxiety, or psychological distress. In summary, previous research has shown that risky ways of using social media tend to be associated with poorer mental health outcomes, but more work is needed to examine positive social media use and associations with adolescent mental health.

Our third finding revealed that none of the studies included in our review examined race or socioeconomic status as stratifying variables, and there were limited results concerning gender. These demographic variables are important to examine because current research suggests that specific groups may be at a higher risk of developing mental illness due to various factors that could impede access to health care or jeopardize overall health.[41] First, the included studies only presented gender stratified results for "female" and "male" participants. Prior research and evidence for best practice points towards the necessity for future research to include a full gender spectrum, inclusive of transgender and nonbinary participants.[42] Sexual orientation is another important topic to consider. Sexual orientation in relation to mental health may be an important stratification to explore, as current research shows that lesbian, gay, bisexual, transgender, and questioning (LGBTQ) individuals experience higher rates of mental illness.[43,44] In addition, because increased racial and ethnic discrimination has been positively associated with symptoms of depression,[45] race and experiences with racism are also important factors to examine when observing the impact of social media use and mental health of adolescents. This finding is supported by our quality review, which found that a common issue across studies was a lack of describing participant demographics. Finally, because prior research shows that the many life stressors of adolescents with a lower socioeconomic status put them more at risk for mental illness,[46] it is also important to investigate how socioeconomic status may play a role in the effect of social media use on mental health in adolescents. Overall, future studies should measure the aforementioned variables to better understand how they may moderate the relationship between social media use and mental health in adolescents.

Furthermore, the review highlighted that certain demographic characteristics were not represented consistently across the final articles. This omission limits the generalizability of the findings and underscores the necessity for more inclusive research practices. Addressing these gaps in future research is crucial to understanding the nuanced ways in which social media use may affect different demographic groups.

This study has limitations to consider. It is important to note the possibility of publication bias in this review, given that unpublished work was not included. The lack of null findings observed may reflect this bias. Furthermore, other mental health outcomes, such as self-esteem, general well-being, and happiness, were not included in the study. Examining these other mental health outcomes might provide more thorough understanding about the nuances of the association between social media use and well-being.

Moreover, a self-reported measure of social media use was not used as an exclusion criterion. New research raises concerns about the validity of findings that use self-reported measures of social media use. A meta-analysis described that self-reported social media use was infrequently a precise representation of logged social media use.[47] However, self-reported screen time is useful to understand the interpretations of social media impacts overall. Moreover, the associations observed could be affected by use of risk-based versus screen time or other measurement types.

Additionally, this systematic review did not explore the relationship between substance use measures and social media use. Past research has found that problematic social media and internet use has been associated with higher odds of consuming substances.[48] Importantly, this association can confound the association between social media use and mental illness.

Lastly, it is important to consider the rapidly changing nature of social media platforms. Many of the studies included in this review focused on platforms such as Facebook. According to a survey by Pew Research Center in 2023, US adolescents age 13 to 17 years old using Facebook has decreased from 71% in 2014-2015 to 33% in 2023, while Snapchat use, which is a more visually oriented platform, has increased from 41% in 2014-2015 to 60% in 2023.[49] This shift in social media usage patterns may influence the nature of associations between social media use and mental health outcomes. Future research should account for the impact of more visually oriented platforms to provide a current and comprehensive understanding of the association between social media and adolescent mental health.

CONCLUSIONS

This systematic review examined the characteristics of studies that assessed the relationship between social media use and

mental health outcomes of depression, anxiety, and psychological distress. Because many social media and mental health studies included in this review were framed around a risk-centered model, future reviews and media reports should consider and report whether the social media measurement they are observing focuses on problematic use or other specific features of use. Moreover, future studies should consider using both a risk-based social media use measure and a benefit-based social media use measure to examine social media use holistically and seek to optimize study quality. Overall, research in this field must focus on a wider spectrum of social media interactions, including those that may have potential benefits. Additionally, clinicians should ask their adolescent patients more specific questions about their social media use to gauge characteristics such as maladaptive or addictive use instead of solely how much time they use social media. Lastly, because a limited number of studies observed results stratified by demographic variables, it is important for future studies to investigate how demographics may moderate the relationship between social media use and adolescent mental health.

Funding/Support: None declared.

Financial Disclosures: None declared.

Acknowledgements: The authors would like to acknowledge the contributions of the research staff who contributed to this systematic review including Anna Jolliff, Manya Shah, Chelsea Olson, Megan Wilt, and Angie Calvin. This study was presented as a poster at Promoting Research in Social Media and Health Symposium 2021 and Pediatric Academic Societies Meeting 2020.

Appendix: Supplemental materials available at www.wmjonline.org

REFERENCES

1. Kessler RC, Angermeyer M, Anthony JC, et al; WHO World Mental Health Survey Consortium. Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative. *World Psychiatry.* 2007;6(3):168-176.

2. Mental health of adolescents. World Health Organization. October 10, 2024. Accessed January 21, 2025. https://www.who.int/news-room/fact-sheets/detail/adolescent-mental-health

3. Heron M. Deaths: leading causes for 2019. *Natl Vital Stat Rep*. 2021;70(9):1-114 doi:10.15620/cdc:107021

4. Lin LY, Sidani JE, Shensa A, et al. Association between social media use and depression among US young adults. *Depress Anxiety.* 2016;33(4):323-331. doi:10.1002/da.22466

5. Anderson M, Jiang J. Teens, social media and technology 2018. Pew Research Center. May 31, 2018. Accessed March 3, 2022. https://www.pewresearch.org/internet/2018/05/31/teens-social-media-technology-2018/

6. Ghaemi SN. Digital depression: a new disease of the millennium? *Acta Psychiatr* Scand. 2020;141(4):356-361. doi:10.1111/acps.13151

7. Hussain Z, Wegmann E, Yang H, Montag C. Social networks use disorder and associations with depression and anxiety symptoms: a systematic review of recent research in China. *Front Psychol.* 2020;11:211. doi:10.3389/fpsyg.2020.00211

8. Erfani SS, Abedin B. Impacts of the use of social network sites on users' psychological well-being: A systematic review. *J Assoc Inf Sci Technol.* 2018;69(7):900-912. doi:10.1002/asi.24015

9. Allen KA, Ryan T, Gray DL, McInerney DM, Waters L. Social media use and social connectedness in adolescents: The positives and the potential pitfalls. *Aust J Educ Deve Psychol*. 2014;31(1):18-31. doi: 10.1017/edp.2014.2

10. Naslund JA, Aschbrenner KA, Marsch LA, Bartels SJ. The future of mental health care: peer-to-peer support and social media. *Epidemiol Psychiatr Sci.* 2016;25(2):113-122. doi: 10.1017/S2045796015001067

11. Keles B, McCrae N, Grealish A. A systematic review: the influence of social media on depression, anxiety and psychological distress in adolescents. *Int J Adolesc Youth.* 2020;25(1):79-93. doi:10.1080/02673843.2019.1590851

12. Piteo EM, Ward K. Social networking sites and associations with depressive and anxiety symptoms in children and adolescents–a systematic review. *Child Adolesc Ment Health.* 2020;25(4):201-216. doi:0.1111/camh.12373

13. Valkenburg PM, Meier A, Beyens I. Social media use and its impact on adolescent mental health: An umbrella review of the evidence. *Curr Opin Psychol.* 2022;44:58-68. doi:10.1016/j.copsyc.2021.08.017

14. Odgers CL, Jensen MR. Annual Research Review: Adolescent mental health in the digital age: facts, fears, and future directions. *J Child Psychol Psychiatry*. 2020;61(3):336-348. doi:10.1111/jcpp.13190

15. Boer M, van den Eijnden RJJM, Boniel-Nissim M, et al. Adolescents' intense and problematic social media use and their well-being in 29 countries. *J Adolesc Health.* 2020;66(6S):S89-S99. doi:10.1016/j.jadohealth.2020.02.014

16. Fabris MA, Marengo D, Longobardi C, Settanni M. Investigating the links between fear of missing out, social media addiction, and emotional symptoms in adolescence: The role of stress associated with neglect and negative reactions on social media. *Addict Behav.* 2020;106:106364. doi:10.1016/j.addbeh.2020.106364

17. Marengo D, Longobardi C, Fabris M, Settanni M. Highly-visual social media and internalizing symptoms in adolescence: The mediating role of body image concerns. *Comput Human Behav.* 2018;82:63-69. doi:10.1016/j.chb.2018.01.003

18. Riehm KE, Feder KA, Tormohlen KN, et al. Associations between time spent using social media and internalizing and externalizing problems among US touth. *JAMA Psychiatry*. 2019;76(12):1266-1273. doi:10.1001/jamapsychiatry.2019.2325

19. Viner RM, Gireesh A, Stiglic N, et al. Roles of cyberbullying, sleep, and physical activity in mediating the effects of social media use on mental health and wellbeing among young people in England: a secondary analysis of longitudinal data. *Lancet Child Adolesc Health.* 2019;3(10):685-696. doi:10.1016/S2352-4642(19)30186-5

20. Drossman DA. Biopsychosocial issues in gastroenterology. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*. 10th ed. Elsevier; 2016:37-350.

21. Karim F, Oyewande AA, Abdalla LF, Ehsanullah RC, Khan S. Social media use and its connection to mental health: a systematic review. *Cureus*. 2020;12(6): e8627. doi:10.7759/cureus.8627.

22. Alegría M, NeMoyer A, Falgàs Bagué I, Wang Y, Alvarez K. Social determinants of mental health: where we are and where we need to go. *Cur Psychiatry Rep.* 2018;20(11):95. doi:10.1007/s11920-018-0969-9

23. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097

24. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Bull World Health Organ.* 2007;85(11):867-872. doi:10.2471/blt.07.045120

25. Louragli I, Ahami AO, Khadmaoui A, Aboussaleh Y, Lamrani AC. Behavioral analysis of adolescent's students addicted to Facebook and its impact on performance and mental health. *Acta Neuropsychol*. 2019;17(4):427-439. doi:10.5604/01.3001.0013.6550

26. Anjum A, Hossain S, Sikder T, Uddin ME, Rahim DA. Investigating the prevalence of and factors associated with depressive symptoms among urban and semi-urban school adolescents in Bangladesh: a pilot study. *Int Health.* 2022;14(4):354-362 doi:10.1093/inthealth/ihz092

27. Barry CT, Briggs SM, Sidoti CL. Adolescent and parent reports of aggression and victimization on social media: associations with psychosocial adjustment. *J Child Fam Stud.* 2019;28:2286-2296. doi:10.1007/s10826-019-01445-1

28. Wartberg L, Kriston L, Thomasius R. Depressive symptoms in adolescents: prevalence and associated psychosocial features in a representative sample. *Dtsch Arztebl Int.* 2018;115(33-34):549-555. doi:10.3238/arztebl.2018.0549

29. Barthorpe A, Winstone L, Mars B, Moran P. Is social media screen time really associated with poor adolescent mental health? A time use diary study. *J Affect Disord.* 2020;274:864-870. doi:10.1016/j.jad.2020.05.106

30. Boers E, Afzali MH, Newton N, Conrod P. Association of screen time and depression in adolescence. *JAMA Pediatr.* 2019;173(9):853-859. doi:10.1001/jamapediatrics.2019.1759

31. Kelly Y, Zilanawala A, Booker C, Sacker A. Social media use and adolescent mental health: findings from the UK millennium cohort study. *EClinicalMedicine.* 2019;6:59-68. doi:10.1016/j.eclinm.2018.12.005

32. Coyne SM, Padilla-Walker LM, Holmgren HG, Stockdale LA. Instagrowth: a longitudinal growth mixture model of social media time use across adolescence. *J Res Adolesc*. 2019;29(4):897-907. doi:10.1111/jora.12424

33. Hawes T, Zimmer-Gembeck MJ, Campbell SM. Unique associations of social media use and online appearance preoccupation with depression, anxiety, and appearance rejection sensitivity. *Body Image.* 2020;33:66-76. doi:10.1016/j.bodyim.2020.02.010

34. Lin C-Y, Broström A, Nilsen P, Griffiths MD, Pakpour AH. Psychometric validation of the Persian Bergen Social Media Addiction Scale using classic test theory and Rasch models. *J Behav Addict.* 2017;6(4):620-629. doi:10.1556/2006.6.2017.071

35. Elphinston RA, Noller P. Time to face it! Facebook intrusion and the implications for romantic jealousy and relationship satisfaction. *Cyberpsychol Behav Soc Netw.* 2011;14(11):631-635. doi:10.1089/cyber.2010.0318

36. Raudsepp L, Kais K. Longitudinal associations between problematic social media use and depressive symptoms in adolescent girls. *Prev Med Rep*. 2019;15:100925. doi:10.1016/j.pmedr.2019.100925

37. Wang P, Wang X, Wu Y, et al. Social networking sites addiction and adolescent depression: A moderated mediation model of rumination and self-esteem. *Pers Individ Diff*. 2018;127:162-167. doi:10.1016/j.paid.2018.02.008

38. Cerniglia L, Griffiths MD, Cimino S, et al. A latent profile approach for the study of internet gaming disorder, social media addiction, and psychopathology in a normative sample of adolescents. *Psychol Res Behav Manag.* 2019;12:651-659. doi:10.2147/prbm.s211873

39. Raudsepp L. Brief report: Problematic social media use and sleep disturbances are longitudinally associated with depressive symptoms in adolescents. *J Adolesc.* 2019;76:197-201. doi:10.1016/j.adolescence.2019.09.005

40. Przepiorka A, Blachnio A. The role of Facebook intrusion, depression, and future time perspective in sleep problems among adolescents. *J Res Adolesc.* 2020;30(2):559-569. doi:10.1111/jora.12543

41. Farley HR. Assessing mental health in vulnerable adolescents. *Nursing*. 2020;50(10):48-53. doi:10.1097/01.NURSE.0000697168.39814.93

42. Malatino H, Stoltzfus-Brown L. Best Practices for Gender Inclusion in Research. October 14, 2020. Accessed July 11, 2022. https://covidupdates.la.psu.edu/wp-content/uploads/sites/9/Gender-Inclusion-in-Research.pdf

43. McDonald K. Social support and mental health in LGBTQ adolescents: a review of the literature. *Issues Ment Health Nurs.* 2018;39(1):16-29. doi:10.1080/01612840.2017.1398283

44. Agardh C, Asamoah BO, Herder T, Larsson M. Risk of poor mental health and experience of violence among a young adult population with same-sex sexuality: a cross-sectional study in southern Sweden. *BMJ Open*. 2022;12(2):e052617. doi:10.1136/bmjopen-2021-052617

45. Quinn DM, Camacho G, Pan-Weisz B, Williams MK. Visible and concealable stigmatized identities and mental health: experiences of racial discrimination and anticipated stigma. *Stigma Health.* 2020;5(4):488-491. doi:10.1037/sah0000210

46. Reiss F, Meyrose A-K, Otto C, Lampert T, Klasen F, Ravens-Sieberer U. Socioeconomic status, stressful life situations and mental health problems in children and adolescents: Results of the German BELLA cohort-study. *PloS One.* 2019;14(3):e0213700. doi:10.1371/journal.pone.0213700

47. Parry DA, Davidson BI, Sewall CJR, Fisher JT, Mieczkowski H, Quintana DS. A systematic review and meta-analysis of discrepancies between logged and self-reported digital media use. *Nat Hum Behav.* 2021;5(11):1535–1547. doi:10.1038/s41562-021-01117-5

48. Liu J, Charmaraman L, Bickham D. Association between social media use and substance use among middle and high school-aged youth. *Subst Use Misuse.* 2024:59(7):1039-1046. doi:10.1080/10826084.2024.2320372

49. Anderson M, Faverio M, Gottfried J. Teens, Social Media, and Technology 2023. Pew Research Center; 2023. Accessed June 25, 2024. https://www.pewresearch.org/internet/2023/12/11/teens-social-media-and-technology-2023/

Valacyclovir Versus Acyclovir for Herpes Simplex Virus Suppression Following Neonatal Infection

Haley A. Olkiewicz, PharmD; Michelle L. Mitchell, MD; Katie M. Ray, PharmD; Evelyn M. Kuhn, PhD; Tracy N. Zembles, PharmD

ABSTRACT

Background: Anecdotal experience suggests efficacious valacyclovir use for neonatal herpes simplex virus (HSV) suppression, with limited published literature. The objective of this study was to evaluate HSV recurrence rates between valacyclovir and acyclovir for suppression of HSV following neonatal infection.

Methods: We conducted a single center, retrospective cohort analysis of patients less than 6 weeks old with a positive HSV polymerase chain reaction who received oral acyclovir or valacyclovir. Demographics, dosing, and recurrence rates were analyzed.

Results: Six patients received acyclovir and 13 received valacyclovir. The recurrence rate was similar in both groups.

Discussion: Valacyclovir may be an alternative to acyclovir for suppression of neonatal HSV, offering less frequent dosing and increased compliance. Larger studies are needed to confirm valacyclovir efficacy for neonatal HSV suppression.

BACKGROUND

Neonatal herpes simplex virus (HSV) is a viral infection affecting 1 per 3200 live births.[1] HSV can present as disseminated, central nervous system (CNS), and/or skin, eye, and/or mucous membrane (SEM) disease. The American Academy of Pediatrics (AAP) recommends intravenous (IV) acyclovir 20 mg/kg/dose every 8 hours for 14 days for SEM treatment and a minimum of 21 days for CNS or disseminated disease in neonates. HSV establishes latency in sensory ganglia following primary infection. It is not known if the virus may also subclinically reactivate in the brain after neonatal CNS infection. However, infants with CNS involvement who received oral suppressive therapy with acyclovir for 6 months were demonstrated to have improved neurodevelopmental outcomes compared to those infants who did not receive suppressive therapy.[2] While neurodevelopmental benefits were not observed for those babies solely with SEM disease, they benefitted from a significant decrease in cutaneous recurrence and presumably the socioeconomic benefits from that.[2] For these reasons, oral suppressive therapy has become relatively standard after neonatal HSV infection. Dosing is 300 mg/m^2/dose 3 times daily for a minimum of 6 months following completion of IV acyclovir.[3] Valacyclovir has not been studied for longer than 5 days in infants.[4] However, valacyclovir is sometimes prescribed for neonatal HSV suppression off-label.[4] Valacyclovir is a nucleoside analogue DNA polymerase inhibitor that rapidly converts to acyclovir and has a similar mechanism of action.[5] Valacyclovir offers the potential benefits of increased bioavailability and less frequent dosing, which could result in improved compliance compared to acyclovir.[5]

There is little published literature comparing the efficacy of valacyclovir and acyclovir for neonatal HSV suppression. However, local anecdotal experience suggests off-label valacyclovir for HSV suppression in infants has been efficacious. The primary objective of this study was to evaluate for a difference in clinical recurrence between valacyclovir and acyclovir for suppression of recurrent HSV following neonatal infection.

METHODS

We retrospectively reviewed records of children less than 6 weeks of age with a positive HSV polymerase chain reaction (PCR)

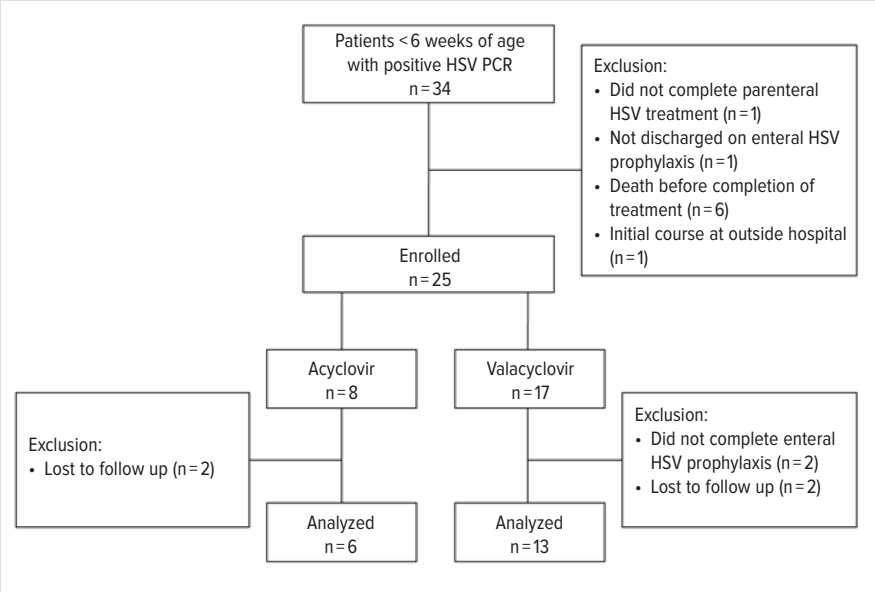
Author Affiliations: Children's Wisconsin, Milwaukee, Wisconsin (Olkiewicz, Ray, Kuhn, Zembles); Medical College of Wisconsin, Milwaukee, Wisconsin (Mitchell).

Corresponding Author: Haley Olkiewicz, PharmD, 8915 W Connell Ct, Milwaukee, WI 53226; email holkiewicz@childrenswi.org; ORCID ID 0000-0003-1932-4673

test who completed parenteral and suppressive therapy from November 2012 to July 2021. Information was collected from patients at a 298 bed children's hospital with a level IV neonatal intensive care unit with 72 licensed beds. Those who were lost to follow-up, died prior to beginning suppressive therapy, or started the course of medication therapy at an outside hospital were excluded. We collected age at diagnosis, sex, type of HSV, antiviral agent and dose, and duration of therapy. We also evaluated medication changes as a surrogate for medication intolerance or failure of therapy. Patients received acyclovir or valacyclovir suppressive therapy at the discretion of the medical provider. Duration of suppressive therapy was also determined by the medical provider. Valacyclovir was dosed at 40-50 mg/kg/day divided twice daily. Acyclovir was dosed at 300 mg/m^2/dose 3 times daily. Patients prescribed the same antiviral agent were analyzed as a cohort. We compared the incidence of recurrence during suppression, as well as time to recurrence. Recurrence was defined as a positive HSV PCR or documentation of a lesion consistent with HSV in the electronic medical record. This project was reviewed by our Institutional Review Board and determined to be a quality improvement project.

Proportions of patients with various characteristics were compared between those who received acyclovir versus those who received valacyclovir using Fisher exact tests. Continuous/numeric variables were compared in the 2 groups using Mann-Whitney tests. Quartiles were calculated using "Tukey's Hinge" method in SPSS. IBM SPSS Statistics 20 (Armonk, New York) was used for statistical analysis.

Figure. Consort Diagram



Abbreviations: HSV, herpes simplex virus; PCR, polymerase chain reaction.

Out of 34 patients who had a positive HSV PCR at less than 6 weeks of age, 9 patients were excluded. Following intravenous therapy, included patients were given oral suppression. In the acyclovir arm, 2 patients were excluded resulting in 6 included patients. In the valacyclovir arm, 4 patients were excluded resulting in 13 patients with complete data for analysis.

Table 1. Demographics

Characteristic	Overall	Acyclovir	Valacyclovir	*P* value
Total, N (%)	19	6 (32)	13 (68)	n/a
Female, N (%)	7 (37)	4 (67)	3 (23)	0.13
Birth weight (kg), median (IQR)	3.26 (2.85–3.52)	3.40 (3.22–3.52)	3.20 (2.78–3.52)	0.38
Gestational age (weeks), median (IQR)	38.0 (36.5–38.5)	38 (38–39)	37 (36–38)	0.12
Herpes simplex virus (HSV) type N (%)				
Type 1	9 (47)	5 (83)	4 (31)	
Type 2	10 (53)	1 (17)	9 (69)	0.06
Diagnosis				
SEM, N (%)	10 (53)	4 (67)	6 (46)	0.63
CNS, N (%)	11 (58)	3 (50)	8 (62)	1.00
Disseminated, N (%)	15 (79)	5 (83)	10 (77)	1.00
Dose, median (IQR)	n/a	900 (900–900) mg/m^2/day	50.0 (40–50) mg/kg/day	n/a
Duration (months), median (IQR)	6 (6–12)	6 (6–6)	11.5 (6–12)	0.03

Abbreviations: SEM, skin, eye, and/or mucous membrane; CNS, central nervous system; IQR, interquartile range.

RESULTS

A total of 34 patients had a positive HSV PCR at less than 6 weeks of age, of which 25 met inclusion criteria (Figure 1). Following IV therapy, included patients received oral suppression with acyclovir (n = 8) or valacyclovir (n = 17). In the acyclovir arm, 2 patients were lost to follow-up, resulting in 6 included patients. In the valacyclovir arm, 2 patients did not complete oral HSV suppression (presumably for adherence) and 2 were lost to follow-up, resulting in 13 patients with complete data for analysis. Patients were lost to follow-up if they did not have documented clinic notes in the electronic health record. There were no differences in demographics between the 2 groups, with the exception of duration of therapy, which was longer in patients prescribed valacyclovir (Table 1). Initial dosing of the antiviral agent was appropriate for both groups. Recurrence while on suppressive therapy was similar between groups (Table 2). Among those who did have a recurrence, the median time to recurrence was 102 days

from diagnosis. Only 1 patient required a medication switch during suppressive therapy, and this was due to nothing by mouth status prior to a procedure, requiring a change to IV acyclovir. No patients had a prescribed change in suppressive therapy for a documented adverse effect.

DISCUSSION

Our data reveal similar rates of recurrence during suppressive therapy when either oral acyclovir or valacyclovir were prescribed. Though oral acyclovir is the drug of choice recommended by the AAP for suppression following neonatal HSV infection, oral valacyclovir is sometimes used off-label. A study completed by Kimberlin et al assessed the safety and pharmacokinetics of valacyclovir dosing.[6] Patients 1 month through 5 years old received one 25 mg/kg dose of valacyclovir. Patients 1 year to 11 years old received 10 mg/kg twice daily or 20 mg/kg 3 times daily for 3 to 5 days. After the authors' pharmacokinetic evaluation, no dosing recommendations could be concluded in patients younger than 3 months old. The authors concluded that valacyclovir 20 mg/kg/dose provided similar exposure of blood concentrations for children aged 3 months to 11 years compared to acyclovir. Our study based appropriate dosing on these findings, as it is the only dosing available and, thus, also what is conventionally used by clinicians for this indication. This pharmacokinetic study demonstrated valacyclovir to be safe and well tolerated. Likewise, patients in our cohort were prescribed doses of 20-25 mg/kg/dose given twice daily without reported side effects.

We did not identify any statistical differences in recurrences, though the recurrence rate while on suppressive therapy overall was low (2 of 19; 10%). This could be a result of our small sample size. Comparatively, a single-center study in the United Kingdom identified a recurrence rate of 33% among 21 infants who presented with HSV at or prior to 90 days of age.[7] The difference might be explained by more reliable follow-up documentation of recurrences given the nationalized health care system. However, most patients (all but 2) were given acyclovir prophylaxis in that study. Additionally, the study by Kimberlin et al reported 41% of babies had at least 2 cutaneous recurrences while on oral acyclovir suppression (37.5% of those infants with CNS disease and 47% of those infants with solely SEM disease).[2] Notably, in our evaluation, both recurrences were related to SEM disease and occurred in the valacyclovir group. However, 1 patient with a gestational age of 36 weeks initially presenting with CNS HSV did not have the dose adjusted for weight gain while on suppressive therapy at the time of the recurrence when nearly 4 months old, potentially explaining the recurrence. The other infant initially had CNS, disseminated, and SEM HSV, with a cutaneous recurrence at around 3 months of age. This patient had a gestational age of 27 weeks, which could impact the pharmacokinetics of the drug, as young infants experience significant kidney maturation in the first few months of life that may alter clearance.[4] Waheed et al also found recurrences in 50% of premature neonates versus 23% of term patients while on suppressive therapy, supporting our concern for dosing and metabolism in premature infants.[7]

Table 2. Outcomes

Medication	Acyclovir (n = 6)	Valacyclovir (n = 13)	*P* value
Medication change, N (%)	0 (0)	1 (8)	1.00
Recurrence while on suppression, N (%)	0 (0)	2 (15)	1.00
Time until recurrence (days), median (IQR)	n/a	102.5 (85–120)	n/a

It was interesting to note patients in our study who were prescribed valacyclovir had longer durations of therapy. Clinicians selected the drug and duration of therapy at their discretion. Given the retrospective nature of this study, we were unable to determine the reason for the selection of drug and duration. However, verbal communication with infectious disease providers suggest that differences in medication selection and duration of therapy may reflect a change in practice over time, favoring a longer duration of 1 year versus 6 months by some clinicians, as many of the valacyclovir patients were from more recent encounters.

Strengths of this study include manual review of patient charts for documentation of a recurrent lesion and/or any PCR for diagnosis of recurrence. All patients included in the analysis had documentation of adherence and were evaluated for appropriate dosing throughout the course of therapy by the authors. Although all patients in this study were reportedly adherent, twice daily valacyclovir dosing allows for ease of administration for neonates and young children, potentially improving compliance over months of therapy. Lastly, complex or questionable patients were reviewed by a pharmacist (HO) and an infectious disease physician (MM) to determine if the patient should be included in the study.

Limitations include small sample size, resulting in insufficient power to detect a potential difference in outcomes, greater number of patients in the valacyclovir arm due to clinician selection, lack of literature guiding dosing in premature neonates, lack of lab assessment for neutropenia, as well as the single center experience. Exclusion of patients who did not complete treatment or who started treatment at another hospital may affect the finding's generalizability.

However, this study provides real world experience on the safety and long-term use of valacyclovir for prevention of recurrent HSV following neonatal infection. Additionally, an ongoing phase 1, open label, single-center study is further assessing the pharmacokinetics and pharmacodynamics of valacyclovir compared to IV acyclovir in neonates.[8] Up to 10 participants aged 2 to 12 weeks with a gestational age greater than 34 weeks will be enrolled. This study may aid in determining optimal dosing of valacyclovir, including those who are late preterm.

Valacyclovir may be an acceptable alternative to oral acyclovir for suppression of neonatal HSV, offering less frequent dosing and possible increased compliance with similar outcomes. Larger studies are needed to determine if there are true differences in outcomes or adverse effects, particularly in premature infants where drug metabolism may differ.

Funding/Support: None declared.

Financial Disclosures: None declared.

Acknowledgments: The authors wish to acknowledge Sue Kehl, PhD, and Ross Hellenbrand for their contributions to data report creation.

REFERENCES

1. Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. *JAMA*. 2003;289(2):203-209. doi:10.1001/jama.289.2.203

2. Kimberlin DW, Whitley RJ, Wan W, et al; National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Oral acyclovir suppression and neurodevelopment after neonatal herpes. *N Engl J Med*. 2011;365(14):1284-1292. doi:10.1056/NEJMoa1003509

3. Kimberlin DW, Baley J; Committee on Infectious Diseases; Committee on Fetus and Newborn. Guidance on management of asymptomatic neonates born to women with active genital herpes lesions. *Pediatrics*. 2013;131(2):e635-e646. doi:10.1542/peds.2012-3216.

4. American Academy of Pediatrics. Herpes Simplex. In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MD, eds. *Red Book: 2021 Report of the Committee on Infectious Diseases*. 32nd ed. American Academy of Pediatrics; 2021:407-416.

5. Valacyclovir. Package insert. GlaxoSmithKline; 2019.

6. Kimberlin DW, Jacobs RF, Weller S, et al. Pharmacokinetics and safety of extemporaneously compounded valacyclovir oral suspension in pediatric patients from 1 month through 11 years of age. *Clin Infect Dis.* 2010;50(2):221-228. doi:10.1086/649212

7. Waheed S, Nuttall L, Fidler K, Dudley J, Bamford A, Lyall H. Neonatal herpes simplex virus: cutaneous recurrence is common on stopping prophylactic suppression therapy. *J Pediatric Infect Dis Soc*. 2022;11(11):518-521. doi:10.1093/jpids/piac098

8. Whitley, RJ. Valacyclovir in neonatal herpes simplex virus disease. ClinicalTrials.gov identifier: NCT04448392. Updated September 9, 2023. Accessed January 2022. https://clinicaltrials.gov/study/NCT04448392

What Aspects of Youth Programming Have Lasting Effects? Perspectives from Wisconsin PATCH Alumni

Tess I. Jewell, BA; Alexandra R. Sabgir, BS; Chelsea J. Aeschbach, MPH, CHES

ABSTRACT

Background: As clinicians and scholars continue to emphasize the importance of actively involving youth in the Maternal and Child Health workforce, this evaluation explores the programmatic elements of the Wisconsin-based Providers and Teens Communicating for Health (PATCH) Program that previous participants found impactful.

Methods: Semistructured interviews were conducted with program alumni. Qualitative thematic analysis utilized a combined deductive and inductive approach.

Results: Fourteen interviews were completed. Analysis revealed 6 key themes highlighting impactful elements of PATCH: education, employment and workforce development, sense of community and belonging, youth-driven programming, facilitating community connections, and youth-adult partnership.

Discussion: Multiple elements of PATCH have led to sustained positive health and development outcomes among program alumni, providing valuable insights for effectively engaging youth.

BACKGROUND

Clinicians and scholars continue to emphasize the importance of actively involving youth in the Maternal and Child Health workforce.[1] Initiatives like the Wisconsin-based Providers and Teens Communicating for Health (PATCH) Program exemplify these efforts. PATCH originated in 2010 as an adolescent health care communications initiative rooted in advocacy and youth-led education to support public health.[2,3] Evolving over time, the program has played a crucial role in authentic youth engagement across Wisconsin, addressing the strong demand for meaningful youth input in adolescent health efforts.[4]

• • •

Author Affiliations: University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Jewell, Sabgir); Providers and Teens Communicating for Health (PATCH) Program, Madison, Wisconsin (Aeschbach).

Corresponding Author: Tess I. Jewell, University of Wisconsin School of Medicine and Public Health, 750 Highland Ave, Madison, WI 53705; email tjewell2@wisc.edu; ORCID ID 0000-0003-2845-5587

At present, PATCH utilizes 2 youth-driven programs to engage youth. The PATCH Teen Consultant Program supports YOUTH in consulting on adolescent health initiatives, policies, and practices, whereas the PATCH Teen Educator Program promotes open, honest, and medically accurate conversations between adolescents and their health care providers via teen-facilitated workshops. Program goals differ, but the approach to engaging youth remains consistent. Teams of 8 to 12 youth (aged 14 to 19) are formed through a deliberate selection process, including the release of job descriptions, submission of applications, interviews, and employment contracts. Each youth makes a 9-month job commitment as either a Teen Consultant or Teen Educator. They are supervised by a program coordinator and paid for their time and expertise to participate in multiday onboarding training; 2-hour, bimonthly enrichment sessions; consulting sessions (Teen Consultants); and/or PATCH workshop facilitation (Teen Educators).

While previous evaluations have demonstrated programmatic effects,[2-4] this manuscript explores specific programmatic elements that have proven impactful or meaningful to past participants, hereafter called alumni. It offers valuable insights into effective practices and strategies, highlighting their importance and implications for enhancing program outcomes and informing future initiatives.

METHODS

This evaluation followed a mixed-methods survey of PATCH alumni administered in the fall of 2023, which identified sustained impacts on participants (Jewell TI, Aeschbach CJ; unpub-

lished data, 2023). Semistructured, follow-up interviews were conducted to gather alumni's insights on (1) the program's impact, (2) the specific aspects of PATCH that contributed to these impacts, (3) important programmatic components, and (4) additional experience or thoughts regarding their participation. Based on the University of Wisconsin–Madison Quality Improvement/Program Evaluation Self-Certification tool, this project was identified as program evaluation that did not meet the federal definition of research pursuant to 45 CFR 46 and did not require review by the Institutional Review Board.

Participant Recruitment

Interview participants were recruited from all previous Wisconsin PATCH alumni (N = 299, from 2010 to completion of the 2022-2023 program cycle). Recruitment was conducted alongside the alumni survey using documented email addresses, a private alumni Facebook group, and direct outreach by staff. After completing the survey, respondents could opt in to a brief follow-up interview via a separate link. Alumni also had the option to bypass the survey and contact the team directly. No incentives were provided for participation in the interviews.

Data Collection

An interview guide was developed in partnership with PATCH's evaluation team, which includes representatives from program leadership, staff, youth participants, and external stakeholders. Study team member TIJ conducted interviews, ranging from 18 to 38 minutes, in January and February, 2024. Interviews were recorded with participant consent, then transcribed and reviewed for accuracy. Detailed demographics were not obtained to ensure anonymity and due to the survey findings indicating no meaningful differences in program impacts. Program records confirmed participation years and the specific PATCH youth engagement programs of interviewees.

Data Analysis

Transcripts were analyzed using a thematic approach. A preliminary codebook was developed deductively based on PATCH's youth engagement model and staff insights. Two independent coders, study team members TIJ and ARS, conducted the analysis to mitigate potential biases. They utilized the preliminary codebook to analyze 3 randomly selected transcripts, resolving discrepancies and refining codes for clarity and additional themes. The revised codebook was used to independently analyze the remaining transcripts. Consensus on all codes was achieved through discussions between coders, who identified key themes and subthemes through an iterative, inductive process.

RESULTS

Forty alumni expressed interest in a phone or virtual interview, with 16 scheduling and 14 completing interviews. Interviewees included 12 former Teen Educators, a former Teen Consultant, and another who participated in both programs. Qualitative analysis revealed 6 key themes highlighting impactful elements of PATCH as identified by alumni (Table). While the vast majority positively described PATCH, a few comments highlighted negative experiences that conveyed the importance of a specific programmatic element.

Education

Most interviewees indicated the importance of being exposed to new information, resources, and connections through training and enrichment. They highlighted how these conversations not only enhanced their understanding of stigmatized health topics but also empowered them to openly talk about these issues with others. One interviewee described the positive effects of learning from local content experts in the community:

> *"Having someone who works in mental health come and talk about mental health is really powerful because they have their own experiences they can share… they can also talk about how the system [is] operating and what needs to be done, what is being done … Not only because then we can give really good workshops, but also because we can have those educational experiences."*

Employment and Workforce Development

Interviewed alumni discussed the value of their paid job responsibilities, such as workshop facilitation and consulting, which helped develop skills and confidence in supportive professional environments. They also had the opportunity to interact with professionals who represented diverse potential career paths. One interviewee discussed how it led to them pursue a career in medicine:

> *"… it made medicine something that was approachable, friendly, and welcoming and something that I could actually—after being part of the program—could actually see myself being a part [of] professionally."*

A Sense of Community and Belonging

Participants highlighted the welcoming and inclusive PATCH environment, which encouraged them to embrace their uniqueness. Bringing together diverse identities and perspectives for a common purpose facilitated personal growth, exploration, a sense of belonging, and the development of meaningful relationships. One interviewee explained, *"… it was a really diverse group of people, and we got to learn a lot about each other and share things with each other about our life experiences and backgrounds that we otherwise maybe wouldn't share."*

Youth-Driven Programming

Individuals emphasized how PATCH leveraged the strengths of both adults and youth, with adults establishing structured program goals and expectations, while youth provided continuous input. They expressed feeling valued for their expertise and observed the tangible effect of their contributions—particularly

Table. Qualitative Insights on Impactful Programmatic Components

Key Theme/Subtheme	% (n) Mentioned	No. of Mentions	Representative Quote
Education			
General education	92.9 (13)	42	"I learned a lot of new information just in general…we had to talk to different people every week, who knew completely different things. And so hearing their knowledge and then learning from them, it was really interesting."
Health education	92.9 (13)	30	"…being taught how to…understand what your doctor is telling you…like knowing whether a positive test or a negative test is actually a positive or negative thing."
Employment and workforce development			
Workshop facilitation	85.7 (12)	34	"… the mere act of getting up and presenting to providers, presenting to other teens…that experience…felt really profound."
General work experience	64.3 (9)	20	"I felt like PATCH was different because it gave me a lot of direct experience…for instance, like art club, wouldn't give you."
Job exploration	50.0 (7)	13	"I think it actually opened my eyes to a lot of different careers within public health that maybe weren't medicine."
Teen consultant work	7.1 (1)	2	"…youth can really talk to adults…and have their voice heard and really have an impact…"
A sense of community and belonging			
Peer connections	92.9 (13)	42	"… it really is different from any other opportunity because you're part of a community that really values community and, like camaraderie. And being a part of PATCH is like having almost like an instant family, you just have people that you can trust and count on, and vice versa."
Sense of belonging	71.4 (10)	26	"…as a team, everybody decided to just kind of accept each other. And that was really nice, because that led to this, freedom of expression that we all got to kind of indulge in…everybody was just really open about who they were, and it made me at least feel like I could do the same."
Youth-driven programming			
Adult-initiated and youth-driven structure	85.7 (12)	29	"PATCH has it down pretty well in terms of getting youth in a space together where they can do this kind of work but also giving them enough space to…still be a kid and like have other commitments."
Youth voices are valued and centered	71.4 (10)	26	"…the mere act of getting up and presenting to providers, presenting to other teens, and having our …voices, be the…drivers of the conversations that we facilitated…when you're kind of held as this like expert, and even if it's an expert in your own lived experience, the way that makes you feel valued and heard and like, the way that impacts our self-esteem, especially as a teen…that was extremely profound for me."
Longitudinal engagement	42.9 (6)	7	"I started PATCH when I was 15…and I stayed in the program until I graduated from high school…being able to have that consistent involvement with the community and the PATCH group itself was really wonderful."
Facilitating community connections			
Engaging with health care providers	78.6 (11)	24	"… it's very empowering to be able to look at these people and also just see them as people who want to learn and really do best for their patients and be in a collaborative setting."
Interacting with the community	64.3 (9)	25	"The nice thing about partnering with the adults in the community is, we are able to learn from their knowledge and learn from their … not necessarily mistakes, but … what they've grown from and what they've learned."
Advocating for issues in the community	42.9 (6)	10	"I felt so involved in the city and the well-being of the state …"
Youth-adult partnership			
Trusted, supportive, reliable adult(s)	92.9 (13)	39	"…I really found it helpful that our program coordinator very clearly…knew all of us, she cared about us, and she was just very hands on…just having like a very supportive, positive person, who's also very passionate about the work, as the team leader, is really good."
Mutual respect	28.6 (4)	7	"They weren't like teachers or camp counselors who can't tell you what's really going on…we were like honest with each other as much as you're honest with the teenager, and they…gave the impression that they…had our backs."
Clear roles, expectations, and boundaries	14.3 (2)	4	"… it was just really nice being treated like an adult…and with that they definitely didnt expect us to behave as adults."

through prolonged engagement with the program. One interviewee said, *"PATCH was one of the first times where I felt like my voice, my perspective, my expertise—and not just mine but our kind of like community of adolescents—was so highly respected and valued."*

Facilitating Community Connections

Alumni recognized how PATCH created safe spaces for youth and professionals to learn from each other, where both parties were seen as experts and learners. They also indicated the value of having guidance, connections, and support to make positive changes within their community. One interviewee described learning about and bolstering community resources:

> *"Some other really big, important aspects of PATCH … are finding what your community resources are and how you can build on them and help them. And utilizing those resources."*

Youth-Adult Partnership

Most alumni mentioned the importance of having a trusted and reliable program coordinator who set clear expectations and

boundaries, held everyone accountable, and treated all participants with respect. One interviewee discussed how the transition from a very experienced coordinator to a new one affected their experience in the program.

> *"The coordinator was new … things weren't up when they were supposed to be, or we didn't get our checks when we were supposed to … it sort of felt like we were teaching [the coordinator] how to do [their] job."*

Limitations

While consistent themes emerged across interviewees, others may not have been captured due to the small sample (14 interviewees among 299 total alumni) and potential bias with those who volunteered for interviews. Moreover, the sample predominantly consisted of Teen Educator alumni, reflecting the longer tenure of this program since 2010 versus the newer Teen Consultant Program established in 2016. While both programs aim to engage youth similarly, it is important to further investigate the newer program's impact. Lastly, alumni participated in PATCH across various years, which enhances diversity in perspectives but also introduces potential recall bias—particularly among those involved many years ago.

DISCUSSION

This evaluation identifies key programmatic elements that PATCH alumni deem impactful, providing insights for effectively engaging youth. Through structured, youth-driven programs and fostering youth-adult partnerships, PATCH creates diverse, safe, and supportive environments for exploration, learning, and growth. Alumni attest that this approach has supported them in exploring their identities and passions, developing essential job and life skills, forming meaningful relationships, and making positive impacts within their communities.

Engaging youth effectively requires significant investments in time, capacity, resources, and expertise. However, these investments can yield substantial returns in terms of youth development and program impact. PATCH serves as a catalyst for workforce and leadership development, promotes positive youth development, improves health outcomes, and supports broader public health goals by amplifying the voices of today's youth.

Funding/Support: This work was conducted as part of the PATCH Program's ongoing evaluation and quality improvement efforts.

Financial Disclosures: Chelsea J. Aeschbach is employed as the Director of Impact and Evaluation for the Providers and Teens Communicating for Health (PATCH) Program.

Acknowledgements: The authors thank Erica Koepsel, PATCH Director of Youth Engagement, and the rest of the PATCH evaluation team for their support and guidance on this project.

REFERENCES

1. Ramos LR, Tissue MM, Johnson A, Kavanagh L, Warren M. Building the MCH public health workforce of the future: a call to action from the MCHB strategic plan. *Matern Child Health J.* 2022;26(Suppl 1):44-50. doi:10.1007/s10995-022-03377-7.

2. Olejniczak A, Otalora-Fadner H, Hanna C, Hudson E, Tess J, Royer H. Evaluation of a curriculum to improve clinician communication with adolescents. *WMJ*. 2015;114(5):213-216.

3. Aeschbach CJ, Olejniczak AB, Koepsel ER, Kusch MM. Enhancing communication among adolescents and health care providers: evolution and evaluation of youth-driven initiative addressing barriers. *WMJ*. 2022;121(4):329-332.

4. Aeschbach CJ, Olejniczak AB, Koepsel ER. Developing a statewide strategy for neaningful youth engagement: insights from a youth-driven program in Wisconsin. *Matern Child Health J.* 2024;28:812-819. doi:10.1007/s10995-023-03867-2.

Utility and Acceptability of Rapid Antigen Testing for Influenza and SARS-CoV-2 in K-12 School Health Offices During and After the COVID-19 Pandemic

Maureen D. Goss, MPH;* Cecilia He, MPH;* Alea Sabry, BS;* Carly Hamer, BS;* Emma L. Svenson, DVM/MPH;* Emily Temte, BA; Shari Barlow, BA; Jonathan L. Temte, MD, PhD

ABSTRACT

Background: Kindergarten through 12th grade (K-12) schools are potential hotspots for infectious disease transmission. We used test results and feedback from school health staff and parents to assess in-school rapid testing during and after the COVID-19 pandemic.

Methods: Rapid testing was conducted in seven K-12 schools during 2021 to 2024. Sofia2-FIA (fluorescent immunoassay) analyzers, test kits, training, and troubleshooting services were provided. School health staff feedback surveys were distributed each year. Parent feedback was collected during the 2023-2024 school year.

Results: Across 3 years, 1710 rapid tests were performed. SARS-CoV-2 (n = 126) and influenza A/B (n = 105) were detected. School health staff found rapid testing "easy" to "very easy" (97%) and supported continuation (90.9%). Parents reported feeling "very relieved" (42.1%) following testing.

Discussion: Rapid testing was highly utilized during and after the COVID-19 pandemic and was well-received by school health staff and parents.

BACKGROUND

Kindergarten through 12th grade (K–12) schools are characterized by high levels of social interaction and close contact, making them potential hotspots for infectious disease transmission. The K–12 school calendar has been linked to outbreaks of acute respiratory infections across the broader community, thus underscoring the role of early detection within schools.[1]

• • •

Author Affiliations: Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health (UW SMPH), Madison, Wisconsin (Goss, He, Sabry, Hamer, E Temte, Barlow, J Temte); Department of Population Health Sciences, UW SMPH, Madison, Wisconsin (Svenson). **Denotes co-first authors.*

Corresponding Author: Maureen D. Goss, MPH, Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, 610 N Whitney Way, Madison, WI 53705; phone 608.301.7730; email maureen.landsverk@fammed.wisc.edu; ORCID ID 0000-0002-7062-1916

The dilemma of preserving educational continuity while implementing mitigation strategies to reduce disease transmission during the COVID-19 pandemic provided the opportunity to introduce rapid antigen tests (RAT) for respiratory pathogens into school settings.[2,3] To navigate the return to in-person learning, some schools implemented testing using RAT to quickly identify and isolate positive cases. Here, we summarize how a school district in Wisconsin utilized school-administered RAT during and after the COVID-19 pandemic. By sharing insights from school health staff and participants, we demonstrate the utility of RAT as an accessible and timely strategy for mitigating respiratory virus transmission in schools.

METHODS

Rapid testing was conducted in the Oregon School District (OSD), where our University of Wisconsin-Madison (UW) research team (hereafter known as the research team) has conducted school-based respiratory disease surveillance since 2015. The OSD is located in South-Central Wisconsin and includes 3 elementary schools (K–4), 1 expanded elementary school (K–6), 1 intermediate school (5–6), 1 middle school (7–8), and 1 high school (9–12), serving over 4000 K–12 students.

In September 2021, we supplied Sofia2 Fluorescent Immunoassay (FIA) analyzers equipped with wireless reporting capability and test kits to OSD schools.[4] This initiative was in conjunction with the Wisconsin Department of Health Services (DHS) during the 2021–2022 school year; the research team contributed consultation, annual training for school health staff on testing and specimen collection, and technical support services

during all 3 school years. The program was solely supported by the research team during the 2022-2023 and 2023-2024 school years. Testing supplies and analyzers were provided by DHS in year 1 and QuidelOrtho (QuidelOrtho Corporation; San Diego, California) in years 2 to 3.

Students presenting to health offices with 2 or more respiratory symptoms (Appendix A) were eligible for RAT by school health staff. Parental consent was obtained during school registration at the beginning of each academic year. Students who received rapid testing were given a printed result to be shared with a parent/guardian. Deidentified RAT results were transmitted wirelessly to the Virena system for export and analysis.[5]

School Health Staff Feedback Surveys

In Spring 2022, we developed a quality improvement survey to assess school health staff's knowledge and experience with Sofia2-FIA analyzer technology and swab collection, and to obtain feedback on the feasibility, acceptability, and generalizability of RAT in school health workflows (Appendix B). Surveys were distributed via email in spring 2022, 2023, and 2024 using Qualtrics XM (Qualtrics; Utah).

Parent Feedback Surveys

In fall 2023, we developed a feedback survey for parents who (1) consented to their children receiving a rapid test, and (2) had a student who received rapid testing at school, to assess their experience with the RAT program (Appendix B). Surveys were distributed weekly by OSD office staff to parents/guardians whose children had received RAT the previous week. Surveys assessed perceived benefits, harms, satisfaction, and acceptability of rapid testing in schools. Individuals who completed the survey were entered into a drawing to win a $50 gift card as an incentive. Surveys were developed and distributed using REDCap electronic data capture tools hosted at the University of Wisconsin–Madison.[6]

Analysis

We utilized descriptive statistics to evaluate the rates of participation, percent positivity of RAT in schools during and after the pandemic, and responses to health office and parent surveys. Qualitative coding of school health staff and parent surveys was performed independently by 4 research team members, and codes were generated and categorized into themes based on thematic analysis. Coders met regularly to ensure consensus of themes and shared understanding of supporting evidence.

RESULTS

Rapid Testing in Schools

From September 1, 2021, through June 7, 2024, school health staff completed 1710 RATs. Of these, 220 (12.9%) were positive, 1482 (86.7%) were negative, and 8 (0.5%) were invalid (Table 1). Most tests were run during the 2021-2022 school year (n = 226, 71.7%), and similar temporal patterns were observed across all 3 years, with a primary testing peak during December to January, followed by a smaller peak during March to May (Figure). Although the high school completed the highest number of tests among the 7 schools (n = 425), grades K-4 collectively conducted the most rapid testing (n = 530). SARS-CoV-2 accounted for 57.3% of detections across all schools and years.

Table 1. Summary Results From Rapid Testing During Academic Years 2021–2022, 2022–2023, and 2023–2024 Across Seven K–12 Schools in the Oregon School District, Dane County, Wisconsin

	2021–2022	2022–2023	2023–2024	Total
Total tests, n	1226	302	182	1710
Positive, n (%)	152 (12.4)	49 (16.2)	19 (10.4)	220 (12.9)
Influenza A, n (%)	35[a] (23)	27 (55.1)	11[c] (57.9)	73 (33.2)
Influenza B, n (%)	20 (13.2)	9[b] (18.4)	3[d] (15.8)	32 (14.5)
SARS-CoV-2, n (%)	103 (67.8)	16 (32.7)	7 (36.8)	126 (57.3)
Negative, n (%)	1068 (87.1)	251 (83.1)	163 (89.6)	1482 (86.7)
Invalid, n (%)	6 (0.5)	2 (0.7)	0	8 (0.5)
Schools, Grades	**Tests Run**	**Influenza A**	**Influenza B**	**SARS-CoV-2**
Elementary 1, K–4	143	6	1	7
Elementary 2, K–4	267	16	7	19
Elementary 3, K–4	120	6	1	11
Elementary 4, K–6	282	7	7	15
Intermediate, 5–6	298	11	11	25
Middle School, 7–8	175	11	3	19
High School, 9–12	425	16	2	30

[a]6 co-detections of influenza A + SARS-CoV-2.
[b]3 co-detections of influenza B + SARS-CoV-2.
[c]1 co-detection of influenza A + SARS-CoV-2.
[d]1 co-detection of influenza B + SARS-CoV-2.

School Health Staff Feedback Surveys

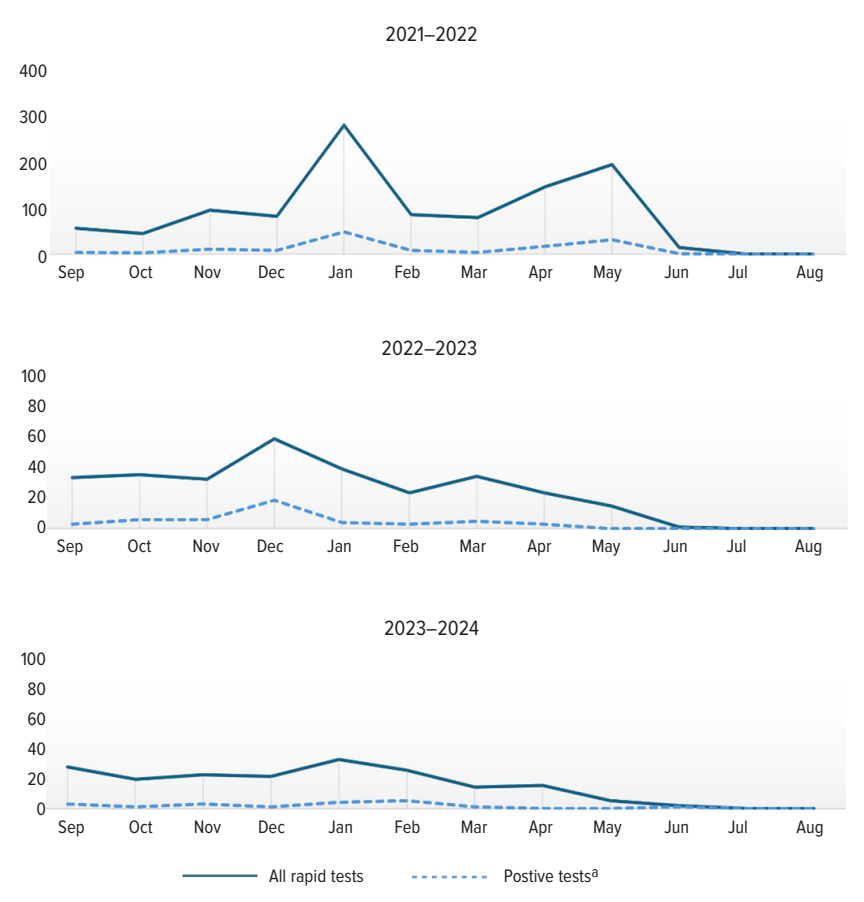
In 2022, 2023, and 2024, 13 out of 13, 11 out of 11, and 9 out of 10 school health staff completed the annual feedback surveys, respectively. Seven school health staff members were OSD employees throughout the testing period and completed the survey all 3 years. After receiving 1 initial training in 2021, staff responses about confidence in performing a RAT changed from "not confident at all" (n = 10, 76.9%) to "very confident" (n = 11, 84.6%). Many staff (54.5%) utilized Sofia2-FIA troubleshooting services offered by the research team. In all 3 years, staff found RAT to be "very easy" or "easy" (97%) and wanted to continue its use (90.9%). Health staff confidence in the accuracy of the RAT result averaged 4.28 on a Likert scale of 1 (low) to 5 (high) over all 3 years. Staff expressed appreciation for the ability to conduct rapid testing, while recognizing time constraints and the need for a more streamlined testing process. Staff underscored the usefulness of being able to test themselves and fellow coworkers when needed. Related themes, codes, and survey questions are documented in Table 2 and the respective legend.

Parent Feedback Surveys

During September 2023 through April 2024, a total of 38/85

(44.7%) surveys were completed by OSD parents whose children received rapid testing. Parents reported feeling grateful for access to this service at school and feeling "very relieved" (n = 16, 42.1%) after their child received a RAT result in school, "very satisfied" (n = 28, 73.7%) with the information/resources received from the school health office, and "very satisfied" (n = 32, 84.2%) with the speed test results were obtained and communicated.

Figure. Monthly Rapid Antigen Tests Performed and Positive Rapid Antigen Tests During Three Consecutive School Years



[a]Positive tests include SARS-CoV-2, influenza A and influenza B combined.

DISCUSSION

Early detection of COVID-19 and influenza in children is crucial for mitigating disease transmission in congregate settings such as schools. Within the OSD, the use of RAT in K-12 schools during and after the COVID-19 pandemic was feasible to implement and widely accepted by school health staff and parents. The opportunity to continue rapid testing in schools was met with positive feedback from both school health staff and families who consented to school-administered RAT.

The number of RATs performed at school decreased each year. This may be due to districtwide mandates in place during the 2021-2022 academic year that required stricter testing, with fewer tests performed as mandates were lifted and during post-pandemic conditions. This also may be attributed to increased accessibility of at-home rapid tests over time and waning concern about the pandemic.

Rapid testing was well-received by school health staff, most of whom were highly confident in RAT results and elected to continue the program in the following years. Surveyed parents also reported high levels of relief when their child received a RAT, which did not vary significantly based on test results. These findings are consistent with other studies demonstrating increased parental and staff peace of mind associated with school-based testing.[7]

This evaluation had several limitations. First, this evaluation was a post-hoc assessment of a community service program. Second, although Sofia2-FIA analyzers were introduced to monitor acute respiratory infection activity among K-12 students, staff were able to obtain rapid testing if they were symptomatic at school. Because analyzers do not label results with students or staff, we can only distinguish an individual as staff or student based on age (>18 years as staff, <18 years as student). In this assessment, we included results of RATs performed on all ages to encompass real-life experiences with RAT in K-12 settings. Third, students and families were required to sign waivers to participate in school RAT and could only be tested if they were symptomatic. Thus, this study excluded asymptomatic or unconsented individuals and may underestimate the true prevalence of influenza and COVID-19 in this population. Lastly, generalizability may be limited due to selection bias of the parent subgroup surveyed, small sample size, and suboptimal response rates from the parent feedback survey, our preexisting relationship with the school district, and the racial/ethnic homogeneity of OSD.[1]

This analysis also has notable strengths, namely the use of quantitative and qualitative approaches to assess feasibility and utility of the RAT platform and acceptance of the program by school health staff and participating parents. School-based testing initiatives can broaden access to rapid testing for school-aged children and contribute to a safer learning environment.[8] While a positive test may affect families by introducing the logistical and financial burden of extra childcare, systematic rapid testing protocols have the potential to reduce overall disease transmission and related absences for students and staff.[9,10] This program was widely utilized and well-received by those surveyed, and sig-

Table 2. Common Themes and Related Codes From School Health Office Staff and Parent Surveys

Theme	Codes	No. of Comments		Example Quotes
		Staff (n=33)	Parents (n=38)	
Rapid testing as a useful resource	Beneficial for both students and staff	11	6	"I very much appreciated the rapid testing as a tool…" (staff)
	Invaluable resource for families			"This resource has also been invaluable to provide a test to those families that it would have been too overwhelming to navigate scheduling a COVID test." (staff)
	Appreciation for access to testing			"Grateful for this service." (parent)
	Helpful, useful tool			"I really appreciate the ability to test at school so I don't have to make a separate doctor appointment." (parent)
Rapid testing as an important tool for school staff	School staff save time by testing at school instead of going elsewhere for testing	13	N/A	"I used [testing] when needed and felt more confident when taking care of students knowing my tests were negative." (staff)
	Staff felt better taking care of students when they were able to test themselves			"I appreciated having the option to test myself if I had a known/ suspected exposure or having symptoms." (staff)
	Faster alternative to making an appointment for a COVID test			"It was reassuring for school staff that they didn't have flu/ COVID, which is easy to spread." (staff)
	Beneficial resource for health office staff and other teachers			"This was so helpful for staff and myself, quick and easy." (staff)
Testing required extra time, resources, and support	Support for testing dependent on staffing availability	11	N/A	"…hard for health room staff to manage testing and a busy health office at the same time." (staff)
	Testing process could be time-consuming			"Slightly time-consuming." (staff)
	Difficult to manage testing during busy times for health office staff			"It was kind of a hassle to get staff tested in between other things going on in the health office." (staff)
	Testing, consenting, and information input could be more streamlined			"Get more families to sign waivers ahead of time." (staff)

[a]A majority (8/11) of responses related to the theme "Testing required extra time, resources, and support" were collected during Year 1, when school health nurses were required to report COVID testing through a state-operated system called COVID Connect, which could anecdotally be time-consuming and cumbersome.

Qualitative responses from school health office staff were collected for 2 short-answer questions: (1) "What are your thoughts on using rapid testing on yourself and/or other school staff?" (2) "Do you have any suggestions on how to improve implementation of rapid testing in a school health office setting?" Qualitative responses from parents were collected from the short-answer question: "How could your family's experience with rapid testing in school be improved? Do you have any questions, or is there any information/resources you would have liked to receive?"

nificant pathogens were effectively detected among participants. Longitudinal testing in more and diverse academic environments may provide additional evidence for the generalizability of such a program in other school districts.

Funding/Support: Quidel Corporation supplied Sofia2 rapid testing analyzers and dual Influenza/SARS-CoV-2 test kits for all school locations. No funding was secured for this study.

Financial Disclosures: None declared.

Acknowledgements: The authors thank the Oregon School District in Oregon, Wisconsin, for ongoing support and cooperation with studies and assessments, and specifically Superintendent Leslie Bergstrom, EdD, and the wonderful school nurses and health office personnel.

Appendices: Available at www.wmjonline.org

REFERENCES

1. Bell C, Goss M, Norton D, et al. Descriptive epidemiology of pathogens associated with acute respiratory infection in a community-based study of K-12 school children (2015-2023). *Pathogens*. 2024;13(4):340. doi:10.3390/pathogens13040340

2. National Academies of Sciences, Engineering, and Medicine; Division of Behavioral and Social Sciences and Education; Board on Children, Youth, and Families; Board on Science Education; Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats; Committee on Guidance for K-12 Education on Responding to COVID-19. *Reopening K-12 schools during the COVID-19 pandemic: prioritizing health, equity, and communities.* Schweingruber H, Dibner K, Bond EC, editors. National Academies Press (US); 2020. doi:10.17226/25858

3. Temte JL, Barlow S, Temte E, et al. Feasibility and functionality of SARS-CoV-2 rapid testing in K-12 school health offices. *WMJ*. 2023;122(5):422-427.

4. Sofia 2 Flu + SARS Antigen FIA. Package insert. Quidel Corporation; 2023. Accessed June 25, 2024. https://www.fda.gov/media/142704/download

5. Quidel. Virena. Accessed June 24, 2024. https://connectme.quidel.com/docs/virena/

6. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

7. Unger JB, Soto D, Lee R, Deva S, Shanker K, Sood N. COVID-19 testing in schools: perspectives of school administrators, teachers, parents, and students in southern California. *Health Promot Pract.* 2023;24(2):350-359. doi:10.1177/152483992110660

8. Teasdale C, Borrell LN, Shen Y, et al. COVID-19 testing among US children, parental preferences for testing venues, and acceptability of school-based testing. *Public Health Rep.* 2022;137(2):362-369. doi:10.1177/00333549211065518

9. Nguyen M, Flores M, Vo AV, Omaleki V, Streuli S, Fielding-Miller R. Barriers and facilitators to COVID-19 testing among staff and parents from San Diego schools. *BMC Public Health*. 2023;23(1):1068. doiDoi:10.1186/s12889-023-15854-x

10. Haroz EE, Kalb LG, Newland JG, et al. Implementation of school-based COVID-19 testing programs in underserved populations. *Pediatrics*. 2022;149(Suppl 2); e2021054268G. doi:10.1542/peds.2021-054268G

Aligning Newborn Hyperbilirubinemia Care With American Academy of Pediatrics Guidelines at an Urban Community Hospital

Cris G. Ebby, MD, MS; Ann H. Allen, MD; Kristin A. Shadman, MD; Nancy Patrick, DNP; Michelle Brenson, RN; Laura P. Chen, MD

ABSTRACT

Background: In August 2022, the American Academy of Pediatrics updated its newborn hyperbilirubinemia guideline. This quality improvement initiative aimed to reduce newborns receiving inpatient phototherapy and subthreshold phototherapy initiation by 50% in 12 months.

Methods: A multidisciplinary team implemented interventions at an urban community hospital in Wisconsin. Retrospective chart review from February 2022 through November 2023 identified newborns receiving phototherapy during birth hospitalization and readmission (primary outcome), subthreshold phototherapy initiation (process measure), and length of stay with meeting escalation of care criteria (balancing measures).

Results: We identified 167 newborns. Median birth hospitalization phototherapy decreased from 10 to 2 newborns per month; there was no change in readmissions. Length of stay and meeting escalation of care criteria were unchanged.

Discussion/Conclusions: This study shows a decrease in inpatient phototherapy use during birth hospitalizations.

INTRODUCTION

Newborn hyperbilirubinemia is a common condition, affecting approximately 80% of newborns in the first week of life.[1] Severe hyperbilirubinemia may lead to permanent neurological damage, including kernicterus,[2] which underscores the importance of screening for and treating hyperbilirubinemia. However, phototherapy can negatively impact caregiver bonding and successful breastfeeding,[3] impose additional costs on the health care system,[4] and has potential long-term harms, such as childhood seizures.[1]

• • •

Author Affiliations: Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Ebby, Allen, Shadman, Chen); SSM Health St. Mary's Hospital, Madison, Wisconsin (Patrick, Brenson).

Corresponding Author: Cris G. Ebby, MD, Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, Madison, WI 53792; email cebby@uwhealth.org; ORCID ID 0009-0000-3653-6630

In August 2022, the American Academy of Pediatrics (AAP) updated the clinical practice guideline for newborn hyperbilirubinemia for newborns born at ≥35 weeks' gestation,[1] raising the phototherapy threshold. While guidelines serve as tools to provide evidence-based care, the publication of guidelines alone may be insufficient to change clinical practice.[5] Furthermore, substantial variation in inpatient management of newborn hyperbilirubinemia was noted with the prior iteration of the AAP guideline.[4]

The global aim of this quality improvement (QI) project was to align newborn hyperbilirubinemia management at our urban, community hospital with the 2022 AAP guidelines. Our specific aim was to decrease both the number of newborns receiving inpatient phototherapy and decrease subthreshold phototherapy initiation by 50% in 12 months.

METHODS

SSM St Mary's Hospital is an urban, community hospital in Madison, Wisconsin, with approximately 2000 births per year, an inpatient pediatric general care unit, and a level III neonatal intensive care unit (NICU). Local data were collected by retrospective chart review from February 2022 through November 2023 as part of the Learning and Implementing Guidelines for Hyperbilirubinemia Treatment (LIGHT) QI initiative from the AAP Pediatric Acute and Critical Care Quality Network. This project was deemed exempt by the local institutional review board. Newborns ≤14 days of age born at ≥35 weeks' gestation receiving phototherapy were included. Newborns received phototherapy either (1) during birth hospitalization in the newborn nursery or (2) during readmission to the pediatric inpatient unit from the

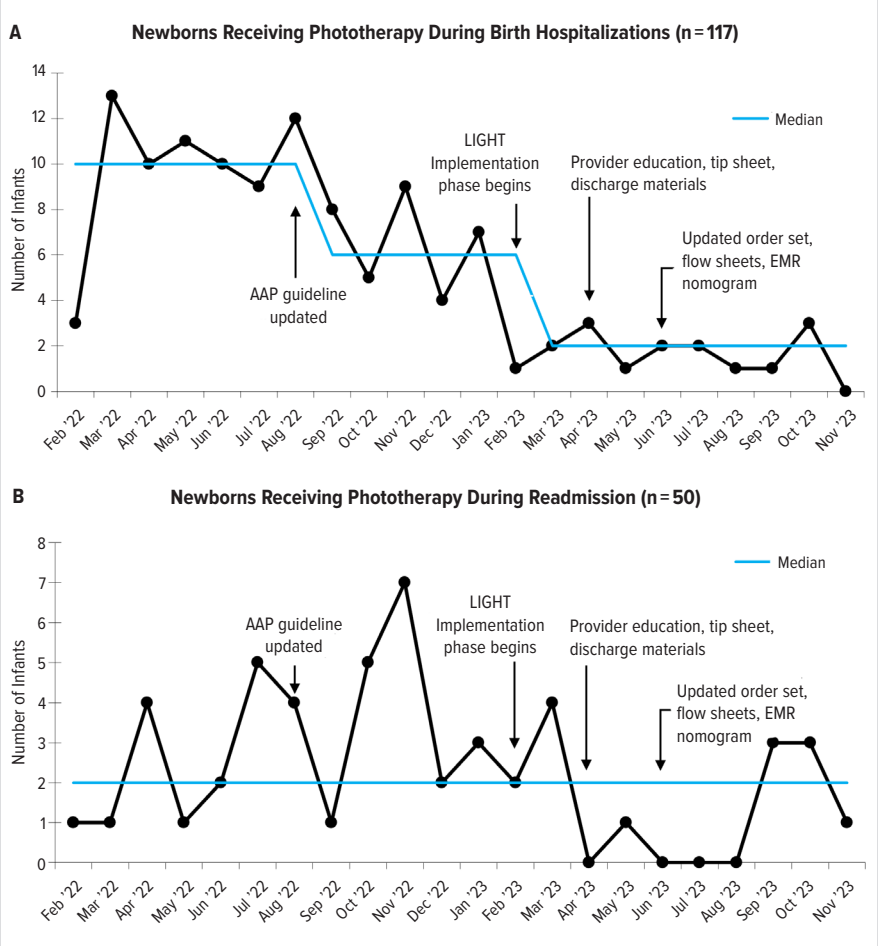
emergency department or outpatient clinics. Newborns requiring NICU admission were excluded. Collected data included patient sex, self-reported race, ethnicity, gestational age, birth weight, weight prior to phototherapy initiation, length of stay (LOS), meeting escalation of care criteria, and whether supplementation with donor milk or formula was started. These metrics were tracked to describe our study population and identify future opportunities for interventions.

Using the model for improvement, a multidisciplinary stakeholder team consisting of a pediatric hospitalist, outpatient pediatrician, neonatologist, and nurses from the NICU, newborn nursery, and pediatric inpatient units gathered to identify key drivers and develop interventions. In April 2023, dedicated education reviewing updated guidelines was instituted for pediatric clinicians and nursing staff in the newborn nursery and inpatient unit. In addition, a tip sheet with key recommendations from the updated guideline was disseminated to all clinicians. The "After Visit Summary," which includes discharge instructions provided to caregivers, was updated and tailored for the newborn nursery and inpatient unit. The next step of interventions took place in June 2023. In the newborn nursery, the order set for routine care was updated to reflect timing of obtaining serum bilirubin. For both settings, order set updates included relevant nursing orders for phototherapy and options for ordering follow-up labs, such as complete blood cell count, hemoglobin, total bilirubin, direct bilirubin, direct Coombs, and blood type. The 2022 gestational age-specific bilirubin treatment nomograms[1] were incorporated within the electronic medical record (EMR) for easy access for clinicians. All nursing flowsheets were updated to optimize documentation within the EMR.

The primary outcome measure was the number of newborns receiving phototherapy per month. The process measure was frequency of subthreshold phototherapy initiation per month, defined as initiating phototherapy at total serum bilirubin ≥ 0.3 mg/dL below the AAP phototherapy threshold. LOS and meeting escalation of care criteria were tracked as balancing measures. Escalation of care was defined as newborns with a total serum bilirubin 2 mg/dL below the exchange transfusion threshold or higher.

Baseline data were collected from February 2022 through January 2023 and implementation data from February 2023 through November 2023. Data were analyzed using Microsoft Excel QI-Charts, version 2.0.23 (Process Improvement Products, San Antonio, Texas). The number of newborns receiving inpatient phototherapy per month and instances of subthreshold phototherapy initiation were tracked on run charts; LOS was tracked on an I-chart. Special cause variation was identified using established run chart rules.[6]

Figure 1. Run Charts Tracking Number of Newborns Receiving Phototherapy Per Month During (A) Birth Hospitalization and (B) Readmissions



Abbreviations: AAP, American Academy of Pediatrics; LIGHT, Learning and Implementing Guidelines for Hyperbilirubinemia Treatment EMR, electronic medical record.

Table. Demographics of Newborns From Birth Hospitalization and Readmitted Newborns (N = 167)

Sex		Admission type	
Male	53%	Birth hospitalization	70%
Female	47%	Readmission	30%
Race		Gestational age	
White	65%	35–36 weeks	12%
Black	9%	37 weeks	29%
Asian	9%	38 weeks	15%
More than 1 race	10%	39 weeks	31%
Other/unknown	7%	40+ weeks	13%

RESULTS

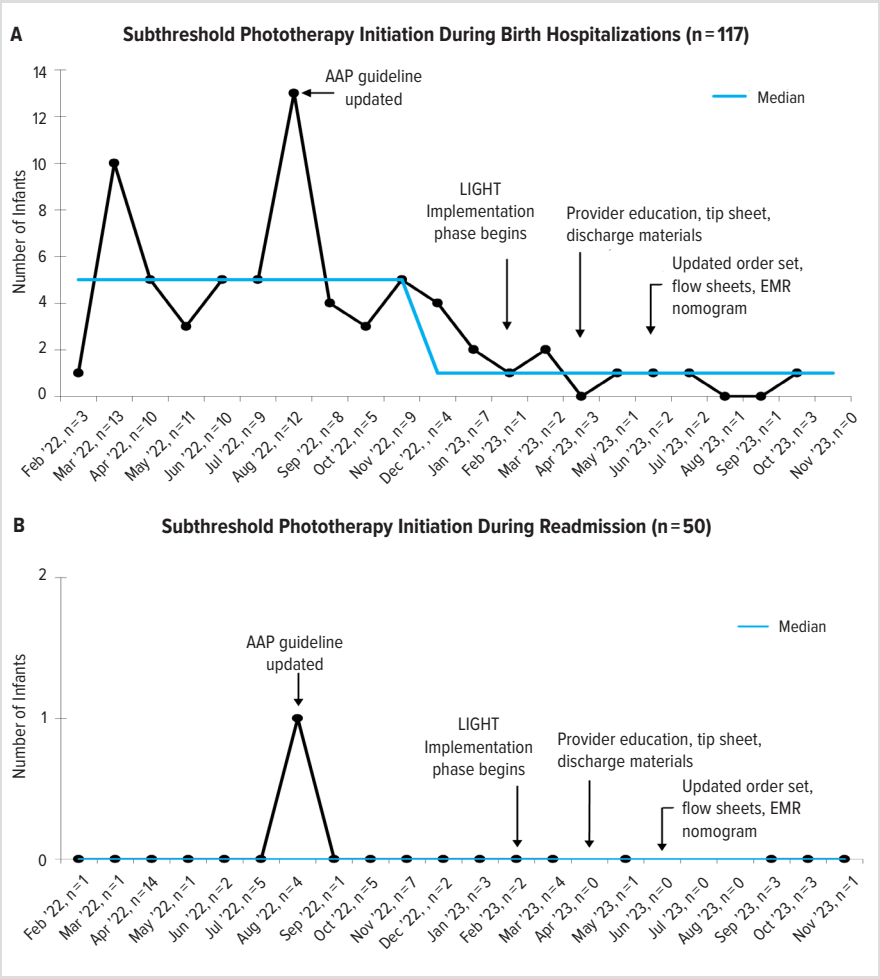
During the study period, 167 newborns received phototherapy: 70% during birth hospitalization and 30% in the inpatient pediatric unit. Newborns were 53% male and 65% White, with the majority born at term (Table).

The median number of newborns receiving phototherapy during birth hospitalization each month decreased from 10 to 6 patients in September 2022, then decreased again in March 2023 to 2 patients. There was no significant change in the median number of newborns readmitted for phototherapy (Figure 1). For birth hospitalizations, the median occurrence of subthreshold initiation of phototherapy decreased from 5 to 1 per month, while there was only 1 instance of subthreshold phototherapy initiation among readmissions (Figure 2).

Average LOS during the baseline phase was 63.8 hours for birth hospitalizations and 28.3 hours for readmissions. For both groups, the centerline was not shifted as there was no sustained change in LOS during the implementation phase (Figure 3). For birth hospitalizations, LOS above the upper control limit (UCL) occurred in 3 patients (patient 98, 105, and 106)—all with concern for active hemolysis—and were transferred to the pediatric inpatient unit. For readmissions, LOS above the UCL occurred in 2 patients: a newborn with Coombs-negative hemolysis likely from hereditary spherocytosis (patient 3) and another with ABO incompatibility (patient 27). Only 6 newborns (3.6%) met criteria for escalation of care: 1 birth admission and 2 readmissions prior to guideline release and 1 birth admission and 2 readmissions postguideline release.

Birth rates at our hospital remained stable throughout the study period, with 161 births per month during the baseline phase and 156 births per month during the implementation phase. Average weight loss at the time of phototherapy initiation for all patients was 5% from birth weight, with 32% of newborns exclusively breastfed, 65% breastfed with donor milk or formula supplementation, and 4% exclusively formula fed.

Figure 2. Run Charts Tracking Number of Instances of Subthreshold Initiation of Phototherapy per Month During (A) Birth Hospitalization and (B) Readmissions



Abbreviations: AAP, American Academy of Pediatrics; LIGHT, Learning and Implementing Guidelines for Hyperbilirubinemia Treatment; EMR, electronic medical record.

DISCUSSION

The publication of the 2022 AAP hyperbilirubinemia guideline[1] has put a national spotlight on newborn hyperbilirubinemia management. Existing literature evaluates pooled data featuring freestanding children's hospitals where reduction in newborns receiving phototherapy has been reported.[7] However, approximately 70% of children receiving care in the United States do so in a community hospital setting,[8] where published data on newborn hyperbilirubinemia are more limited. This QI study highlights the practical implementation of the updated AAP guidelines at an urban, community hospital.

In the newborn nursery, there was a significant decrease in the number of newborns receiving phototherapy and subthreshold phototherapy initiation. Not only does this decrease health care costs and harm, it also minimizes disruption to breastfeeding and caregiver bonding. While there was a reduction in subthreshold phototherapy initiation for birth hospitalizations, this trend is confounded by the decrease in the overall number of newborns receiving phototherapy. However, the 3 months with no occurrences of subthreshold phototherapy initiation occurred in the last 8 months, reflecting positive progress.

Despite interventions to implement the 2022 clinical practice guideline, the median number of newborns readmitted for phototherapy was unchanged. The lack of subthreshold phototherapy initiation during the implementation phase suggests patients were appropriately readmitted for phototherapy. We hypothesized that raised phototherapy thresholds should have reduced the number of newborns requiring readmission; however, reduced rates of phototherapy treatments during birth hospitalizations may have led to increased hyperbilirubinemia in discharged newborns. Notably, the 4 months without readmissions occurred exclusively during the implementation phase. Ongoing data monitoring is necessary to capture trends in the number of readmitted newborns.

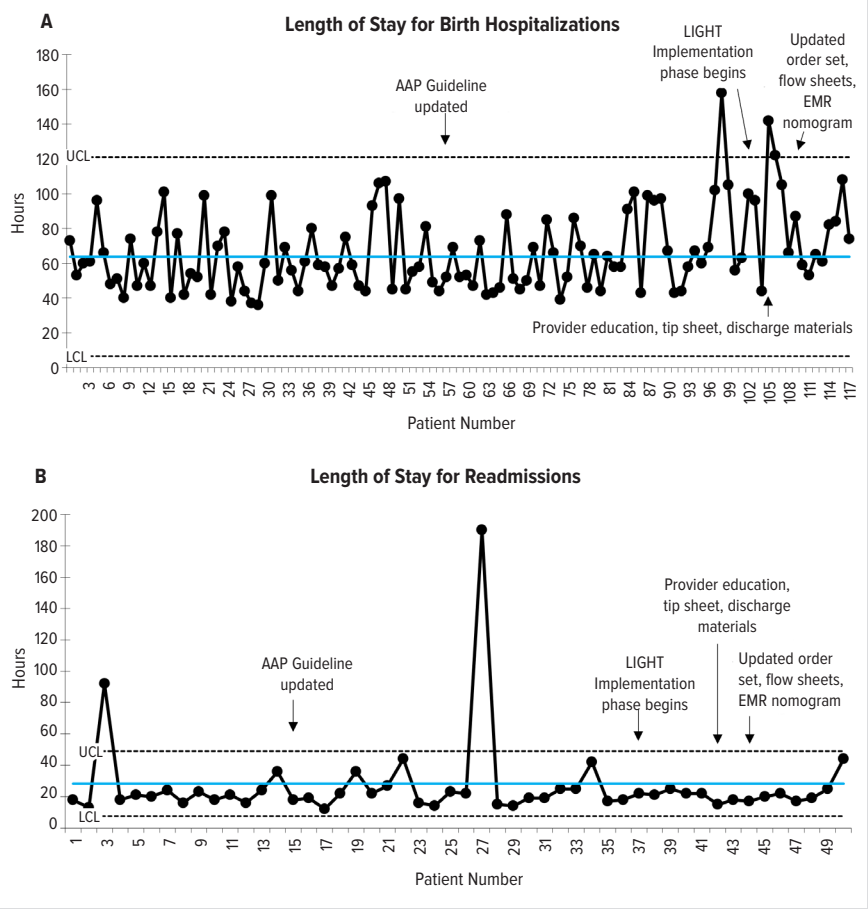
Potential adverse outcomes associated with the higher phototherapy threshold include increased symptoms from hyperbilirubinemia, increased risk of meeting escalation of care criteria, and prolonged hospitalization or requiring transfer to the NICU. However, in this study, LOS and occurrence of meeting escalation of care criteria remained unchanged in both populations. The average readmission LOS of 28.3 hours in this study was similar to LOS at freestanding children's hospitals.[4,9] Average LOS for birth hospitalizations in this study was significantly longer at 63.8 hours, likely due to feeding difficulty, newborn comorbidities, or maternal medical care affecting birth hospitalization. There was no difference in the number of newborns meeting escalation of care criteria in both populations, indicating no increase in newborn morbidity with the 2022 guidelines.

In our study, 65% of newborns were breastfed and received supplemental donor breast milk or formula. While newborns with excessive weight loss (>10% from birth weight) require intervention with supplementation, the average weight loss in our study was only 5%, indicating that supplementation was not solely initiated for excessive weight loss. Furthermore, the nadir weight loss was not captured in this study. Additional studies exploring reasons for initiating supplementation may inform future interventions to decrease jaundice from suboptimal intake.

This study was performed at a single center, limiting generalizability to other health systems. Additionally, the study period may be insufficient to capture long-term outcomes related to the implementation of new guidelines. With no change in birth rates during the study period, the overlap of the study period with the COVID-19 pandemic likely did not impact the findings.

This QI initiative demonstrates a significant decrease in the number of newborns receiving inpatient phototherapy and reduction in initiation of subthreshold phototherapy during birth hospitalization at an urban, community hospital in Wisconsin. Inpatient newborn care is provided at over half of Wisconsin hospitals, and adapting national guidelines to local settings requires leveraging local resources for successful QI implementation.[10] This process can be tailored to community hospital settings for local improvement efforts with a multidisciplinary team to standardize care of newborns with hyperbilirubinemia. At our institution, next steps will focus on continued engagement of clinicians and data surveillance to ensure sustained trends.

Figure 3. I-Charts Tracking Length of Stay for (A) Birth Hospitalization and (B) Readmissions



Abbreviations: AAP, American Academy of Pediatrics; LIGHT, Learning and Implementing Guidelines for Hyperbilirubinemia Treatment; EMR, electronic medical record; UCL, upper control limit; LCL lower control limit.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Kemper AR, Newman TB, Slaughter JL, et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics*. 2022;150(3):e2022058859. doi:10.1542/peds.2022-058859

2. Kasirer Y, Kaplan M, Hammerman C. Kernicterus on the spectrum. *Neoreviews*. 2023;24(6):e329-e342. doi:10.1542/neo.24-6-e329

3. Muchowski KE. Evaluation and treatment of neonatal hyperbilirubinemia. *Am Fam Physician*. 2014;89(11):873-878.

4. DePorre AG, Hall M, Puls HT, et al. Variation in care and clinical outcomes among infants hospitalized with hyperbilirubinemia. *Hosp Pediatr.* 2020;10(10):844-850. doi:10.1542/hpeds.2020-0161

5. Palmer RH, Clanton M, Ezhuthachan S, et al. Applying the "10 simple rules" of the Institute of Medicine to management of hyperbilirubinemia in newborns. *Pediatrics*. 2003;112(6 Pt 1):1388-1393. doi:10.1542/peds.112.6.1388

6. Provost LP, Murray SK. *The health care data guide: learning from data for improvement.* 2nd ed. Jossey-Bass; 2022.

7. Sarathy L, Chou JH, Romano-Clarke G, Darci KA, Lerou PH. Bilirubin measurement and phototherapy use after the AAP 2022 Newborn Hyperbilirubinemia Guideline. *Pediatrics*. 2024;153(4): :e2023063323. doi:10.1542/peds.2023-063323

8. Leyenaar JK, Ralston SL, Shieh MS, Pekow PS, Mangione-Smith R, Lindenauer PK. Epidemiology of pediatric hospitalizations at general hospitals and freestanding children's hospitals in the United States. *J Hosp Med*. 2016;11(11):743-749. doi:10.1002/jhm.2624

9. Tartaglia KM, Campbell J, Shaniuk P, McClead RE. A quality project to improve compliance with AAP guidelines for inpatient management of neonatal hyperbilirubinemia. *Hosp Pediatr.* 2013;3(3):251-257. doi:10.1542/hpeds.2012-0103

10. Busch S, Allen A, Birstler J, Ildiko Martonffy A. Inpatient pediatric care and clinician workforce in Wisconsin: the state of the state. *WMJ*. 2023;122(3):164-170.

Human Parechovirus Infection in an Infant Presenting with Hyperferritinemia

Kayla Rose McConnaha, BS; Zachary Kenneth Bracken, BS; Rebecca Rose Mastey, BS; Drew Koeppl, CPNP-AC; Pradeep Bangalore Prakash, MD

ABSTRACT

Introduction: Human parechovirus (HPeV) is recognized as a cause of severe infections in infants.

Case Presentation: A 4-week-old febrile female with HPeV infection presented with persistent fevers and hyperferritinemia with normal C-reactive protein, suggestive of cytokine storm syndrome.

Discussion: HPeV is known to cause encephalitis, hepatitis, sepsis, and organ dysfunction. However, few have documented hyperferritinemia and the role of cytokines in disease progression and the role of intravenous immunoglobulins (IVIG) used in the treatment of HPeV-induced hyperinflammation/cytokine storm.

Conclusions: HPeV infections in infants can present with hyperinflammation and sepsis-like syndrome. IVIG may have a role in the treatment of severe parechoviral infections in children who present with hyperferritinemia.

INTRODUCTION

Human parechovirus (HPeV) is a single-stranded RNA virus belonging to the Picornaviridae family.[1] HPeV-1 is the most common type and is associated with mild gastrointestinal illnesses and respiratory tract infections in children. HPeV-3 is less common and linked with severe diseases, including sepsis and meningoencephalitis.[1] Recently, HPeV has been recognized as a cause of severe viral infections presenting with encephalitis, hepatitis, sepsis, neurological impairments, and organ dysfunction—especially in neonates and young infants.[1] Furthermore, there have been findings to suggest cytokine storm may contribute to more severe HPeV infections.[2] Here we report a case of an infant infected by HPeV who presented with persistent fevers, transaminitis, and hyperferritinemia who was treated with intravenous immunoglobulin (IVIG) and subsequently had a remarkable improvement in clinical symptoms and laboratory values.

CASE PRESENTATION

The patient is a 4-week-old female born at 37 weeks 6 days with a birth history complicated by marginal cord insertion and Group B streptococcal infection in the mother, which was adequately treated prenatally. She was brought to the pediatrician with primary concerns consisting of fussiness, reduced oral intake, emesis, and a rectal temperature of 100.1 °F. At this visit, it was reported that prior to falling ill, she was exposed to her cousin, who had tested positive for parechovirus. Physical exam was unremarkable, COVID-19 test was negative, and she was discharged home.

The following day, the patient continued to have similar symptoms, with the addition of looking "stiff," so she was reevaluated and sent to the emergency department for further workup. There, her vitals demonstrated a pulse of 182 beats per minute, respiratory rate of 36, oxygen saturation of 98% on room air, and a rectal temperature of 102.6 °F. A broad workup was ordered, which included a complete blood cell count (CBC) with differential, comprehensive metabolic panel (CMP), C-reactive protein level (CRP), procalcitonin, urinalysis (UA) with culture, blood culture, respiratory polymerase chain reaction (PCR) panel, and cerebrospinal fluid (CSF) studies. Her labs were significant for white blood cell (WBC) 4.6 x 103 /uL (7.0-20.0 x 103 /uL) with 34% lymphocytes and 11% (0%-11%) bands, sodium 130 mmol/L (136-

Author Affiliations: Medical College of Wisconsin-Green Bay, Green Bay, Wisconsin (Bracken, McConnaha, Mastey); HSHS St Vincent Children's Hospital, Green Bay, Wisconsin (Bangalore, Koeppl).

Corresponding Author: Pradeep Bangalore Prakash, MD; email pradeep.prakash@prevea.com.

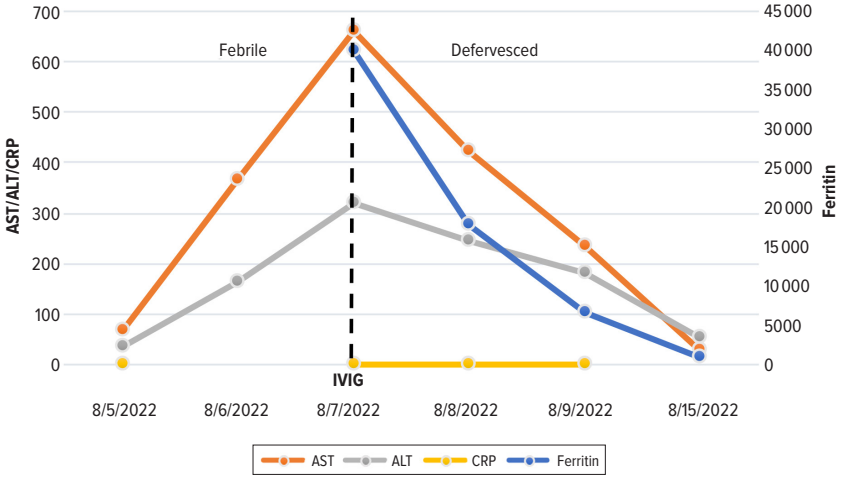
145 mmol/L), aspartate aminotransferase (AST) 69 U/L (15-60 U/L), alanine aminotransferase (ALT) 35 U/L (13-45 U/L), CRP < 0.29 mg/dL (< 0.31 mg/dL), procalcitonin of 0.41 ng/mL (< 0.50 ng/mL), unremarkable UA, negative respiratory PCR, blood-tinged CSF with few WBCs, positive CSF PCR for human parechovirus, normal CSF glucose, and normal CSF protein. The patient was transferred to the pediatric intensive care unit (PICU) for observation and further evaluation with pending blood and urine cultures.

In the PICU, she was started on IV fluids, antipyretics, famotidine, and ondansetron. Empiric antimicrobials were not started because laboratory findings were suggestive of viral etiology (parechovirus) for the febrile illness. On the second day of admission, she remained febrile, and her transaminases continued to rise with ALT climbing above the reference range to 164 U/L (AST 367 U/L). Her CBC was without leukocytosis, differential had 72% lymphocytes, blood cultures resulted negative, and she was started on continuous electroencephalogram monitoring to rule out seizures. Hyponatremia resolved on the second day of illness, and she did not have any clinical signs of dehydration. Given her status, the plan was to monitor liver function tests (LFT) daily.

On the third day of admission and due to persistent fevers, we suspected hyperinflammation secondary to parechoviral infection and checked a ferritin level. The repeated labs were notable for increased transaminases (AST 662 U/L, ALT 318 U/L) ferritin of > 40 000 ng/mL (200.0-600.0 ng/mL) and a CRP < 0.29 mg/dL. We hypothesized the parechoviral infection triggered an inflammatory hepatic process, likely producing clinical and diagnostic evidence of hyperinflammation/cytokine storm. IVIG 2g/kg (Octagam 10%) was administered over 6 hours.

Additionally, an echocardiogram and electrocardiogram were ordered to rule out cardiac involvement. These tests showed no acute cardiac pathology, but there was a non-hemodynamically significant patent foramen ovale with small left-to-right shunting. The patient defervesced immediately after IVIG administration and had improved oral intake. Laboratory values were trending down (AST 423 U/L, ALT 244 U/L, ferritin 17818 ng/mL, differential 65% lymphocytes with no bands) with a normal international normalized ratio and CRP. IV fluids were stopped, and pediatrics infectious disease was consulted; they felt supportive care was appropriate. On day 5 of admission, the patient remained afebrile, and laboratory values were reassuring. She was discharged and scheduled for a 1-week follow-up with her pediatrician for reevaluation and lab work. On discharge, notable labs included a WBC of 9.5 x 103 /uL, AST of 236 U/L, ALT of 180 U/L, and ferritin of 6707 ng/mL. At her 1-week follow-up, notable labs included a WBC of 14.7 x 103 /uL, AST of 30 U/L, ALT of 53 U/L, and a ferritin of 907 ng/mL (Figure).

Figure. Laboratory Values



Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein.

DISCUSSION

HPeVs are common childhood pathogens that predominantly cause mild infections in children between 6 months to 5 years of age. In children less than 3 months of age, HPeV can cause severe sepsis-like illness, meningitis, and hepatitis.[3] Our patient presented with sepsis-like illness with high fevers, decreased oral intake, emesis, and elevated transaminases and subsequently was found to have a markedly high ferritin value of > 40 000 ng/ml – levels that have not been well-documented in prior cases.[4]

There have been reports of neonates with severe HPeV infections presenting with hemophagocytic lymphohistiocytosis (HLH)-like illness with hyperferritinemia, cytokinemia, and cytopenia treated with corticosteroids and cyclosporine.[5] It is not well understood why HPeV triggers hyperinflammation in some infants. It is possible that immune pathways activated with HPeV are different from other viruses given multiple reports of children presenting with normal CRP and elevated serum ferritin, which was similarly observed in our patient. Serum ferritin has been studied extensively by immunologists. It is a known marker of inflammation and serves to enhance the immune system response. Ferritin is associated with inflammation as it is released from macrophages during infection and induces pro-inflammatory cytokines and immunosuppression, causing a positive feedback loop of inflammation via TLR-9 stimulation and activation of macrophage inflammasomes resulting in increased ferritin.[6] Elevated serum ferritin can cause uncontrolled inflammation with positive feedback loop resulting in tissue damage and increased morbidity and mortality in patients.[6]

The mechanism of HPeV induced-hyperferritinemia is unclear. It is possible that elevated serum ferritin levels could be a result of viral or immune-mediated hepatitis. Ferritin is stored in the liver cells and may leak out into the blood due to the damage caused by the virus.[6] Elevated serum ferritin known to fuel inflammation could cause cytokine storm via positive feedback loop triggered by elevated ferritin. While a cytokine panel would have been useful in understanding the cytokine response in our patient, we were limited by timely availability of results, and it would have incurred unnecessary costs and ultimately not changed the course of treatment at that point in time.

There are multiple reports of HPeV-induced cytokine storm. The largest known cohort of 118 infants infected with HPeV was reported from Australia in 2015. Two children in that cohort had hemophagocytic lymphohistiocytosis (HLH) or Kawasaki disease-like illness. One child received IVIG and defervesced; the other child recovered without any immunomodulatory therapy.[7] Another case report showed elevated cytokine levels (MCP-1, IL-6, IL-10, IFN-γ, and TNF-α) in 2 HPeV-3 infected infants, suggesting the role of cytokine storm in the pathophysiology of parechoviral infection.[2] Our 4-week-old patient met criteria for systemic inflammatory response syndrome with an elevated core temperature above >38.5°C and a depressed leukocyte count for the patient's age. Additionally, elevated transaminases and extremely elevated ferritin levels with normal CRP supported the idea of HPeV-induced hyperinflammation as the cause of her illness.[8] The clinical decision was made to administer a single, high dose of IVIG.

Prior experience of using IVIG to treat hyperinflammation is primarily in Kawasaki disease and more recently in treating COVID-19-associated multisystem inflammatory syndrome in children (MIS-C). IVIG had been used alone as well as in combination with other therapies for cases of viral encephalitis in the pediatric population – primarily for enterovirus, parvovirus, and mumps.[9,10] IVIG is currently the recommended first-line treatment for Kawasaki disease due to its anti-inflammatory effects, which subsequently reduces myocarditis and arterial abnormalities in treated patients.[11] IVIG has been successful in treating MIS-C, a clinical syndrome of children with a history of SARS-CoV-2 infection, which is followed by systemic inflammation, fever, and multiorgan dysfunction.[12] IVIG has been used to neutralize a select strain of parechovirus in vitro and in supportive therapy for encephalitis in prior case reports.[13] Despite each of these prior documented uses for IVIG, our literature review did not reveal any reported parechoviral-induced cases of viral hepatitis in infants associated with hyperferritinemia that had been treated specifically with IVIG.

Without prior literature to base treatment selection on, IVIG was chosen as the treatment for this infant given our suspicion for cytokine storm syndrome and the similarities of the patient's clinical presentation with other inflammatory diseases for which IVIG has been used – particularly Kawasaki disease and MIS-C. Ultimately, the strong association between the time of administration of IVIG and the stark decrease in ferritin levels, LFTs, and defervescence suggests IVIG may be considered for treatment of parechovirus-induced viral hepatitis presenting with hyperferritinemia. Importantly, this patient's LFTs and ferritin levels remained low at her follow-up appointment, and she was doing well clinically 1 week after discharge. It is important to note that laboratory and clinical improvement may have been seen without the use of IVIG; however, given the worsening clinical symptoms and similarities of the case to Kawasaki and MIS-C patients successfully treated with IVIG, we felt it was an appropriate intervention for our patient. The dosage of IVIG was based upon the treatment of hyperinflammation states such as Kawasaki and MIS-C, which is 1 dose followed by observation for a response and a second dose if not improved. Our patient improved with a single dose.

The administration of IVIG does not come without risks, which need to be considered for each patient. Given that it is a blood transfusion, there is the risk of an adverse reaction or even anaphylaxis. Infection is also a risk that is not negligible. Furthermore, for children who receive IVIG, it is recommended that they do not get any live vaccines for a year after. This would postpone administration of the MMR vaccine as well as others that could increase risk of exposure to additional viruses.

Our patient was discharged on day 5 of admission, while some infants treated with antibiotics alone were discharged 6 to 8 days after admission.[1,2] Although 1 infant with a suspected severe systemic inflammatory response was treated with IVIG and was first discharged on day 8 of admission, it is important to note IVIG was not administered until day 5 of admission. Retrospectively, our hypothesis would support the idea that had IVIG been administered sooner, it is possible this infant may have been discharged earlier.[14]

One limitation of this study is that a cytokine panel was not collected to confirm the cytokine storm. This was not deemed necessary as the patient defervesced and had remarkable improvement. However, if she was not responsive or if her condition was worsening, a cytokine panel would have been ordered, and other therapies, such as steroids, anakinra (an interleukin-1 antagonist), plasma exchange, and interleukin-6 antagonists would have been potential next steps. Furthermore, it would be of interest to see which cytokines are elevated and perhaps an additional target for future therapeutics. Another limitation was that we did not obtain titers of neutralizing antibodies against HPeV before and after IVIG administration; future studies or clinical cases would likely benefit from such measurement to better understand the potential mechanism of IVIG.

CONCLUSIONS

In children with HPeV infection presenting with persistent fever and hepatitis, a check of serum ferritin level might help assess if

the patient has HPeV-induced hyperinflammation. Currently, there is not enough evidence to recommend IVIG as a treatment for HPeV-induced hyperferritinemia. IVIG use must be based on the best clinical judgement after weighing its risks and benefits.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Olijve L, Jennings L, Walls T. Human parechovirus: an increasingly recognized cause of sepsis-like illness in young infants. *Clin Microbiol Rev.* 2017;31(1):e00047-17. doi:10.1128/CMR.00047-17

2. Sugiura K., Ogura A, Takanashi J, Hamada H. Multiple hypercytokinemia in human parechovirus-3 infection in infants with pediatric systemic inflammatory response syndrome. *Chiba Med J*. 2020;96E:73-77. doi:10.20776/S03035476-96E-6-P73

3. Center for Preparedness and Response. Recent reports of human parechovirus (PeV) in the United States—2022. Center for Disease Control and Prevention. CDCHAN-00469. Published July 12, 2022. Accessed September 12, 2022. https://emergency.cdc.gov/han/2022/han00469.asp

4. Selvarangan R, Nzabi M, Selvaraju SB, Ketter P, Carpenter C, Harrison CJ. Human parechovirus 3 causing sepsis-like illness in children from midwestern United States. *Pediatr Infect Dis J*. 2011;30(3):238-242. doi:10.1097/INF.0b013e3181fbefc8

5. Hara S, Kawada J, Kawano Y, et al. Hyperferritinemia in neonatal and infantile human parechovirus-3 infection in comparison with other infectious diseases. *J Infect Chemother.* 2014;20(1):15-19. doi:10.1016/j.jiac.2013.11.002

6. Carcillo JA, Kernan KK, Horvat CM, Simon DW, Aneja RK. Why and how is hyperferritinemic sepsis different from sepsis without hyperferritinemia? *Pediatr Crit Care Med*. 2020;21(5):509-512. doi:10.1097/PCC.0000000000002285

7. Khatami A, McMullan BJ, Webber M, et al. Sepsis-like disease in infants due to human parechovirus type 3 during an outbreak in Australia. *Clin Infect Dis.* 2015;60(2):228-236. doi:10.1093/cid/ciu784

8. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med*. 2005;6(1):2-8. doi:10.1097/01.PCC.0000149131.72248.E6

9. Wagner JN, Leibetseder A, Troescher A, Panholzer J, von Oertzen TJ. Efficacy and safety of intravenous immunoglobulins for the treatment of viral encephalitis: a systematic literature review. *J Neurol*. 2022;269(2):712-724. doi:10.1007/s00415-021-10494-w

10. Yen MH, Huang YC, Chen MC, et al. Effect of intravenous immunoglobulin for neonates with severe enteroviral infections with emphasis on the timing of administration. *J Clin Virol.* 2015;64:92-96. doi:10.1016/j.jcv.2015.01.013

11. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. 2017;135(17):e927-e999. doi:10.1161/CIR.0000000000000484

12. Wang Z, Zhao S, Tang Y, et al. Potentially effective drugs for the treatment of COVID-19 or MIS-C in children: a systematic review. *Eur J Pediatr.* 2022;181(5):2135-2146. doi:10.1007/s00431-022-04388-w

13. Miura W, Momoki E, Fuchigami T, et al. Encephalitis related to human parechovirus type 3. *Int J Clin Pediatr.* 2019;8(2):37-40. doi:10.14740/ijcp333

14. Casas-Alba D, Martínez-Monseny A, Monfort L, et al. Extreme hyperferritinemia in dizygotic twins with human parechovirus-3 infection. *Pediatr Infect Dis J.* 2016;35(12):1366-1368. doi:10.1097/INF.0000000000001333

Perinatal Femur Fracture Following Difficult Cesarean Delivery: A Case Report

Sarthak Aggarwal, BS; Sudhish Chandra, MD

ABSTRACT

Introduction: Neonatal femur fractures from birth trauma are rare, occurring in 0.1 to 2 per 1000 live births, with unclear associations with cesarean delivery. Limited literature leaves gaps in early detection, injury mechanisms, and management.

Case Presentation: This is the case of a full-term female neonate with a femur fracture following a cesarean delivery for breech presentation. The delivery involved a difficult extraction, and the fracture was diagnosed immediately due to crepitus and a "popping" sound. Treatment was complicated by insurance. The patient received a Pavlik harness with good healing.

Discussion: In the literature, diagnosis averages 4 days, relying on late-arising classic signs. The literature is mixed on risks associated with mode of delivery.

Conclusions: Challenging cesarean extractions pose a risk for femur fractures. Early diagnosis is essential and may be expedited by comprehensive screening and early physical exam findings, such as crepitus, a "popping" sound, or decreased limb mobility. Poor access to pediatric orthopedic clinicians may complicate treatment.

INTRODUCTION

Neonatal femur fractures in the setting of birth trauma are exceedingly rare. The estimated incidence of perinatal femur fracture has been reported to be roughly 0.1-2 per 1000 live births.[1-3] Clavicle and humerus fractures from birth trauma are relatively more common, though still infrequent.[4,5] Long bone fractures may occur during both vaginal delivery or cesarean delivery and, while cesarean deliveries have long been thought of as protective against birth trauma, literature has not been definitive on which mode of delivery purports greater risk for femoral fracture. Some studies have posited that most birth-related femur fractures occur in vaginal breech deliveries,[6-9] whereas other studies report a greater incidence with cesarean delivery.[2,3,10] More established risk factors for femoral fracture at delivery include malpresentation, low birth weight, macrosomia, prematurity, osteogenesis imperfecta, fetal osteoporosis, and difficult extraction.[9,11] Given limited literature on these fractures, information on their early clinical detection, mechanism of injury, and preferred management is lacking, and current practices on identifying such fractures partly rely on the extrapolation of practices from other contexts. Further elucidating the epidemiology and risk factors associated with neonatal femur fractures can inform clinical decision-making and contribute to improved outcomes for affected infants. We report the case of a full-term neonate found to have a closed fracture of the femoral shaft following cesarean delivery for breech presentation.

CASE REPORT

This is the case of a female neonate born at 39 weeks 0 days via cesarean section to a gravida 1 para 1 (G1P1) mother in a community hospital. The mother's prenatal course was uncomplicated, and she received routine care throughout her pregnancy. She did not have a history of diabetes or drug use, nor was there any family history of musculoskeletal diseases, such as osteogenesis imperfecta. Cesarean delivery was ultimately indicated due to breech presentation, and the neonate was born via a low transverse incision with Apgar scores of 7 and 9 at 1 and 5 minutes, respectively. Delivery was complicated by a difficult extraction, in which the leg was internally rotated to deliver the infant through the hysterotomy. Given the challenging positioning of the neonate and relatively limited space provided by the hysterotomy, additional

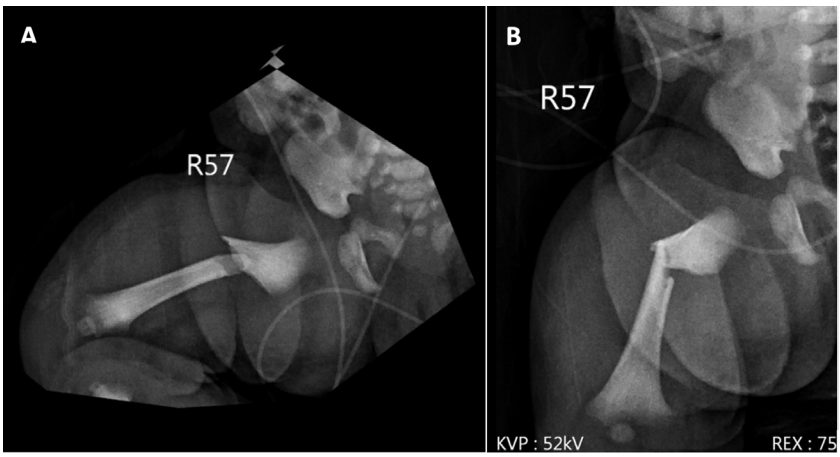
Author Affiliations: University of Chicago Pritzker School of Medicine, Chicago, Illinois (Aggarwal); Department of Pediatrics, St. Mary Medical Center, Hobart, Indiana (Chandra).

Corresponding Author: Sarthak Aggarwal, email sarthak.aggarwal@uchicagomedicine.org; ORCID ID 0000-0001-9887-1223

traction and rotation was deemed necessary to successfully extract the neonate. Upon this internal rotation, a "pop" was felt at the level of the hip, and this exam finding was noted by the obstetrician.

The attending obstetrician communicated this finding with the attending neonatologist, who promptly examined the infant. The infant was found to have crepitus upon palpation of the right thigh, with only slight swelling of the area. The circumference of the right thigh was noted be 1 centimeter greater than that of the left thigh. Neurovascular exam was intact, with distal pulses, sensation, and motor tone intact immediately following delivery. The infant was noted to be irritable, though this observation was largely nonspecific. Laboratory workup was also unremarkable at the time. Anterior posterior and lateral view x-rays were obtained given the high index of suspicion for fracture, and imaging demonstrated an oblique fracture of the proximal femoral diaphysis with a rotational component (Figure). Of note, there was no dislocation at the hip noted on radiographic imaging, and gentle manipulation while holding proximal to the fracture site produced no frank dislocation. The infant was admitted to the neonatal intensive care unit for perinatal femur fracture and remained stable. Given the rare nature of this pathology and the lack of pediatric orthopedic specialists in the area, she was transferred to a tertiary medical center in a nearby city for further care.

Figure. Anterior Posterior View (A) and Lateral View (B)



At the tertiary center, a pediatric orthopedic surgeon and resident on call performed a physical exam. The exam ultimately revealed no gross deformity or skin changes over the extremity, and the patient continued to be neurovascularly intact; however, she cried upon manipulation of the affected extremity. Given the clinical context and imaging studies, as well as the lack of significant neurovascular compromise, she received a Pavlik harness for right lower extremity fracture immobilization and was discharged with plans for outpatient follow-up. The chest strap of the Pavlik harness was applied allowing space for respiration, the anterior leg strap was fastened to maintain hip flexion of roughly 90 degrees, and the posterior leg strap was fastened to produce roughly 45 degrees of abduction. It was advised that the harness be worn at all times with the exception of brief removal for bathing and sanitation. Follow-up was complicated by the tertiary center's specialists being out of network given the patient's insurance, and she was unable to return for follow-up. Instead, specialist follow-up with pediatric orthopedic surgery was pursued at another tertiary center. Healthy callus formation was noted at 3 weeks, and improved alignment and excellent healing were seen at subsequent follow-up visits. There were no complications during the follow-up period, and the patient's parents strictly adhered to immobilization recommendations and appropriate harness usage. She ultimately demonstrated a full recovery with complete healing of the femur and return to age-appropriate activity and function.

DISCUSSION

We observed a perinatal femur fracture in a full-term neonate following cesarean delivery for breech presentation. Cesarean delivery is recommended for breech delivery, but its role in reducing risk of birth trauma is a matter of debate. Even so, femur fractures related to delivery are exceptionally rare.[2,7]

A case series by Kancherla et al found the mean time to diagnosis to be 4 days for perinatal femur fractures, similar to prior studies.[7] While some femur fractures may be diagnosed soon after delivery due to more dramatic presentations, other cases may not be identified until much later due to a lack of symptoms or poor access to care.[2] In our case, the fracture was diagnosed immediately following delivery due to collaboration between the attending obstetrician and neonatologist, as well as identification of key physical exam findings. Close observation of neonates with risk factors for perinatal femur fracture—especially breech presentation or difficult extraction—also may help with early detection. A screening protocol may best address this, in which neonatologists examine such high-risk neonates to detect the aforementioned early physical exam signs.[7] Parents of at-risk neonates also should be educated on classic symptoms, as this may reduce delays in care after discharge.

Common presentations of perinatal femur fractures include thigh swelling, decreased mobility of the affected leg, focal tenderness, and irritability.[2,5,11] In the case presented here, a sound was heard during delivery, which prompted further examination by the neonatologist. Many of the classic symptoms noted above, such as soft tissue swelling, focal tenderness, and irritability, may present late and thus were not prominent on initial examination in our case.[2] However, the presence of crepitus was a key early exam finding in our case, even though it is one that may not be checked for

routinely. In the timeframe immediately following delivery, careful clinical examination for crepitus and decreased mobility may quicken diagnosis of perinatal femur fracture, as opposed to waiting for the emergence of other classic physical findings and may avoid unnecessary investigation for nonaccidental trauma associated with delayed discovery.

Perinatal femur fractures tend to be spiral fractures of the proximal femur, suggesting a torsional mechanism of injury in the delivery process.[1,7] In the case of a cesarean delivery, this may be due to poor maneuverability of the fetus given anatomic challenges (eg, uterine anatomy, small incision, fetal positioning) or poor delivery technique. In our case, a difficult extraction with torsion of the leg likely contributed to the fracture.[7,8] In vaginal deliveries, breech fixation at the pelvis may lead to excessive leg traction.[7] Unanticipated fracture patterns in the absence of excessive traction may necessitate further workup for other causes of fracture, including metabolic and musculoskeletal disorders. Nonaccidental trauma is another important consideration in fractures discovered after discharge. Notably, any forceful traction may result in long bone injury, and our case highlights the definite risk for femur fracture with cesarean delivery.[10]

Prognosis of birth-related femur fracture is generally excellent with appropriate diagnosis and treatment, and treatment is mostly nonoperative.[1,12] Given the superior healing capacity of infants and children relative to adults, surgical intervention is very rarely indicated. Furthermore, fractures generally heal well through secondary bone healing without any long-term sequelae, such as deformity, neurologic deficit, or limb-length discrepancy.[1] However, early diagnosis and treatment limits prolonged distress for both the infant and family and may avoid the need for nonaccidental trauma investigation. A variety of treatment options exist, all of which ultimately aim to immobilize the femur. Pavlik harness, splint, spica cast, and Bryant traction are all acceptable treatment methods that have been shown to be effective.[7,12]

A Pavlik harness was used in the present case, as it is inexpensive, simple to use, and allows for quick discharge. Though treatment with these harnesses is generally uncomplicated, Pavlik harnesses should still be monitored for possible complications, most notably femoral nerve palsy, avascular necrosis of the femoral head, and skin breakdown.[5,9] Femoral nerve palsy may result from excessive hip flexion, and patient families must be vigilant for leg weakness—particularly with knee extension. In contrast, avascular necrosis may occur with excessive abduction or otherwise improper positioning and is often accompanied by increasingly limited, painful hip movement that families may notice during diaper changes. Finally, skin irritation may occur due to excess tightness or poor positioning of harness straps, which should be checked regularly for underlying irritation. If symptoms arise, patient families should consult their care provider, who may then adjust the harness and perform a careful physical exam.

Given the necessity for such close follow-up and monitoring, a study by Givon et al posited that Pavlik harnesses may cause unnecessary distress to new parents versus inpatient care with Bryant traction, allowing for continuous professional nursing care.[12] However, in addition to Bryant traction being logistically challenging, the efficacy of this method may be rooted in the increased frequency and quality of communication between clinicians and family. Thus, while the ability of caretakers to closely provide care at home for their infant should be considered when weighing treatment options, high-quality communication with families and convenient follow-up should be prioritized when caring for such fractures.

In our case, a lack of orthopedic specialists comfortable with Pavlik harness application in the community required the patient to be transferred to a tertiary care facility in an adjacent state for Pavlik harness placement, and insurance issues necessitated follow-ups at a separate facility located significantly farther away. Thus, the present case not only highlights hurdles to timely and effective care but also underscores the logistical challenges of outpatient management and need for pediatric orthopedic care that is easily accessible. This is particularly relevant to socioeconomically disadvantaged families, who may not have the resources to travel hours for care and follow-up. Even in the absence of orthopedic specialist care, training in the basics of fracture care and immobilization techniques could allow for improved care in community settings. Such training may be directed towards neonatologists, pediatricians, and family medicine clinicians and may include training on reduction techniques, Pavlik harness and spica cast application, and general cast application workshops and principles. In the case presented here, a lack of local treatment options required the patient to seek regular care hours from home, contributing unnecessary stress to an already distressing situation.

Thus, despite advances in perinatal care, challenges persist in the timely diagnosis and management of perinatal femur fractures—particularly in regions with limited access to pediatric orthopedic expertise. Developing standardized protocols for the screening and management of neonates at risk for birth-related fractures could enhance early detection, decrease family distress, and expedite timely treatment and should be achieved through multidisciplinary efforts by obstetricians, pediatricians, and orthopedists. Such screening ideally would allow for pediatricians and obstetricians to identify key risk factors related to prenatal history and delivery method to stratify patients at high risk for such fractures and prompt further workup. Similar efforts to create screening guidelines have begun at our own institution to guide the identification and care of these fractures.

Additionally, efforts to improve access to specialized care, such as telemedicine consultations or regional referral networks, may mitigate the logistical barriers faced by families and clinicians in underserved areas. These relationships may begin through networking with local orthopedists as well as through the creation of formalized procedures for referrals and transfers to tertiary centers, as has recently begun in our institution. Further research is warranted to

explore the long-term implications of perinatal femur fractures and evaluate the effectiveness of different treatment modalities in optimizing outcomes for affected infants. Collaboration among perinatal and orthopedic specialists is essential to ensure comprehensive and coordinated care for these vulnerable patients. Ultimately, while the need for pediatric orthopedic specialists in the community may not be fixable immediately, mitigating patient and family distress is a critical part of improving care. Providing educational materials and clear communication about the excellent outcomes of these fractures, maintaining frequent follow-up with pediatric specialists and care coordinators, and building relationships with academic centers for smoother transitions of care are key strategies to make a meaningful impact.

CONCLUSIONS

We present a case of perinatal femur fracture following cesarean delivery for breech presentation. Perinatal femur fracture is a rare but distressing complication and should be diagnosed promptly with appropriate screening and exam. Cesarean delivery—especially difficult extractions with rotation of the leg—carries a definite risk for such fractures, and excessive traction should be avoided when possible. Early diagnosis is important and may be quickened by comprehensive screening and demonstration of early physical exam findings, such as crepitus—a "popping" sound upon delivery—and decreased limb mobility. These signs may emerge before other classic physical exam findings characteristic of fractures. Poor access to pediatric orthopedic providers may complicate the treatment course and be a source of additional distress for patients and their families. However, access to such care may be improved by educating local clinicians on the application of Pavlik harnesses, utilizing local orthopedists as immediate resources, and fostering robust partnerships with tertiary care centers for telemedicine consultations and clinical outreach.

Funding/Support: None declared.

Financial Disclosures: None declared.

Acknowledgements: Written and signed informed consent was provided by the patient's guardian for patient information and images to be published (in print and online).

REFERENCES

1. Morris S, Cassidy N, Stephens M, McCormack D, McManus F. Birth-associated femoral fractures: incidence and outcome. *J Pediatr Orthop.* 2002;22(1):27-30. doi:10.1097/01241398-200201000-00007

2. Kanai Y, Honda Y, Honda T, Sanpei M. Delayed birth-related femur fracture after cesarean section: a case report. *AJP Rep*. 2018;8(3):e158-e160. doi:10.1055/s-0038-1667190

3. Curtelin C, Delille E, Bailly C, et al. Femoral fracture during breech vaginal delivery: a case report. *J Gynecol Obstet Hum Reprod.* 2022;51(3):102310. doi:10.1016/j.jogoh.2022.102310

4. von Heideken J, Thiblin I, Högberg U. The epidemiology of infant shaft fractures of femur or humerus by incidence, birth, accidents, and other causes. *BMC Musculoskelet Disord.* 2020;21(1):840. doi:10.1186/s12891-020-03856-4

5. Pavone V, Vescio A, Montemagno M, et al. Perinatal femoral fracture: a ten-year observational case series study. *Children*. 2020;7(10):156. doi:10.3390/children7100156

6. Bombah FM, Ngalame AN, René E, et al. Obstetric fracture of the femur during cesarean section in a preterm baby: a case report. *J Orthop Orthop Surg.* 2021;2(3):22-24. doi: 10.29245/2767-5130/2021/3.1150

7. Kancherla R, Sankineani SR, Naranje S, et al. Birth-related femoral fracture in newborns: risk factors and management. *J Child Orthop*. 2012;6(3):177-180. doi:10.1007/s11832-012-0412-4

8. Rijal L, Ansari T, Trikha V, Yadhav CS. Birth injuries in caesarian sections: cases of fracture femur and humerus following caesarian section. *Nepal Med Coll J.* 2009;11(3):207-208.

9. Awariwar MD, Iqbal MS, Jayamol MK, Bhat V. Management of a neonatal femoral shaft fracture following breech presentation: a case report. *J Mar Med Soc*. 2022;24(3) S104-S106. doi:10.4103/jmms.jmms_193_20

10. Vellingiri K, Venkataraman S, Shanthappa AH, Seenappa H. Femur shaft fracture in newborns: a report of two cases. *Cureus*. 2021;13(1):e12504. doi:10.7759/cureus.12504

11. Moore MK, Zwemer E, Lohr JA. Femur fracture in a newborn. *Consultant*. 2018;58(11):316-317.

12. Givon U, Sherr-Lurie N, Schindler A, Blankstein A, Ganel A. Treatment of femoral fractures in neonates. *Isr Med Assoc J.* 2007;9(1):28-29.

Extremely Early Onset Type 1 Diabetes in the Emergency Setting: A Unique Presentation of a Common Childhood Onset Disease

Erin Whiteford, MD, MS; Amy Drendel, DO, MS

ABSTRACT

Introduction: As the prevalence of type 1 and type 2 diabetes continues to increase, hospitals have developed protocols for managing its many complications, particularly diabetic ketoacidosis. However, extremely early onset type 1 diabetes, defined as onset at age < 2 years old, remains a diagnostic challenge to the community clinician.

Case Presentation: We report a case report of a 19-month-old female thought to have acute on chronic constipation who presented to our pediatric emergency department and was subsequently found to be in diabetic ketoacidosis.

Discussion: This case emphasizes the importance of maintaining a high suspicion for this potentially lethal disease presentation, as well as the variety of symptoms that can occur with it.

Conclusions: The limited communicative ability of the pediatric population often results in unclear or vague initial complaints at disease onset. This has led to a paucity of literature and knowledge surrounding the diagnosis of extremely early onset type 1 diabetes, making delayed diagnosis and its associated complications commonplace.

INTRODUCTION

Diabetes is a disorder in which the body does not produce enough insulin or does not respond appropriately to insulin, in turn causing the blood glucose level to be abnormally high.[1] As diabetes has become increasingly common over the past decade, an abundance of research has surfaced.[2-4] A robust portion of this research is devoted to determining the etiology of the disease, of which both genetic and environmental factors have been implicated.[1-3] Although type 1 diabetes classically has been considered a disease of childhood and type 2 a disease of adults, there has been an uptrend in the prevalence of both across each age group.[2-3] Despite this, among those diagnosed with type 1 diabetes, it is most frequently discovered in a biphasic distribution: from the ages of 4 to 7 and later, from the ages of 10 to 13 years.[2-4] Although diabetes is associated with several comorbidities as well as mortality in the long term, the challenges of a timely diagnosis in the pediatric population, coupled with the high prevalence of diabetic ketoacidosis (DKA) at initial presentation (30%) in this group, has prompted the development of several guidelines and protocols at major children's hospitals in an attempt to quickly identify and treat this condition.[5,6]

DKA is defined as diabetes with the following features: hyperglycemia (blood glucose > 200 mg/dL), metabolic acidosis (serum bicarbonate < 18 mmol/L or venous pH < 7.3), and ketosis (ketones in the urine or blood).[7] A 2022 systematic review revealed the following major risk factors as being associated with an increased likelihood that a patient would present in DKA: age < 2 years at onset/diagnosis, being part of an ethnic minority population, delayed diagnosis/missed diagnosis, and presenting during the COVID-19 pandemic.[8] In particular, it is postulated that younger children are at increased risk of delayed diagnosis and, thus, DKA at presentation due to the inability or difficulty of obtaining a concrete clinical history – especially pertaining the classic triad of polyuria, polydipsia, and polyphagia (often with associated weight loss).[10-12] Alternatively, others have hypothesized that the higher rate of DKA at time of diagnosis in this population is due to a more severe autoimmune phenotype, as evidenced by higher titers of multiple diabetes-associated antibodies as well as lower c-peptide levels at diagnosis.[13]

• • •

Author Affiliations: Children's Hospital of Wisconsin - Milwaukee Campus and Medical College of Wisconsin and Affiliated Hospitals, Milwaukee, Wisconsin (Whiteford, Drendel).

Corresponding Author: Erin Whiteford, MD, MS, Children's Hospital of Wisconsin - Milwaukee Campus, 8915 W Connell Ct, Milwaukee, WI 53226; email Ewhiteford@mcw.edu; ORCID ID 0009-0009-3658-3803

TableE4: . Patient's Vital Sign Trends Throughout Emergency Department (ED) Course and at Time of Discharge

	Heart Rate[a] (RR 90-140 bpm)	Blood Pressure[a] (RR 86-106/42-63 mmHg)	Respiratory Rate[a] (22-37 rpm)	Temperature (axillary)	SpO_2
On presentation to the ED	138	135/90	36	36 °C (96.8 °F)	100%
After 1st intravenous fluid bolus	128	109/78	24	N/A	100%
After 2nd intravenous fluid bolus	124	101/51	31	N/A	100%
At time of discharge from hospital	116	104/62	22	36.4 °C (97 °F)	100%

Abbreviations: RR, references ranges; bpm, beats per minute; rpm, respirations per minute; mmHg, millimeters of mercury; SpO_2, peripheral oxygen saturation.
[a]RRs are provided based on Pediatric Advanced Life Support (PALS) through the American Heart Association (AHA) 2020.
Consider individual's baseline values, as aberrations are expected depending on illness condition, stress

Although the most common presenting complaint at initial type 1 diabetes diagnosis in the overall pediatric population is polyuria (92% in 1 study), the most common complaint in children < 2 years old with new onset type 1 diabetes is poorly defined.[7]

Given the rarity of this early life diagnosis, literature is relatively sparse. However, Quinn et al noted that parents frequently brought their young children to medical attention for nonspecific complaints, including abdominal pain, dehydration, and fatigue.[14] Further, the classic symptoms of hyperglycemia, such as enuresis, polydipsia, polyuria, polyphagia, candidiasis, and fatigue, were reported less frequently in patients less than 2 years of age compared to those from 2 to 4 years old and 4 to 6 years old.[14] Several studies suggest this is due to limited communicative ability, diaper wearing, and shorter duration of symptoms prior to progression to significant metabolic derangement and critical illness.[11,14-15]

In addition to delayed diagnosis, the severity of clinical status at presentation is often worse due to the overall higher metabolic rate of these young patients, exacerbating the effects of dehydration, as well as their immature cerebral autoregulatory systems, predisposing them to cerebral edema, a feared and often fatal complication of DKA.[9-11,14-15] Despite the rarity of extremely early onset type 1 diabetes, the high risks associated with delayed or missed diagnosis make it imperative for the emergency medicine provider to remain vigilant when tasked with caring for the acutely ill toddler.

The following case demonstrates the importance of directed questioning and the need for maintenance of high suspicion for underlying occult pathology in the young pediatric population presenting with common complaints.

CASE PRESENTATION

A 19-month-old female presented to our pediatric emergency department (ED) with worsening constipation and abdominal pain. She was born near term (37 weeks 6 days gestation) and was small for gestational age at birth (1.59 percentile based on weight for age data from the Centers for Disease Control and Prevention [CDC] and the World Health Organization [WHO]). According to her parents and chart review, the patient had a long history of constipation (since the "first couple months of life"). It was documented that she did pass meconium within the first 48 hours of life. Regular primary pediatrician office visits documented a long-term history of constipation that previously had been well controlled with daily prune juice administration. Her recorded weights were at or below the 10th percentile for age (based on weight for age data from CDC and WHO) prior to the month leading up to presentation, consistently following her individual growth curve as would be expected. Her parents reported no changes in diet or suspicion for toxic/abnormal ingestions leading up to this presentation. Prior encounters clinicians in the week leading up to presentation noted decreased oral intake, increased fatigue, abdominal distension and pain, and lack of a recent bowel movement.

On arrival to the ED, the patient was notably fussy, dehydrated, and had a distended abdomen with hypoactive bowel sounds and a palpable stool burden. Vital signs throughout the clinical course are documented in the Table. She appeared thin and small for her age, which was corroborated on review of her growth chart (2nd percentile weight for age, down from the 10th percentile at a well child checkup 1 month prior). Abdominal x-ray was notable for a large stool burden with otherwise unremarkable findings. Chart review noted that she had lost approximately 1 kg over the prior month. Based on stool burden, exam, and history, a normal saline enema was administered without subsequent bowel movement over the next hour, after which a soap suds enema was administered, with modest stool production.

On repeat exam, the patient was fatigued with dry mucous membranes with persistent abdominal distension and tenderness, at which point a peripheral intravenous (IV) line was placed and a 1-time 20 ml/kg normal saline bolus was administered. Gastroenterology was consulted due to impressive stool burden and concern for weight loss in the setting of life-long constipation, warranting additional workup for failure to thrive. Repeat exam and vital sign review revealed a persistently dehydrated child, prompting an additional 20 ml/kg normal saline bolus. Given her minimal response to therapies, a comprehensive metabolic panel was run using blood initially obtained and held at the time of IV placement, to assess baseline electrolyte status in addition to general kidney and liver function prior to hospital admission. Laboratory results were notable for a severe

metabolic acidosis with a bicarbonate of < 8 mg/dL and an elevated anion gap of > 19 (using bicarbonate of 8), as well as blood glucose of 250 mg/dL.[1] The patient remained hemodynamically stable on maintenance IV fluids while further workup was done to evaluate the anion gap metabolic acidosis, including serum lactic acid, beta-hydroxybutyrate, and urinalysis. The urinalysis quickly revealed large ketones and glucosuria, consistent with DKA and associated new onset diabetes. Subsequently, the lactic acid was found to be normal and the beta-hydroxybutyrate level was elevated, also consistent with DKA. Because of the patient's severe metabolic acidosis and young age, she was admitted to the pediatric intensive care unit for further stabilization and management.

After diagnosis, the patient was placed on the "2 bag system" (simultaneous administration of an insulin drip and dextrose-containing fluid), after which her DKA quickly corrected within the next 24 hours, along with return to baseline neurologic status. She was subsequently transferred to the acute care floor for new onset diabetes parental teaching, as well as subcutaneous insulin administration training and titration prior to discharge. Close follow-up in the diabetes clinic was scheduled for later that week. Serum testing for type 1 diabetes-associated autoantibodies returned positive for GAD65 and highly sensitive insulin autoantibodies, confirming the diagnosis. She continues to follow-up with endocrinology and regularly attends her local primary pediatrician appointments with significant improvement in her weight trends (at age 35 months, weight was approximately 30th percentile for age consistently).

DISCUSSION

Unexpectedly, this patient who presented to the ED with complaints of constipation and abdominal pain was diagnosed with new onset type 1 diabetes after laboratory evaluation was obtained for dehydration and concern for failure to thrive. Given her young age, she was classified as extremely early onset type 1 diabetes, which carries a more severe prognosis.[3] It is postulated that individuals who develop type 1 diabetes at < 2 years of age have a more severe autoimmune phenotype, which leads to excessive beta cell destruction early in life.[3,14-16] Although extremely early onset diabetes is rare, the clinical pearls associated with such cases remain valuable across age groups for the pediatrician and emergency medicine provider, particularly for the patient presenting to the ED for acute on chronic abdominal pain with or without a history of constipation.[17-19]

The onset of constipation early in life, as in this case (around 4 to 6 months of age), requires additional investigation.[20-21] Our patient experienced constipation that had initially improved with over-the-counter therapies but worsened acutely leading up to presentation.

Constipation is a common childhood complaint that rarely has a known causative etiology, nor does every child warrant an extensive workup to determine one.[20-21] In this patient's case, her growth trends were consistently tracking along the 10th percentile or less for age, which is low but not necessarily pathologic if consistent for that individual patient.[22] The acute worsening of her baseline constipation prompted a medical encounter at which time she was appropriately referred to our ED. A combination of factors likely led to the false assumption that her symptoms all were linked to acute on chronic constipation. This point is evidenced by her notable down-trending growth curve percentiles ("falling off her growth curve") despite an intact appetite. Additionally, more directed discussions with the patient's parents after the diagnosis revealed the presence of polyuria and polyphagia. Although diabetes is a generally common diagnosis in the pediatric population, this patient's young age and her previously diagnosed constipation (although of unknown etiology) likely led to provider anchoring bias, affecting clinical judgement and decision-making pertaining to additional evaluation on subsequent presentations.[23]

Regardless of the etiology, there were additional clues making the astute clinician unable to write off her conglomeration of symptoms as secondary to solely constipation. The first of these key clues is weight loss and/or drop in growth percentiles. Consistently tracking in a low weight percentile can be normal but warrants frequent reassessment and monitoring.[22] Alternatively, weight loss in a young pediatric patient without explanation or with intact appetite is not normal, nor is constipation a sufficient explanation for it. A slew of gastrointestinal (GI) complaints/disorders are common in patients with type 1diabetes.[24] In a study of patients < 2 years old diagnosed with type 1 diabetes, 45% were noted to have weight loss prior to presentation, while about 10% reported constipation.[25] Although weight loss was reported among the majority of age groups at diagnosis, constipation was reported most in toddlers diagnosed at < 2 years of age.[25] Quinn et al found that parents were significantly less likely to report symptoms of hyperglycemia, such as polydipsia, polyuria, and polyphagia, in patients < 2 years old.[14] Although GI complaints are common in the emergency setting, we recommend quick review of the patient's growth curve to help guide the provider in terms of the true chronicity of the presenting condition as well as the severity of the issues described. Evaluation for the etiology of chronic constipation – especially in patients with symptom onset early in life coupled with marginal or no response to standard first-line medical therapies – is warranted as it can be associated with multiple additional health issues or be masking an occult systemic pathology.[18-21,24,26-28] The patient presenting with acute on chronic abdominal pain requires astute history gathering and examination with each presentation in order to ensure an underlying condition is not missed. Abdominal complaints – especially lower gastrointestinal complaints such as constipation, diarrhea, or an alternating pattern – can be a symptom of undiagnosed diabetes.[24]

The patient's altered mental status represented another diagnostic clue. This can be difficult to ascertain in a 19 month old

who is not feeling well, as there is often a high component of stranger anxiety in the hospital setting.[29] However, her transition from apprehensive of the medical team to sleeping uninterrupted despite their presence, was a notable derivation from baseline. With increased rates of DKA at diagnosis in younger patients, the risk of cerebral edema and, thus, neurologic status aberrations secondary to metabolic derangement also is increased.[8,10-13,30,31] This highlights the importance of serial exams and evaluation after each intervention. Serial exams in this patient appropriately cued the physicians to consider a broader differential and perform laboratory testing that led to the diagnosis.

Lastly, vital sign aberrations and examination findings out of proportion to the described clinical course or medico-social history warrant further evaluation, especially in the pediatric population where history gathering is often difficult. In the case presented here, the patient was significantly more dehydrated than would be expected based on history and context. This was evidenced by her minimal response to the initial fluid bolus and signs of hemoconcentration on lab evaluation. In a child with decreased oral intake but no emesis or diarrhea, one would not expect such profound dehydration as was demonstrated here. Seemingly small or insignificant hemodynamic changes are often the first manifestation of an underlying pathology at play.[32-34] Continued review—especially by adult emergency medicine providers—of normal age range standards is imperative, as is monitoring of hemodynamic trends in patients throughout their stay (ie, heart rate before and after fluid bolus).[35]

CONCLUSIONS

Extremely early onset type 1 diabetes is a rare diagnosis of a well-known pediatric disease that often presents with a vague constellation of symptoms. We present the case of a young child thought to have acute on chronic constipation who was subsequently found to be in DKA. Clinicians should remain vigilant when caring for this unique population to avoid anchoring bias and obtain appropriate work-up as to not miss this high-risk condition.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Baumer-Mouradian SH, Gray M, Wolfgram P, et al. Improving emergency department management of diabetic ketoacidosis in children. *Pediatrics*. 2019;144(4):e20182984. doi:10.1542/peds.2018-2984

2. National and State Diabetes Trends. Centers for Disease Control and Prevention. Last reviewed May 17, 2022. Accessed September 2023. https://archive.cdc.gov/www_cdc_gov/diabetes/library/reports/reportcard/national-state-diabetes-trends.html.

3. Diabetes in Young People is on the Rise. Centers for Disease Control and Prevention. Updated May 15, 2024. Accessed September 2023. https://www.cdc.gov/diabetes/data-research/research/young-people-diabetes-on-rise.html?CDC_AAref_Val=https://www.cdc.gov/diabetes/research/reports/children-diabetes-rates-rise.html.

4. Wagenknecht LE, Lawrence JM, Isom S, et al; SEARCH for Diabetes in Youth study. Trends in incidence of youth-onset type 1 and type 2 diabetes in the USA, 2002-18: results from the population-based SEARCH for Diabetes in Youth study. *Lancet Diabetes Endocrinol*. 2023;11(4):242-250. doi:10.1016/S2213-8587(23)00025-6.

5. Jensen ET, Stafford JM, Saydah S, et al. Increase in prevalence of diabetic ketoacidosis at diagnosis among youth with type 1 diabetes: The SEARCH for Diabetes in Youth study. *Diabetes Care.* 2021;44(7):1573-1578. doi:10.2337/dc20-0389.

6. Zee-Cheng JE, Webber EC, Abu-Sultaneh S. Adherence to pediatric diabetic ketoacidosis guidelines by community emergency departments' providers. *Int J Emerg Med.* 2017;10(1):11. doi:10.1186/s12245-017-0137-8.

7. Wolfsdorf JI, Glaser N, Agus M, et al. ISPAD clinical practice consensus guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *Pediatr Diabetes.* 2018;19 Suppl 27:155–177. doi:10.111/pedi.12701.

8. Rugg-Gunn CEM, Dixon E, Jorgensen AL, et al. Factors associated with diabetic ketoacidosis at onset of type 1 diabetes among pediatric patients: a systematic review. *JAMA Pediatr.* 2022;176(12):1248-1259. doi:10.1001/jamapediatrics.2022.3586.

9. Wolfsdorf, J. I. The International Society of Pediatric and Adolescent Diabetes Guidelines for management of diabetic ketoacidosis: Do the guidelines need to be modified? *Pediatr Diabetes.* 2014;15(4):277–286. doi:10.1111/pedi.12154

10. Daneman D, Frank M, Perlman K, Wittenberg J. The infant and toddler with diabetes: Challenges of diagnosis and management. *Paediatr Child Health.* 1999;4(1):57-63. doi:10.1093/pch/4.1.57.

11. Bui H, To T, Stein R, Fung, K, Daneman D. Is diabetic ketoacidosis at disease onset a result of missed diagnosis? *J Pediatr.* 2010;156(3):472-477. doi:10.1016/j.jpeds.2009.10.001

12. Usher-Smith JA, Thompson MJ, Sharp SJ, Walter FM. Factors associated with the presence of diabetic ketoacidosis at diagnosis of diabetes in children and young adults: a systematic review. *BMJ*. 2011;343:d4092. doi:10.1136/bmj.d4092.

13. Sales Luis M, Alcafache M, Ferreira S, et al. Children with type 1 diabetes of early age at onset - immune and metabolic phenotypes. *J Pediatr Endocrinol Metab*. 2019;32(9):935-941. doi:10.1515/jpem-2019-0103.

14. Quinn M, Fleischman A, Rosner B, Nigrin DJ, Wolfsdorf JI. Characteristics at diagnosis of type 1 diabetes in children younger than 6 years. *J Pediatr.* 2006;148(3):366-371. doi:10.1016/j.jpeds.2005.10.029.

15. Johnson MB, Patel KA, De Franco E, et al; EXE-T1D Consortium; Ellard S, Flanagan SE, Hattersley AT, Oram RA. Type 1 diabetes can present before the age of 6 months and is characterised by autoimmunity and rapid loss of beta cells. *Diabetologia*. 2020;63(12):2605-2615. doi:10.1007/s00125-020-05276-4.

16. de Vries L, Oren L, Lazar L, Lebenthal Y, Shalitin S, Phillip M. Factors associated with diabetic ketoacidosis at onset of Type 1 diabetes in children and adolescents. *Diabet Med*. 2013;30(11):1360-1366. doi:10.1111/dme.12252.

17. The anion gap. *Lancet*. 1977;309(8015):785–786. doi: 10.1016/s0140-6736(77)92963-4

18. Rodrigues ML, Motta ME. Mechanisms and factors associated with gastrointestinal symptoms in patients with diabetes mellitus. *J Pediatr (Rio J)*. 2012; 88(1):17-24. doi:10.2223/JPED.2153.

19. Menchise AN, Condino AA, Levitt MA, Hebra A, Wilsey MJ. Celiac disease and diabetes mellitus diagnosed in a pediatric patient with Hirschsprung disease. *Fetal Pediatr Pathol.* 2013;31(1):7-12. doi:10.3109/15513815.2012.659396.

20. Arakoni R, Kamal H, Cheng SX. Very early onset perinatal constipation: Can it be cow's milk protein allergy? *World J Gastroenterol.* 2023;29(33):4920-4926. doi:10.3748/wjg.v29.i33.4920.

21. Rao SS, Meduri K. What is necessary to diagnose constipation? *Best Pract Res Clin Gastroenterol.* 2011;25(1):127-140. doi:10.1016/j.bpg.2010.11.001

22. Fenton TR, Merlino Barr S, Elmrayed S, Alshaikh B. Expected and desirable preterm and small infant growth patterns. *Adv Nutr.* 2024;15(6):100220. doi:10.1016/j.advnut.2024.100220.

23. Iwai K, Tetsuhara K, Ogawa E, Kubota M. Hidden diagnosis behind viral infection: the danger of anchoring bias. *BMJ Case Rep*. 2018;2018:bcr2018226613. doi:10.1136/bcr-2018-226613.

24. Leeds JS, Hadjivassiliou M, Tesfaye S, Sanders DS. Lower gastrointestinal symptoms are associated with worse glycemic control and quality of life in type 1 diabetes mellitus. *BMJ Open Diabetes Res Care.* 2018;6(1):e000514. doi:10.1136/bmjdrc-2018-000514.

25. Roche EF, Menon A, Gill D, Hoey H. Clinical presentation of type 1 diabetes. *Pediatr Diabetes*. 2005;6(2):75-78. doi:10.1111/j.1399-543X.2005.00110.x.

26. Pini Prato A, Erculiani M, Novi ML, et al. Delayed diagnosis in Hirschsprung disease. *Pediatr Surg Int.* 2024;40(1):65. doi:10.1007/s00383-024-05657-5.

27. Bianchi PI, Lenti MV, Petrucci C, et al. Diagnostic delay of celiac disease in childhood. *JAMA Netw Open*. 2024;7(4):e245671. doi:10.1001/jamanetworkopen.2024.5671.

28. Freedman SB, Rodean J, Hall M, et al. Delayed diagnoses in children with constipation: multicenter retrospective cohort study. *J Pediatr.* 2017;186:87-94.e16. doi:10.1016/j.jpeds.2017.03.061.

29. Lerwick JL. Minimizing pediatric healthcare-induced anxiety and trauma. World J Clin Pediatr. 2016;5(2):143-150. doi:10.5409/wjcp.v5.i2.143.

30. Gregory J, Basu S. Diabetic ketoacidosis, hyperuricemia and encephalopathy intractable to regular-dose insulin. *J Pediatr Endocrinol Metab*. 2017;30(12):1317-1320. doi:10.1515/jpem-2017-0225.

31. Mackay MT, Molesworth C, Northam EA, Inder TE, Cameron FJ; DKA Brain Injury Study Group. Diabetic ketoacidosis and electroencephalographic changes in newly diagnosed pediatric patients. *J Pediatr Diabetes*. 2016;17(4):244-248. doi:10.1111/pedi.12284.

32. Loomba RS, Villarreal EG, Farias JS, Flores S, Bronicki RA. Fluid bolus administration in children, who responds and how? A systematic review and meta-analysis. *Paediatr Anaesth*. 2022;32(9):993-999. doi:10.1111/pan.14512.

33. Janak JC, Howard JT, Goei KA, et al. Predictors of the onset of hemodynamic decompensation during progressive central hypovolemia: comparison of the peripheral perfusion index, pulse pressure variability, and compensatory reserve index. *Shock*. 2015;44(6):548-553. doi:10.1097/SHK.0000000000000480.

34. Suresh MR, Chung KK, Schiller AM, Holley AB, Howard JT, Convertino VA. Unmasking the hypovolemic shock continuum: the compensatory reserve. J Intensive Care Med. 2019;34(9):696-706. doi:10.1177/0885066618790537.

35. Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric basic and advanced life support 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. American Academy of Pediatrics, 2021. doi:10.17615/eejb-xq50

The University of Wisconsin Undiagnosed Disease Program: Unveiling Rare Neurodevelopmental Disorders in Exome-Negative Patients

Jadin M. Heilmann; April L. Hall, PhD, MS, CGC; Janet M. Legare, MD; Gregory M. Rice, MD; Kristin A. Seaborg, MD; Derek M. Pavelec, PhD; Xiangqiang Shao, PhD; Vanessa Horner, PhD; M. Stephen Meyn, MD, PhD; Bryn D. Webb, MD

ABSTRACT

Introduction: The University of Wisconsin Undiagnosed Disease Program employs a "beyond the exome" approach to diagnose rare disease patients.

Case Presentations: We present 2 cases of rare neurodevelopmental disorders identified by whole genome sequencing. The first is a 12-year-old boy with global developmental delay/intellectual disability (GDD/ID) and congenital hypotonia who was diagnosed with *CAPZA2*-related disorder. The second is a 13-year-old boy with microcephaly, GDD/ID, and seizures who was diagnosed with neurodevelopmental disorder with language delay and behavioral abnormalities, with or without seizures (NEDLAS).

Discussion: Our use of whole genome sequencing identified the fifth reported case of *CAPZA2*-related neurodevelopmental disorder. Fewer than 40 patients have been reported with NEDLAS, and we identified the fourth patient with the *AGO1* in-frame deletion p.Glu376del.

Conclusions: Whole genome sequencing can be effective in diagnosing patients with suspected genetic disorders despite negative standard of care clinical genetic testing and enables the practice of precision medicine.

INTRODUCTION

Over 26 million Americans are affected by rare genetic disorders, resulting in significantly higher annual health care costs than common conditions such as heart disease and cancer. Both pediatric and adult patients with rare diseases experience longer hospital stays, higher admission charges, increased readmissions, and elevated mortality rates compared to individuals with common conditions.[1] Rare diseases also remain the leading cause of infant mortality.[2] Intellectual disability (ID) and global developmental delay (GDD) are among the most frequently reported impairments in children, with GDD affecting 1% to 3% of children under the age of 5 and ID affecting 1.10% of children ages 3 to 17 years old.[3,4]

GDD is defined as significant delays in 2 or more developmental domains in children less than 5 years of age, while ID is defined as having significant limitations in both intellectual functioning and adaptive behavior.[5] Numerous testing routes can be pursued to determine the etiology of GDD/ID, including chromosomal microarray and whole exome sequencing, which are now standard-of-care tests ordered in outpatient clinics. A chromosomal microarray is a test that detects regions of genomic imbalances termed copy number variation. Whole exome sequencing involves sequencing the protein-coding regions of the genome. This "coding" portion of the genome is called the exome. The human exome represents < 2% of the genome but contains approximately 85% of known disease-related variants.[6] The diagnostic yield of chromosomal microarray in cases of GDD/ID ranges from 4.5% to 28.0% (median 13.7%), while the diagnostic yield of whole exome sequencing ranges from 28% to 43% (average 34%).[7] However, the majority of patients with GDD/ID remain undiagnosed after these evaluations, indicating the need for further work to provide specific diagnoses for these patients and families. The University of Wisconsin Undiagnosed Disease Program (UW UDP) employs whole genome sequencing to discover novel disease genes and variants to enable diagnoses of ultra-rare genetic

• • •

Author Affiliations: Center for Human Genomics and Precision Medicine, University of Wisconsin School of Medicine and Public Health (UW SMPH); Madison, Wisconsin (Heilmann, Hall, Meyn, Webb); Department of Pediatrics, UW SMPH, Madison, Wisconsin (Hall, Legare, Rice, Shao, Meyn, Webb); Gunderson Health System, LaCrosse Clinic, LaCrosse, Wisconsin (Rice); Department of Neurology, UW SMPH, Madison, Wisconsin (Seaborg); Biotechnology Center, UW – Madison; Madison, Wisconsin (Pavelec); Wisconsin State Laboratory of Hygiene; Madison, Wisconsin (Shao, Horner); Department of Pathology, UW SMPH; Madison, Wisconsin (Horner).

Corresponding Author: Bryn D. Webb, MD, 1111 Highland Ave, Office 2792, Madison, WI 53705; phone 608.262.2559; email bdwebb@wisc.edu; ORCID ID 0000-0001-6174-4677

disorders. We choose whole genome sequencing as a first-line test given that most referred patients already have had negative clinical whole exome sequencing, and a whole exome sequencing to whole genome sequencing approach leads to higher program costs. Here, we present 2 cases of suspected neurodevelopmental disorders of genetic etiology with negative clinical exome testing that we diagnosed using whole genome sequencing.

CASE PRESENTATIONS

Case 1

A 12-year-old male was referred to the UW UDP for neurodevelopmental concerns, including motor and speech delays and severe congenital hypotonia. He was born at 38 weeks gestation by emergency cesarean delivery due to fetal heart rate deceleration and failure to progress. At birth, he experienced breathing difficulties requiring supplemental oxygen and had a small right pneumothorax, which resolved spontaneously. His Wisconsin state newborn screen was normal. At 3 weeks of age, he presented to the emergency department with excessive vomiting and was diagnosed with pyloric stenosis, which was treated surgically. Between 7 and 10 months, he was hospitalized 4 times for respiratory infections exacerbated by hypotonia, making it difficult for him to clear his airway, and he was later diagnosed with early childhood asthma. At 10 months, At 10 months, he was identified to have significant developmental delays, achieving expressive language skills expected of a 3- to 4-month old, receptive language skills expected of an 8-month old, fine motor skills expected of a 4- to 5-month old, and gross motor skills expected of a 5-month old. At 12 months, his head circumference was measured at the 98th percentile (Z-score = 2.16). Magnetic resonance imaging (MRI) and head ultrasound revealed an incidental finding of a 3 mm cystic intradural lesion, but it was otherwise normal. At 14 months, a screening electrocardiogram showed sinus arrhythmia and findings of biventricular hypertrophy; however, an echocardiogram was normal. He was able to sit alone at 2 years and walk without help between 3 and 4 years. He was able to run at 9 years.

At 9 years and 6 months of age, moderate dilation of the ascending aorta was noted on echocardiogram (2.6 cm, Z-score = 4.3) with normal aortic root size. Follow-up echocardiogram at 12 years and 7 months revealed moderate dilation of the ascending aorta to similar degree (3.1 cm, Z-score = 4.2) with normal aortic root size. At 10 years old, the patient was diagnosed with autism after presenting with echolalia, repetitive verbalizations, and sensory-seeking behaviors. He also had thrombocytopenia identified consistently from age 19 months to 13 years, ranging from 75 K/uL to 145 K/uL and most often <120 K/uL.

Since age 12 years, the patient has used words in combination with a communication device to communicate. He is able to follow simple commands with a gesture. He is unable to walk long distances and uses a wheelchair or stroller. His physical exam at this time indicated weight of 34.5 kg (19.37%), height of 1.444 m (26.92%), and head circumference of 55.5 cm (88.03%).

At 13 years old, neurological exam revealed generalized hypotonia with decreased muscle bulk and size in biceps, triceps, quadriceps, soleus and gastrocnemius bilaterally. He has intrinsic hand muscles with decreased tone and bulk. He sits in a "W" position, and he is unable to rise from lying down to a seated position independently but can sit up from lying down with gentle assistance. He rises to stand from a seated position on the ground using ground and nearby structures to support himself in a modified Gower sign. He is not able to hold a squatting position. He has an intention tremor at reach in upper extremities bilaterally but no dysmetria. His upper extremity biceps and brachioradialis reflexes are 2+ and symmetric. His bilateral patellar reflexes are 1+, and he has a trace Achilles reflex bilaterally. He has a shuffling gait with limited plantarflexion and bilateral pronation at the ankles and knees.

Genetic testing for spinal muscular atrophy, myotonic dystrophy, Prader Willi, and Fragile X syndromes, as well as chromosomal microarray analysis, were negative. For metabolic evaluation, his acylcarnitine profile, plasma amino acids, urine organic acids, plasma and cerebrospinal fluid lactate and neurotransmitter profiles, and muscle biopsy for electron microscopy and mitochondrial depletion studies were normal. Whole exome sequencing completed in 2021 did not provide a definitive diagnosis, and the patient was referred to the UW UDP where whole genome sequencing was completed. For this sequencing, DNA was isolated from peripheral blood samples from the proband and mother; the father was unavailable for testing. Libraries were prepared and short-read, paired end, 150 base pair sequencing was obtained. FASTQ files were aligned to the human reference genome (GRCh38), and germline variant calling was performed using DRAGEN, which identifies single nucleotide variants, copy number variations, and structural variations. Variant calls were analyzed by the study team, which includes a board-certified clinical molecular geneticist. The team identified a disease-causing missense variant in *CAPZA2* c.776G>T; p.Arg259Leu, which was not inherited from the mother, and diagnosed the proband with *CAPZA2*-related disorder. See Case 1 discussion below for details.

Case 2

A 13-year-old male with global developmental delays, intellectual disability, seizures, and postnatal microcephaly was referred to the UW UDP. He was born at full term by normal spontaneous vaginal delivery after an uncomplicated pregnancy. After birth, he failed his newborn hearing screen twice and was diagnosed with mild bilateral sensorineural hearing loss at 2 months old. At 3 months, he was evaluated by genetics, who noted plagiocephaly, high-arched palate, minor ear anomalies, low hairline, umbilical hernia, and bilateral clubfoot. By 7 months, he developed postna-

Table 1. Clinical Features of All Known Individuals With CAPZA2-related Disorder

	UW UDP	Huang et al[9]		Pi et al[10]	Zhang et al[11]
	Case 1 Patient	Patient 1	Patient 2	Patient 1	Patient
Origin	European	Chinese	European	Chinese	ND
Variant	p.Arg259Leu	p.Arg259Leu	p.Lys256Glu	p.Arg260del	c.219+1G>A Splicing
Inheritance	Not inherited from mother, father unavailable	*de novo*	*de novo*	*de novo*	*de novo*
Gender	Male	Female	Female	Female	Male
Age	12 years	2.5 years	9 years	10 months	3 years
Growth					
Short stature	–	–	–	ND	–
Microcephaly	–; macrocephalic	–	–	+	–
Dysmorphic features	–	–	–	ND	ND
Development					
Speech delay	+	+	+	NA	–
Motor delay	+	+	+	+	–
Intellectual disability	+	NA	+	NA	+
Neurological					
Autism	+	NA	+	NA	–
Hypotonia	+	+	+	+	–
Seizure history	–	+; atypical febrile seizure	+; developed seizures at 7 months and infantile spasm occurred at 10 months	+; developed spasms at 3 months	+; 7 seizure episodes, 5 of which were febrile seizures
Magnetic resonance imaging abnormality	+; 3-mm cystic intradural lesion on spine	–	+; mild abnormal myelination in frontal area, mild perivascular space dilation in parietal and occipital area	–	+; septal pellucidum cyst and bilateral mastoiditis
Others					
Neonatal feeding difficulty	+	+	+	+	–
Additional findings	+; moderate dilation of ascending aorta; history of thrombocytopenia; pyloric stenosis; toe walking	–	+; hypopigmentation on right lower leg, hyper pigmentation upper legs; toe walking	–	–

Abbreviations: UW UPD, University of Wisconsin Undiagnosed Disease Program; +, feature present; –, feature absent; NA, not applicable due to patient age; ND, not determined.

tal microcephaly, with his head circumference measuring at the 1st percentile (Z-score = -2.10).

By 22 months, the patient had eye-rolling spells and was diagnosed with epilepsy after an electroencephalogram showed frequent occipital spike and wave discharges and severely abnormal background with absence of sustained posterior dominant rhythm and sleep architecture. At 26 months, head MRI showed mild delay in white matter myelination in the parietal and temporal regions bilaterally, prominence of the lateral and third ventricles, and simplification of the sulcal pattern along the sylvian fissures. He began walking at 4 years old and spoke his first word at 5 years old.

Repeat MRI at 7 years old showed similar configuration of brain morphology with interval maturation of the sulcation and myelination in both frontal and temporal lobes. T2/FLAIR signal abnormalities were seen in the periatrial white matter of both cerebral hemispheres with additional involvement of the subcortical white matter in both parietal lobes. At 11 years old, neurology noted focal seizures, choreoathetotic movements, truncal hypotonia with spasticity of the extremities, and an ataxic gait. Currently, at 13 years old, the patient has a happy demeanor, is largely nonverbal, and uses a walker.

Extensive genetic testing, including chromosome analysis, chromosomal microarray, connexin *GJB2* sequencing for hearing loss, and Prader-Willi methylation polymerase chain reaction, were negative. In 2021 at age 11 years, whole exome sequencing revealed a heterozygous pathogenic variant in the *ADSL* gene, which causes an autosomal recessive inborn error of metabolism; however, the patient is presumed to be unaffected as biallelic variants were not identified. In addition, he was identified to have a heterozygous, maternally inherited, likely pathogenic variant in *PTPRQ* (c.4015+1G>A). Pathogenic variants in *PTPRQ* are known to cause autosomal dominant or autosomal recessive hearing loss.[8] Notably, the mother has no history of hearing loss, and few families have been reported with disease. At age 13 years, whole genome sequencing by the UW UDP identified a de novo

Table 2. Clinical Features of Individuals With the de novo *AGO1* p.Glu376 Deletion Pathogenic Variant

	UW UDP	Schalk et al[16]		Niu et al[17]
	Case 2 Patient	Patient in Family 21	Patient in Family 22	Patient 1
Origin	African American/ European	European	ND	ND
Variant	p.Glu376del	p.Glu376del	p.Glu376del	p.Glu376del
Gender	Male	Male	Female	Female
Age	13 years	3 years	ND	ND
Growth				
Postnatal microcephaly	+	+	+	+
Dysmorphic features	+	+	ND	ND
Development				
Speech delay	+	+	+	+
Motor delay	+	+	–	+
Intellectual disability	+	+	+	+
Neurological				
Autism	–	–	+	ND
Hypotonia	+	+	+	+
Seizure history	+	+; generalized seizures with corpus callosotomy at age 7 secondary to intractable seizure	–	–
Abnormal movements	+	ND	+	–
Abnormal brain magnetic resonance imaging (MRI)	+; prominent ventricles, signal abnormality in the periatrial and subcortical white matter	–; normal MRI at 10 months	ND	+; myelin dysplasia, mild widening of bilateral frontotemporal space, and mild widening and deepening sulcus fissure
Others				
Neonatal feeding difficulty	+	–	–	+
Additional findings	+; Bilateral sensorineural hearing loss; bilateral club foot	–	–	+; Mild deafness

Abbreviations: UW UPD, University of Wisconsin Undiagnosed Disease Program; +, feature present; –, feature absent; ND, not determined.
[a]Schalk et al reported 33 individuals with NEDLAS including 2 patients with the same p.Glu376del variant.

in-frame deletion in *AGO1* (c.901_903delGAG; p.Glu376del), diagnosing him with neurodevelopmental disorder with language delay and behavioral abnormalities, with or without seizures (NEDLAS). See Case 2 discussion below for details.

DISCUSSION

The UW UDP's use of whole genome sequencing identified the fifth reported case of *CAPZA2*-related disorder and the fourth patient with the in-frame deletion p.Glu376del in *AGO1*, which causes NEDLAS.

Case 1

CAPZA2 encodes an F-actin capping protein, CapZ, which is critical for dendritic spine development and neurodevelopment. Capping proteins such as CapZ terminate the elongation of actin filaments by binding at the barbed end of the tentacle domain.[12] This regulation is essential for maintaining the proper length and stability of actin filaments, which are integral to the cytoskeleton and play a pivotal role in cellular morphology, motility, and various intracellular processes.[12,13] Knockdown of capping proteins α and β2 subunits in hippocampal cultures results in a marked decline in spine density, altered spine morphology, and a reduced number of functional synapses.[13] This suggests that *CAPZA2* significantly influences the function of capping proteins in dendritic spine development, thus playing a critical role in neurodevelopment. It is postulated that variants in or near the highly conserved basic residues of the *CAPZA2* tentacle domain disrupt the regulatory function of CapZ, contributing to the pathogenesis of neurodevelopmental disorders.[14]

The variant we identified in *CAPZA2* c.766G>T (p.Arg259Leu) previously has been reported as pathogenic in the literature, and this variant, along with the other 2 previously reported variants p.Lys256Glu and p.Arg260del, affect highly conserved basic residues.[9,10] According to American College of Medical Genetics and Genomics (ACMG) guidelines, this variant is classified as "likely pathogenic" (PS2, PM2, PP3, and PP5 criteria).[15] The identification finding of our patient with *CAPZA2*-related disease further confirms the known phenotype of this disease. Our patient shares features of speech and motor delays, hypotonia, and neonatal feeding difficulties with the previously reported patients (Table 1). Notably, our patient has not had any known seizures, unlike the

4 other reported patients. Additionally, our patient had pyloric stenosis, moderate dilation of the ascending aorta, and thrombocytopenia. As additional patients are identified, further exploration can determine whether these features are a part of the clinical spectrum of *CAPZA2*-related disease.

Case 2

AGO1 encodes Argonaute-1, a protein essential for gene silencing mediated by small non-coding RNAs. In transcriptional gene silencing, *AGO1* forms RNA-induced transcriptional silencing complexes that recruit chromatin-modifying proteins to create heterochromatin, thereby preventing mRNA synthesis. In post-transcriptional gene silencing, *AGO1* binds small RNAs, guiding them to complementary mRNA targets to induce mRNA degradation or inhibit translation.[18] Pathogenic variants in *AGO1*, including the p.Glu376del variant, are predicted to alter the flexibility of the *AGO1* linker domains, which likely impairs function in mRNA processing.[16] The variant identified in this patient is classified as "likely pathogenic" per ACMG guidelines (PS2, PM2, PM4, and PP5 criteria).[15]

Our patient is the fourth reported case with the same pathogenic variant p.Glu376del, and all 4 cases have postnatal microcephaly, GDD/ID, and hypotonia (Table 2).[16,17] Forty-six percent of patients with NEDLAS have variable brain MR anomalies, and 46% of affected individuals have a history of seizures.[16] Notably, our patient also has bilateral clubfoot and bilateral sensorineural hearing loss. Another patient with this variant also has mild deafness, potentially expanding the known clinical spectrum of disease.[17] However, it is also possible that the hearing loss is not directly caused by the *AGO1* variant but, instead, is secondary to the previously identified likely pathogenic variant in *PTPRQ*, which is known to be associated with hearing loss. Further investigation into the etiology of our patient's bilateral sensorineural hearing loss is warranted.

CONCLUSIONS

The UW UDP employs whole genome sequencing to diagnose Mendelian diseases in previously undiagnosed patients. Our identification of the fifth reported case of *CAPZA2*-related disorder and the fourth case of NEDLAS with the *AGO1* in-frame deletion p.Glu376del highlights the power of participation in research studies when clinical whole exome sequencing is unrevealing.

In Case 1, an in-depth exploration of the coding regions by our team identified a disease-causing variant that was not reported on clinical whole exome sequencing. In Case 2, the identification of a disease-causing variant was enhanced by new scientific literature published after clinical whole exome sequencing was completed, highlighting the crucial role of undiagnosed disease programs in reexamining challenging cases where prior clinical whole exome sequencing results were negative.

In general, the UW UDP performs whole genome sequencing as the first-tier test as: (1) patients are most often referred to our program following negative clinical whole exome sequencing, (2) it has superior mapping quality over whole exome sequencing,[19] and (3) it is more comprehensive in the ability to detect noncoding variants, large structural rearrangements, and copy number variation.[19,20]

Making a rare disease diagnosis reduces the uncertainty experienced by patients, families, and caregivers and may improve the overall quality of care. Integrating advanced genomic techniques and continuous reanalysis of genome data holds significant promise for improving diagnostics, patient care, and outcomes through more effective and personalized health care solutions. Our findings reinforce the importance of long-term follow-up for patients, including exome reanalysis or additional genomic testing through whole genome sequencing, to ensure ongoing diagnostic accuracy as new genetic insights and technologies emerge.

Funding/Support: None declared.

Financial Disclosures: None declared.

Acknowledgements: The authors extend their gratitude to the patients and their families who participated in this study.

REFERENCES

1. Navarrete-Opazo AA, Singh M, Tisdale A, Cutillo CM, Garrison SR. Can you hear us now? The impact of health-care utilization by rare disease patients in the United States. *Genet Med.* Nov 2021;23(11):2194-2201. doi:10.1038/s41436-021-01241-7

2. Ely DM, Driscoll AK. Infant mortality in the United States, 2020: data from the period linked birth/infant death file. *Natl Vital Stat Rep*. 2022;71(5):1-18.

3. Mithyantha R, Kneen R, McCann E, Gladstone M. Current evidence-based recommendations on investigating children with global developmental delay. *Arch Dis Child*. 2017;102(11):1071-1076. doi:10.1136/archdischild-2016-311271

4. Zablotsky B, Black LI, Maenner MJ, et al. Prevalence and trends of developmental disabilities among children in the United States: 2009-2017. *Pediatrics*. 2019;144(4):e20190811. doi:10.1542/peds.2019-0811

5. Vasudevan P, Suri M. A clinical approach to developmental delay and intellectual disability. *Clin Med (Lond).* 2017;17(6):558-561. doi:10.7861/clinmedicine.17-6-558

6. Bamshad MJ, Ng SB, Bigham AW, et al. Exome sequencing as a tool for Mendelian disease gene discovery. *Nat Rev Genet*. 2011;12(11):745-755. doi:10.1038/nrg3031

7. Savatt JM, Myers SM. Genetic testing in neurodevelopmental disorders. *Front Pediatr*. 2021;9:526779. doi:10.3389/fped.2021.526779

8. Eisenberger T, Di Donato N, Decker C, et al. A C-terminal nonsense mutation links PTPRQ with autosomal-dominant hearing loss, DFNA73. *Genet Med.* 2018;20(6):614-621. doi:10.1038/gim.2017.155

9. Huang Y, Mao X, van Jaarsveld RH, et al. Variants in CAPZA2, a member of an F-actin capping complex, cause intellectual disability and developmental delay. *Hum Mol Genet.* 2020;29(9):1537-1546. doi:10.1093/hmg/ddaa078

10. Pi S, Mao X, Long H, Wang H. A de novo inframe deletion variant in CAPZA2 tentacle domain with global developmental delay and secondary microcephaly. *Clin Genet.* 2022;102(4):355-356. doi:10.1111/cge.14186

11. Zhang XM, Xu KL, Kong JH, et al. Heterozygous CAPZA2 mutations cause global developmental delay, hypotonia with epilepsy: a case report and the literature review. *J Hum Genet.* 2024;69(5):197-203. doi:10.1038/s10038-024-01230-z

12. Akin O, Mullins RD. Capping protein increases the rate of actin-based motility by promoting filament nucleation by the Arp2/3 complex. *Cell*. 2008;133(5):841-851. doi:10.1016/j.cell.2008.04.011

13. Fan Y, Tang X, Vitriol E, Chen G, Zheng JQ. Actin capping protein is required for dendritic spine development and synapse formation. *J Neurosci.* 2011;31(28):10228-10233. doi:10.1523/JNEUROSCI.0115-11.2011

14. Kim T, Cooper JA, Sept D. The interaction of capping protein with the barbed end of the actin filament. *J Mol Biol.* 2010;404(5):794-802. doi:10.1016/j.jmb.2010.10.017

15. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015;17(5):405-424. doi:10.1038/gim.2015.30

16. Schalk A, Cousin MA, Dsouza NR, et al. coding variants in the. *J Med Genet.* 2022;59(10):965-975. doi:10.1136/jmedgenet-2021-107751

17. Niu Y, Qian Q, Li J, et al. De novo variants in AGO1 recapitulate a heterogeneous neurodevelopmental disorder phenotype. *Clin Genet.* 2022;101(4):459-465. doi:10.1111/cge.14114

18. Janowski BA, Huffman KE, Schwartz JC, et al. Involvement of AGO1 and AGO2 in mammalian transcriptional silencing. *Nat Struct Mol Biol.* 2006;13(9):787-792. doi:10.1038/nsmb1140

19. Bagger FO, Borgwardt L, Jespersen AS, et al. Whole genome sequencing in clinical practice. *BMC Med Genomics.* 2024;17(1):39. doi:10.1186/s12920-024-01795-w

20. Brlek P, Bulić L, Bračić M, et al. Implementing whole genome sequencing (WGS) in clinical practice: advantages, challenges, and future perspectives. *Cells*. 2024;13(6):504. doi:10.3390/cells13060504

The 'Passport' to Inclusive Research Participant Engagement: Integrating Families in a Research Journey

Veronika Mak, MSc; Julia Schiller, PT, DPT; Alina Grimaldo; Ellen N. Sutter, PhD, PT, DPT; Kellie M. Collins, PT, DPT; Bernadette T. Gillick, PhD, MSPT, PT

In medical research, establishing partnerships among clinicians, researchers, and participants can be facilitated by effective communication and collaboration. This synergy becomes critical when considering vulnerable populations, such as children and their families. The nuances of communication and collaboration play a pivotal role in ensuring the ethical and respectful inclusion these groups in research endeavors.

Family-centered care, shared decision-making, transdisciplinary collaboration, and culturally responsive practices can be incorporated within research design and recruitment retention efforts. These techniques influence successful engagement and optimize the overall research participation experience for all involved, exemplifying how to conduct ethically sound and impactful medical research with vulnerable populations.

• • •

Author Affiliations: Waisman Center, University of Wisconsin–Madison, Madison, Wisconsin (Mak, Schiller, Grimaldo, Sutter, Collins, Gillick); Department of Rehabilitation Medicine, University of Minnesota, Minneapolis, Minnesota (Sutter); University of Wisconsin School of Medicine and Public Health (UW SMPH), Madison, Wisconsin (Collins); Department of Pediatrics, UW SMPH, Madison, Wisconsin (Gillick).

Corresponding Author: Veronika Mak, MSc, 1500 Highland Ave #421, Madison, WI 53705, phone 608.381.2699, email vmak@wisc.edu; ORCID ID 0009-0004-0836-7891

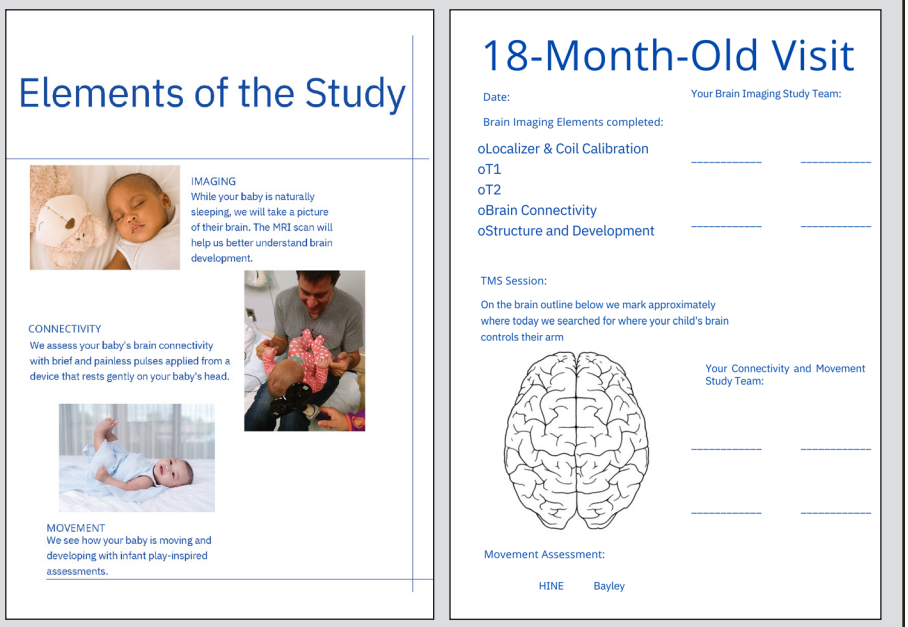
Current best practices recommend a heightened emphasis on advancing pediatric research through a collaborative approach that actively involves families. There is a shift from merely conducting research on children to working with children in research as they are integral to the outcomes. Several strategies facilitate this shift, including promoting diversity, equity, and inclusion initiatives; considering social determinants of health; creating community advisory boards; using face-to-face recruiting and financial incentives; and increasing parent and child engagement throughout the study.[1] These methods have proven effective in recruiting and retaining families in pediatric medical research, with the latter emerging as one of the most effective strategies recommended by families and researchers.[2] Consequently, prioritizing meaningful and educational engagement with families and children is a crucial focus for our research teams, aiming to enhance families' understanding of their participation in research.

The Pediatric Neuromodulation Lab at the Waisman Center of the University of Wisconsin-Madison is currently conducting a longitudinal observational study exploring the impact of perinatal brain injury on motor development and risk for cerebral palsy (NIH-1R01HD098202). Following consultations with medical professionals, discussions with families of past participants, and relevant literature on perinatal brain injury, the research team recognized that families may have complex emotions regarding research participation based on their experiences while navigating their child's health care needs. Respecting the families' journey, we aim to facilitate communication between the research team and participating family. Knowledge of families' experiences and research indicating that families prefer active engagement with research teams prompted the lab to create a "Travel Passport." This tool guides families throughout each of the study visits in their research journey over the first 2 years of their child's life.

The Travel Passport aims to provide easily understandable information about the study, individualized detail of each assessment, and a tangible tool for tracking and documenting participation before the publication of results.

The Travel Passport aims to provide easily understandable information about the study,

Figure. Sample Pages From the Travel Passport



individualized detail of each assessment, and a tangible tool for tracking and documenting participation before the publication of results. On the first day of study participation, each family receives a customized passport packet. After each visit, they receive a "stamp" and summaries detailing the activities their child completed during their visit. Each study visit includes several different research assessments, and the Travel Passport describes each element in plain language, with a calculated Flesch-Kincaid readability score at approximately a 10th grade reading level. Additionally, the Travel Passport includes pictures and names of the individuals involved in the study and positions the family as the "center" of the research team to highlight that their involvement remains at the core of our work. The Passport remains with the family, allowing them to take it home for their reference.

To evaluate the effectiveness and impact of the Travel Passport, the Pediatric Neuromodulation Lab actively seeks feedback from families, clinicians, and researchers. Through a short, anonymous survey, families provide feedback after their study visits. Survey questions cover perceptions and use of the passport, suggestions for improvement, and likes and dislikes. Eleven of the 16 families involved in the study who received a Travel Passport provided input. Eight of the 11 respondents found the Travel Passport "helpful" or "very helpful" in explaining their child's participation in the study. Additionally, 82% of families expressed either having used or intending to use the Travel Passport to describe their experiences in the study to family, friends, or their children. Favorite components of the Passport included reference materials, the ability to track visits and development, and the inclusion of team pictures. One parent noted, "We found the breakdown of what was going to happen at each visit helpful. We also enjoyed the pictures of the team who helped facilitate each visit being attached to the passport." For future improvements of the Travel Passport, respondents recommended a digital version and further descriptions of study results.

Various research team members, including the medical monitor and medical director have recognized the Travel Passport as an innovative method to engage participants in the research process. It has been presented at local and national conferences to reach a diverse audience and gather valuable feedback. The response from researchers and medical professionals has been overwhelmingly positive, with some clinicians contemplating the integration of a tool like the Travel Passport into their specialty practices. They see its potential to offer education, facilitate conversations, and track development by incorporating patients' medical experiences.

We aim to share this tool as a catalyst for increasing science literacy, enhancing comprehension of research participation, and promoting participant engagement. To integrate families as active research team members, the Pediatric Neuromodulation Lab created the Travel Passport to facilitate meaningful involvement throughout the observational, longitudinal study. We remain committed to assessing participants' perspectives on the passport to cultivate a collaborative and informative research environment.

Funding/Support: The project described was supported by a grant from the National Institutes of Health (NIH-1R01HD098202) and Promotion of Doctoral Studies Level I and II Scholarships from the Foundation for Physical Therapy Research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Financial Disclosures: None declared.

REFERENCES

1. Huntington C, Newton JT, Donaldson N, et al. Lessons learned on recruitment and retention in hard-to-reach families in a phase III randomised controlled trial of preparatory information for children undergoing general anaesthesia. *BMC Oral Health.* 2017;17(1):122. doi:10.1186/s12903-017-0411-4

2. Weintraub JA, Breland CE. Challenges, benefits, and factors to enhance recruitment and inclusion of children in pediatric dental research. *Int J Paediatr Dent.* 2015;25(5):310-316. doi:10.1111/ipd.12176

Glucose-6-Phosphate Dehydrogenase Deficiency in Wisconsin Newborns: Missed Opportunity for Screening

Laura P. Chen, MD; Vinod K. Bhutani, MD; Paola J. Fliman, MD; Roberto Mendez, PhD; Ann H. Allen, MD

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common genetic red blood cell enzyme disorder worldwide.[1] Its incidence varies based on population demographics; it is more common among individuals of sub-Saharan African, Mediterranean, Middle Eastern, Asian, Latin American, and Native American descent. In a study of US military members, overall prevalence of G6PD deficiency was 2.2%; however, over 11% of non-Hispanic Black males have the disorder.[2]

In newborns, G6PD deficiency is often asymptomatic. However, in the first week of life, G6PD deficiency can cause unpredictable, severe hyperbilirubinemia and kernicterus if not monitored or treated appropriately. Kernicterus, or chronic bilirubin encephalopathy, occurs with severe neonatal hyperbilirubinemia. Unbound bilirubin crosses the blood-brain barrier and can cause choreoathetoid cerebral palsy, sensorineural hearing loss, and other permanent, irreversible neurologic impairments.[3] Ethnic and racial disparities exist in newborns who sustain kernicterus,[4] with Black infants constituting 14% of US births, yet accounting for 25% of infants with kernicterus.[5] The most common condition accounting for this outcome disparity is G6PD deficiency.[4,5]

Author Affiliations: Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Chen, Mendez, Allen); Department of Pediatrics, Stanford University School of Medicine, Stanford, California (Bhutani); SSM Health St. Mary's Hospital, Madison, Wisconsin (Fliman); Wisconsin Newborn Screening Laboratory, Wisconsin State Laboratory of Hygiene, Madison, Wisconsin (Mendez).

Corresponding Author: Laura P. Chen, MD, Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, Madison, WI 53792; email lpchen@wisc.edu; ORCID ID 0000-0001-5267-0565

G6PD Deficiency in Wisconsin

In August 2022, the American Academy of Pediatrics (AAP) released updated guidelines for treating newborn hyperbilirubinemia, emphasizing G6PD deficiency as a risk factor for severe hyperbilirubinemia and bilirubin neurotoxicity, as well as outlining clinical indications for testing.[6] The University of Wisconsin American Family Children's Hospital and SSM St Mary's Hospital in Madison were two of the approximately 150 hospitals nationally that participated in the AAP quality improvement project called LIGHT (Learning and Implementing Guidelines for Hyperbilirubinemia Treatment). The updated clinical practice guideline recommended screening for G6PD deficiency in patients with evidence of Coombs-negative hemolysis, but our local findings from the LIGHT initiative revealed that testing for G6PD deficiency is rarely obtained. Utilizing state diversity indices and applying race-specific adult prevalence estimates, it is estimated that approximately 1350 newborns annually in Wisconsin have G6PD deficiency; however, true statewide prevalence is unknown (Table).[7] Identifying statewide prevalence along with continued clinician education and surveillance for G6PD deficiency supports the advancement of equitable newborn care in Wisconsin.

Identifying statewide prevalence along with continued clinician education and surveillance for G6PD deficiency supports the advancement of equitable newborn care in Wisconsin.

Screening for G6PD Deficiency

G6PD deficiency is not routinely tested or universally screened in the United States. Washington, DC, is currently the only place that mandates universal newborn screening for G6PD deficiency.[8] However, the timing of diagnosis of G6PD deficiency is crucial to prevent kernicterus. The majority of infants with G6PD deficiency in the USA Kernicterus Registry were readmitted to the hospital within the first week after birth.[5] Newborn state screens via dried

Table. Expected Number[a] of Newborns With G6PD Deficiency in Wisconsin, 2021[b]

Race	Males		Females		Total	
	Births	G6PDd Newborns	Births	G6PDd Newborns	Births	G6PDd Newborns
American Indian/Alaska Native	364	3	343	2	707	6
Asian/Pacific Islander	1432	45	1345	20	2778	80
Non-Hispanic Black	3192	358	3073	144	6265	595
Non-Hispanic White	25 703	107	24 716	65	50 419	202
Other/Unknown	826	21	787	14	1613	37
Overall	31 517	721	30 264	465	61 781	1359

[a]Expected numbers were calculated from racial G6PD deficiency (G6PDd) prevalence data from Lee et al, 2019.[2]

[b]Wisconsin births for the year 2021 obtained CDC Wonder, Centers for Disease Control and Prevention. Accessed August 3, 2022. http://wonder.cdc.gov/wonder/help/Natality-expanded.html.

Table adapted with permission from Vidavalur R and Bhutani VK.[7]

blood spot testing typically are not available for 5 to 7 days or more,[8] which is beyond the high-risk period for kernicterus.

Recent legislation in New York mandated newborn G6PD deficiency screening, but only for high-risk infants based on specific factors including race and ancestry.[9] Utilizing race to guide clinical decision-making contributes to continued racial disparities in health care[9,10] and G6PD deficiency can occur in racial groups that are considered low risk.[11] The optimal time for testing and results is before birth hospital discharge to enhance test accuracy, facilitate family education regarding jaundice and avoidance of triggers for breastfeeding caregivers, and ensure close follow-up.[12] In addition, prehospital discharge screening has been shown to be cost-effective.[13] Thus, G6PD enzyme screening of newborns has been proposed with a focus on rapid turnaround time.[14]

Next Steps

Universal G6PD enzyme screening of all newborns is the most equitable strategy for detecting G6PD deficiency.[15] The emergence of quantitative, point-of-care testing opens opportunities for rapid screening results in the newborn period. There is potential for streamlining point-of-care screening utilizing umbilical cord blood or coordinating with the time of newborn screen collection.[9,16] Future studies are needed to further assess the accuracy of point-of-care tests and improve turnaround time for timely delivery of results to families.

Conclusions

G6PD deficiency is an established neurotoxicity risk factor for severe hyperbilirubinemia in newborns. Identification at birth allows for timely management and intervention to prevent irreversible brain injury. Universal screening of newborns prior to discharge from birth hospitalization is a crucial step towards equitable diagnosis of G6PD deficiency, so that all G6PD-deficient individuals can lead a healthier lifestyle protected from unpredictable adverse dietary, chemical, and environmental triggers.

Funding/Support: None declared.
Financial Disclosures: None declared.

REFERENCES

1. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: a systematic review and meta-analysis. *Blood Cells Mol Dis.* 2009;42(3):267-278. doi:10.1016/j.bcmd.2008.12.005

2. Lee J, Poitras BT. Prevalence of glucose-6-phosphate dehydrogenase deficiency, U.S. Armed Forces, May 2004-September 2018. *MSMR*. 2019;26(12):14-17.

3. Kasirer Y, Kaplan M, Hammerman C. Kernicterus on the spectrum. *Neoreviews*. 2023;24(6):e329-e342. doi:10.1542/neo.24-6-e329

4. Okolie F, South-Paul JE, Watchko JF. Combating the hidden health disparity of kernicterus in black infants: a review. *JAMA Pediatr*. 2020;174(12):1199-1205. doi:10.1001/jamapediatrics.2020.1767

5. Johnson L, Bhutani VK, Karp K, Sivieri EM, Shapiro SM. Clinical report from the pilot USA Kernicterus Registry (1992 to 2004). *J Perinatol.* 2009;29 Suppl 1:S25-45. doi:10.1038/jp.2008.211

6. Kemper AR, Newman TB, Slaughter JL, et al. Clinical practice guideline revision: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2022;150(3): e2022058859. doi:10.1542/peds.2022-058859

7. Vidavalur R, Bhutani VK. Georacial epidemiological estimates of glucose-6-phosphate dehydrogenase deficiency among newborns in the United States. *Am J Perinatol*. 2024; 41(S 01):e1841-e1849. doi:10.1055/a-2082-4859

8. Newborn Screening Information Center. Health Resources & Services Administration. Accessed November 13, 2024. https://newbornscreening.hrsa.gov/

9. Milburn S, Bhutani VK, Weintraub A, Guttman K. Implementation of universal screening for G6PD deficiency in newborns. *Pediatrics*. 2024;154(2):e2024065900. doi:10.1542/peds.2024-065900

10. Hernandez-Boussard T, Siddique SM, Bierman AS, Hightower M, Burstin H. Promoting equity in clinical decision making: dismantling race-based medicine. *Health Aff (Millwood).* 2023;42(10):1369-1373. doi:10.1377/hlthaff.2023.00545

11. Chinevere TD, Murray CK, Grant E, Jr., Johnson GA, Duelm F, Hospenthal DR. Prevalence of glucose-6-phosphate dehydrogenase deficiency in U.S. Army personnel. *Mil Med.* Sep 2006;171(9):905-907. doi:10.7205/milmed.171.9.905

12. Watchko JF, Kaplan M, Stark AR, Stevenson DK, Bhutani VK. Should we screen newborns for glucose-6-phosphate dehydrogenase deficiency in the United States? *J Perinatol.* 2013;33(7):499-504. doi:10.1038/jp.2013.14

13. Vidavalur R, Bhutani VK. Economic evaluation of point of care universal newborn screening for glucose-6-Phosphate dehydrogenase deficiency in United States. *J Matern Fetal Neonatal Med*. 2022;35(25):5745-5753. doi :10.1080/14767058.2021.1892067

14. Nock ML, Johnson EM, Krugman RR, et al. Implementation and analysis of a pilot in-hospital newborn screening program for glucose-6-phosphate dehydrogenase deficiency in the United States. *J Perinatol*. 2011;31(2):112-117. doi:10.1038/jp.2010.69

15. Uduwana SR, Nemerofsky SL. Recent G6PD screening mandate: we are missing the mark. *Hosp Pediatr*. 2024;14(8):e369-e37. doi:10.1542/hpeds.2023-007681

16. Anderle A, Bancone G, Domingo GJ, Gerth-Guyette E, Pal S, Satyagraha AW. Point-of-care testing for G6PD deficiency: opportunities for screening. *Int J Neonatal Screen*. 2018;4(4):34. doi:10.3390/ijns4040034

Common Ground

Ava Rowe

Digital Art

Artist Statement:

I'm an artist who delves into dark themes with an underlying message of promoting world peace. "Common Ground" is about the similarities of a stray cat and an underprivileged homeless teenager—both trying to survive in a world that was not made to help them thrive.

Thank You!
to our Reviewers

The *WMJ* would like to thank everyone who served as a manuscript reviewer in 2023. Manuscript review is an important collegial act and is essential to the integrity of *WMJ*. We are grateful for the assistance of these individuals in ensuring authors receive objective and insightful feedback on their work.

Kartikey Acharya, MD, MPH
Sol del Mar Aldrete, MD
Kathleen M. Antony, MD, MSCI
Erica Arrington, MD
Karina A. Atwell, MD, MPH
Fahad Aziz, MD
Quratul Aziz, MD
Jessica C. Babal, MD
Aurengzab Baber, MD
Howard H. Bailey, MD
Lauren Bauer, MD, MPH, MS
Adam Bauer, MD
Tomer Begaz, MD
Jason M. Bellak, MD
Paul Anthony Bergl, MD
Saswati Bhattacharya, PhD
Laura Birkeland, CGC
Joseph Blustein, MD
Rohan Bodapati, MD
Nicole Bonk, MD
Amber Brandolino, MS, CCRC
Meghan Beth Brennan, MD
Morgan Briggs, MD
John R. Brill, MD, MPH
Chasity Brimeyer, PhD
Bonnie Brown, MD
Charles Brummitt, MD
Brian P. Buggy, MD
Kristen Bunnell, PharmD
Kristin Busse, PharmD
Steven Butz, MD
Thomas Carver, MD
Shannon Casey, PhD
William E. Cayley, MD, MDiv
Adithya Chennamadhavuni, MD, MBBS
Michael P. Cinquegrani, MD, FACC, FSCAI
James H. Conway, MD, FAAP
Margaret Cook, PharmD, BCPS
Juan Felipe Coronado, MD
Kenneth W. Crabb, MD, FACOG
Paul D. Creswell, PhD
Christopher J. Crnich, MD
Jessica Dalby, MD
Richard A. Dart, MD
Matthew Dellinger, PhD
John C. Densmore, MD
Donn Dexter, MD
Subarna M, Dhital, MD
Sean Duffy, MD
Thomas J. Ebert, MD, PhD
Mary L. Ehlenbach, MD
Christina Eldredge, MD, PhD
Ann E. Evensen, MD
Leonard Ezenagu, MD
Sancia Ferguson, MD, MPH
Neil Dominic Fernandes, MD
Elizabeth Fleming, MD
Jeff Freund, PharmD
John J. Frey, MD
David Galbis-Reig, MD, DFASAM
Ali Gardezi, MD
Rohini Garg, MBBS
Richard J. Gauthier, MD
Valerie J. Gilchrist, MD
Maureen D Goss, MPH
Tyler J Grunow, MD
Nathan Gundacker, MD
Stephen J. Halliday, MD, MSCI
Lawrence P. Hanrahan, PhD
Paul P. Hartlaub, MD, MSPH
Buddhi Hatharaliyadda, MD
Robin Helm, MD
Brian Hilgeman, MD
Mary Homan, DrPH, MA, MSHCE
William Hueston, MD
Paul Hunter, MD
Corlin Jewell, MD
Sheri P. Johnson, PhD
Greer Jordan, MBA, PhD, BSEE
John Kalmanek, MD
Andrew Kastenmeier, MD
Michael Kessler, MD
Ezza Aslam Khan, MD
Abdul Khan MBBS, MD
Laura Kopplin, MD, PhD
Karol Kremens, MD
Greta J. Kuphal, MD
Matthew Lambert, MD
Swapnil Lanjewar, MD
Magnolia Larson, DO
Joseph L'Huillier, MD
Amy E. Liepert, MD
Jennifer E. Lochner, MD
Leigh S. LoPresti, MD
Maichou Lor, PhD
Taja Lozar, MD
George E. MacKinnon III, PhD, MS, RPh, FASHP
Aman Mahajan, MD, MRCPsych
David Mallinson, PhD
Venkata Manchala, MD
Chetna Mangat, MBBS, MD
Andrea Ildiko Martonffy, MD
Tina C. Mason, MD, MPH, FACOG
Benson T. Massey, MD
Eduard Matkovic, MD
Lindsey McAlarnen, MD, MSc
Joseph A. McBride, MD
Tracy E. McCall, MD, FACS
Michael McCormick, MD
Andrew J. McLean, MD, MPH
Alex Means, MD
Jill R. Meilahn, DO
Marlene Melzer-Lange, MD
Linda N. Meurer, MD, MPH
Cezarina Mindru, MD
Lana Minshew, PhD
Mansoor Mirza, MD, FACP
Asim A. Mohammed, MD
Varun Monga, MD
Maria C. Mora Pinzon, MD, MS
George Lee Morris III, MD, MPH, DIC
Jeffrey A. Morzinski, PhD
Brenda Muth, NP
Marine Nalbandyan, MD, PhD, MPH
Paul W. Nannis, MSW
Sonya Naryshkin, MD, FIAC, FCAP
Subramanian Natarajan, MD
Suzanne Norby, MD
Shinoj Pattali, MD
Barry J. Pelz, MD
Andrew E. Petroll, MD, MS
Elizabeth M. Petty, MD
David M. Poetker, MD, MA
Seema M. Policepatil, MD
Ron Prince, MS
David Quimby, MD
Lisa Quinn-Lee, PhD, MSSW, LICSW
Peter S. Rahko, MD
Erik A. Ranheim, MD, PhD
David Rebedew, MD
Patrick L. Remington, MD, MPH
Richard H. Reynertson, MD
Jean Marie Riquelme, MD
Brenda Rooney, PhD
Ani Saryan Kopf, MD
Justin A. Sattin, MD
Sima Sayyahmelli, MD
Alexander Scharko, MD
Andrew T. Schramm, PhD
Amy Schultz, PhD, MS
Robert Sedlacek, MD, FAAFP
Umesh Sharma, MD, FACP
Umar A. Sheikh, PhD
Marianna Shershneva, MD, PhD
Harmit Singh, MD
Tripti Singh, MD
David A. Sonetti, MD
Richard H. Strauss, MD
Rebekah Summey, MD
Geoffrey R. Swain, MD, MPH
Kurtis J. Swanson, MD
Matthew Swedlund, MD
Erick Tarula, MD
Rachna Tiwari, MBBS
Shahul Valavoor, MD
Suzanne van Landingham, MD
Basil Varkey, MD
Anna Vasquez, MD, MS
Manasa Velagapudi
Ryan J. Wagner, DO
Njeri Wainaina , MD, FACP
Shafik Wassef, MD
Alexis Waters, PA-C
John M. Watkins, MD
Donald Weber, MD
Benjamin Weber, MA
Susan Wenker, PhD
Benjamin Weston, MD, MPH
Joshua Wiegel, PharmD
Thalia Williams, MD, PhD
Harvey Woehlck, MD
Ke Yan, PhD
David T. Yang, MD
Craig C. Young, MD
Misbah Zaeem, MD
Susan Zahner, DrPH, RN
Laura Zakowski, MD
Amy Zelenski, PhD
Amy Zosel, MD, MSCS

• • •

The *WMJ* continually seeks to expand our list of highly qualified reviewers. To learn more or to sign up, visit wmjonline.org and click on "Reviewers."