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WMJ

2024 • volume 123 • issue 1

IN THIS ISSUE

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WMJ

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COVER ART

Mitosis

Vincent Cryns, MD

Digital art created on an iPad with Brushes Redux

Artist's Statement

"In cancer, the carefully orchestrated process of mitosis or cell division is hijacked to promote uncontrolled growth, often resulting in cells with abnormal numbers of chromosomes. This digital painting portrays the cellular chaos of a cancer cell."

About the Artist

Vincent Cryns is a physician-scientist who has been influenced as an artist by years of cancer research and careful observation. "I try to break down complex images into colors and repeating shapes."

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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.

EDITORIAL

ORIGINAL RESEARCH

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.

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BRIEF REPORTS

CASE REPORTS

Optimizing Inpatient Patient Experience

Dear Editor:

Quality of patient care, service, and communication is critical for patient satisfaction. This is tied to several benefits for the health system, including increased patient compliance, loyalty, referral to new patients, and improved clinical productivity. The efficacy of a hospital is often dependent on the admitted patients' experiences with different clinicians. These experiences factor into the patients' likelihood to refer the clinician to other potential patrons. Patients are likely to refer a clinician when they feel heard and included in the decision-making process. When patient satisfaction is low, it is reflected in the percentage of the "likelihood to refer." A below-average score indicates a need to address departmental practices and potentially change how clinicians interact with their patients. A cross-sectional study by Leow and Liew noted that the length of time a physician spends with their patient is one of the strongest determinants for patient satisfaction.[1]

At Froedtert Hospital in Milwaukee, Wisconsin, the 9NT medicine floor continuously reported a likelihood to refer score between 50% and 67% from July 2022 through January 2023, with 76% being the desired goal. To improve likelihood to refer parameter, we started a project in February 2023 focusing on improving clinicians' scores by interventions to promote the communication between clinicians and their patients. We implemented 3 focused intervention strategies to target patient satisfaction improvement. First, physicians should press the "Provider in room" button on the Rauland's panel upon entering a patient's room, which alerts the bedside nurse to come into the room. The physician then discusses the plan of care (POC) with the patient and nurse, utilizing this time to address any questions or concerns intentionally focused on shared decision-making and collaboration. Next, the clinician should update the whiteboard with the patient's POC for the day and the expected discharge date and place. Then, at the end of the day, the physician will reconnect with the patient either in person or via the patient's in-room phone. During this time, the physician will share potential POC updates and ask if any changes occurred and if they can assist with anything before departing for the day.

Prior to introduction of these interventions, "the likelihood to refer" percentage consistently remained below 67%. Within the first month of implementation of this pilot project, this rate increased to 75%. Throughout the study span, the "likelihood to refer" for 9NT reached 78%, surpassing the desired target.

With 3 targeted intervention tactics, an increased "likelihood to refer" percentage demonstrates improved patient satisfaction. Based on the successful pilot project, we are implementing this on all medicine units at the hospital. This initiative will enhance the efficiency and productivity of the institution, improve patient retention, and foster trust between patients and their medical care team.

—Precious Anyanwu, BS; Sparsh Jain, BS; Sushma Raju, MD; Sanjay Bhandari, MD; Jeanette Carreras, MPH; Pinky Jha, MD, MPH; Barbara Slawski, MD

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Comment on 'Can Metronidazole Cause a Disulfiram-Like Reaction? A Case-Control Study Propensity Matched By Age, Sex and Ethanol Concentration'

Dear Editor,

We read with great interest the recently published article by Feldman and Jaszczenski regarding the possibility of a disulfiram-like reaction brought about by the use of metronidazole.[1] According to their results, there were no patients who experienced such a reaction after concomitant use of alcohol and metronidazole. Based on this finding, they suggest that metronidazole should not be avoided due to concern about an interaction with ethanol. Because of our continuous research on disulfiram, we find the issue very interesting and we would like to comment briefly on this report.

In a previous work of our laboratory team published in 2007, we clearly showed that metronidazole does not provoke a disulfiram-like reaction, because it does not inhibit the hepatic aldehyde dehydrogenase nor increase blood acetaldehyde in the Wistar rat.[2] In addition, in this study, we demonstrated for the first time that metronidazole produces a tremendous increase in the levels of brain serotonin, while the enhancing effects of ethanol on the central levels of serotonin are well established.[3] Likewise, we concluded that the reaction to ethanol exhibited by metronidazole may be the result of an interaction in the context of a type of a serotonin syndrome (SS), as in the case of the concomitant administration of agents possessing serotonergic activity. In support of this notion, it has been demonstrated that the combination of ethanol with serotonergic agents may induce a SS.[4]

The clinical manifestations of SS are a triad of altered conscious state, autonomic dysfunction, and neuromuscular excitability. However, in a retrospective study by Radomski et al,[5] it was shown that the clinical picture of SS may be highly variable, and, in fact, all the symptoms observed during a "disulfiram reaction" are included in the detailed list of symptoms provided by this study.

In conclusion, we suggest that the authors should be aware of the serotonergic properties of metronidazole and ethanol, the combination of which might lead, at least in theory, to a SS, with symptoms very similar to those of a disulfiram-like reaction. Hence, we believe that they might reconsider their suggestion that patients under treatment with metronidazole can safely use alcohol due to lack of interaction between these two agents. Given the low incidence of SS, the fact that none of the 18 patients of the study who received metronidazole and ethanol had a suspected disulfiram-like reaction cannot rule out the possibility of alcohol intolerance produced by metronidazole.

—Petros N. Karamanakos, MD, MSc, PhD; Eleftheria S. Panteli, MD, MSc, PhD, DESA; Marios Marselos, MD, PhD

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Leprosy in the Upper Midwest: Vigilance Needed for Contacts

Dear Editor,

A case report by Bach et al has brought to attention a case of leprosy in the upper Midwest.[1] Several critical points need emphasis for the management of the patient's contacts and to prevent future complications for the patient. Specifically, the possibility of administering a single dose of rifampicin[2] or rifapentine[3] to the patient's contacts should be explored, as the patient is classified with borderline lepromatous leprosy, which carries a higher risk of transmission due to high bacillary loads.

It is imperative to conduct physical examinations of all the patient's contacts and provide them with a single dose of rifampicin or rifapentine as a preventive measure. A contact is defined as an individual who has had significant, prolonged exposure to a leprosy patient, such as living in close proximity for at least 20 hours per week over a 3-month period annually. This would typically include family members, neighbors, friends, classmates, and coworkers.

The World Health Organization's single-dose rifampicin recommendations are based on age and weight. For individuals 15 years and older weighing around 60 kg, the prescribed dose is 600 mg; for those aged 10-14 years, it is 450 mg; for those aged 6 to 9 years weighing 20 kg or more, it is 300 mg; and for children aged 2 years or older weighing less than 20 kg, the dose is calculated at 10-15 mg/kg.

It should be further emphasized that this patient is at a significant risk of developing erythema nodosum leprosum, which is a type 2 reaction, due to the abundant presence of bacilli. It is recommended to manage such cases with steroids, especially considering the neural involvement, but it should be done cautiously due to the associated decreased visual acuity and the increased risk that steroids present. If severe reactions with systemic involvement are not controlled by steroids and methotrexate, thalidomide may be considered as an alternative treatment.[4] The initial dose of thalidomide is 100 mg 3 times daily, with subsequent dose reduction as appropriate.

—Pugazhenthan Thangaraju, MD, Sajitha Venkatesan, MD

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The Safety Net's Safety Net

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Fahad Aziz, MD, FASN

Reflecting on Excellence: The *Wisconsin Medical Journal's* Year in Review

Fahad Aziz, MD, FASN; *WMJ* Editor-in-Chief

Since its beginning in 1903, the *Wisconsin Medical Journal (WMJ)* has been a vital platform for the Midwest's medical community. This peer-reviewed, indexed journal has a long history of publishing significant scientific works, focusing on educating health care professionals and promoting scientific research. Initially published by the Wisconsin Medical Society (Wismed), ownership shifted in 2019 to the Medical College of Wisconsin (MCW) and the University of Wisconsin School of Medicine and Public Health (SMPH). A publishing board, with members from each institution and a representative from Wismed, now oversees *WMJ* operations.

I started my journey as editor-in-chief one and a half years ago with the expert guidance of esteemed Publishing Board members Jonathan Temte, MD, Elizabeth Petty, MD, and Robyn Perrin, PhD, from the SMPH and Asirani Chiu, MD, Amalia Lyons, MD, and Sara Wilkins, MA, MPA, from the MCW. Their collective wisdom and support were instrumental in my transition into this role. Additionally, the opportunity to collaborate closely with Kendi Neff-Parvin, our highly skilled managing editor, and Robert Treat, PhD, our insightful deputy editor, has been a privilege and a profound learning experience. Their guidance and support have contributed significantly to my professional development and comprehension of the publishing process.

The mission of the *WMJ* goes beyond just sharing groundbreaking research in all areas of medicine. Our goal is also to nurture and improve the abilities of medical students and emerging medical professionals, empowering them to use their expertise beyond the confines of any single institution. In this editorial, our goal is to shine a spotlight on the progress made by our journal in 2023 and lay out our ambitious goals for 2024. We strive to encourage advancements in the medical field by fostering a community that shares knowledge and promotes professional growth.

> We are immensely grateful for this community's contributions, which underpin the journal's success and enable us to continue advancing the field of medicine.

REFLECTING ON PROGRESS: 2023 ACHIEVEMENTS AND MILESTONES

Publications

Last year marked a pivotal period of growth and achievement for WMJ as we experienced unprecedented manuscript submissions. These submissions span diverse categories, including original research, comprehensive reviews, detailed case reports, and insightful commentaries. We received 161 submissions, surpassing all previous years. Our publication efforts matched this vigor, with 100 manuscripts successfully published.

In response to the rising number of submissions, we strategically decided to increase our publication frequency, expanding from four to six issues per year, with the latter two combining to form a special issue. This expansion has proven highly effective in accommodating the breadth of contributions we receive and allowing us to showcase a wide array of vital medical research and insights.

Moreover, 2023 saw us embark on a significant transformation, shifting the journal from its traditional printed format to a fully online platform. This transition modernizes our distribution method and aligns with our commitment to environmental stewardship. By going digital, we

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have taken a considerable step towards minimizing our paper consumption and actively supporting the mission of a greener environment.

Publication of Special Issue

In December 2023, the *WMJ* significantly contributed to the collective understanding of the COVID-19 pandemic by publishing a special double issue. This landmark edition compiled the expertise and experiences of more than 120 health professionals, researchers, students, and artists from Wisconsin, all reflecting on the myriad challenges and learnings from the pandemic. The issue delves into various critical themes, including the evolution of patient care, the profound impact on health care workers, the strategic public health responses, and the disparities and inequities highlighted or exacerbated by COVID-19. Each manuscript contributed to a broader narrative of resilience, adaptation, and the ongoing quest for knowledge in the face of a global health crisis.

Editorial Fellowships

The *WMJ* took a significant stride forward in 2023 with the launch of its editorial fellowship program, a visionary initiative designed to equip the next wave of medical professionals with the tools necessary to advance medical knowledge and continue the journal's legacy. We developed this program specifically to foster and enhance the skills needed to lead in the distribution and management of medical literature, thus shaping the future leaders of the *WMJ* mission.

We proudly welcomed four accomplished editorial fellows, each bringing a wealth of medical expertise and unique perspectives to the journal. Our inaugural group of fellows consists of Saswati Bhattacharya, PhD, a scientist in the Department of Pediatrics at SMPH; David Mallinson, PhD, a post-doctoral fellow in the SMPH Department of Family Medicine and Community Health; Corlin Jewell, MD, assistant professor of emergency medicine at SMPH; and Eduard Matkovic, MD, assistant professor of pathology and laboratory Medicine at SMPH. The collective efforts of these fellows have already resulted in substantial contributions towards the progression of the *WMJ's* goals and objectives.

Looking ahead, we eagerly anticipate recruiting the second cohort of editorial fellows in the fall of 2024, following the successful completion of the current fellows' tenure. This ongoing cycle of fellowship and mentorship is integral to our commitment to fostering editorial excellence and ensuring that *WMJ* remains at the forefront of medical scholarship and communication.

2024 OUTLOOK

In 2024, we reaffirm our commitment to maintaining the publication cadence of six issues annually, including a special themed issue in December. This issue will serve as a platform for novel research, comprehensive reviews, and thought leadership on the myriad topics around maternal and child health, providing our readership with in-depth analysis and discussion on relevant and emergent topics. Submissions are due July 15, and we are currently putting together an advisory board to help inform the content of this issue. Learn more by visiting wmjonline.org/featured-content/call-for-papers-mch/.

Seeking Editorial Talent

In response to the surge in submissions and the corresponding increase in publication volume, the WMJ is actively seeking to expand its editorial team by recruiting additional deputy editors. This strategic move is designed to enhance our journal's operational efficiency, notably by reducing the time required to process manuscripts editorially. This expansion will also allow new professionals to gain firsthand experience with the nuances of editorial processing, thereby nurturing the next generation of editors within the field.

Simultaneously, WMJ is looking to augment the composition of its esteemed editorial board. This diverse and dynamic group of physicians, researchers, and other allied health professionals is instrumental in shaping the journal's policies and guiding its direction. As some of our board members approach the conclusion of their tenure, we are keen to invite new members who represent a broad spectrum of medical specialties and can contribute to realizing the journal's vision and mission.

In addition, the crucial work of peer reviewers cannot be overstated, as they are central to the progression of scientific knowledge. In light of this, WMJ is also seeking additional reviewers. Expanding our reviewer pool will enable us to improve our manuscript review turnaround times, thereby enhancing the overall editorial and review process. We seek individuals committed to upholding the high standards of our journal and contributing to the advancement of medical science. Sign up to become a reviewer at wmjonline.org/for-reviewers/wmj-reviewer-sign-up-form/ or email wmj@med.wisc.edu.

Finally, on behalf of our editorial team, I wish to express our heartfelt appreciation for the enduring support and dedication of SMPH Dean Robert N. Golden, MD, and MCW Joseph E. Kerschner, MD, the publishing board, editorial board, esteemed authors, meticulous reviewers, and valued readers. Their collective commitment and relentless pursuit of excellence are the cornerstone of the journal's high standards, ensuring the quality and integrity of its published content and enhancing its esteemed reputation.

Together, these joint endeavors have yielded publications that are not just informative but influential. Through shared knowledge and rigorous peer review, we have created a platform that makes a significant and lasting impact on the medical community. We are immensely grateful for this community's contributions, which underpin the journal's success and enable us to continue advancing the field of medicine.

The Safety Net's Safety Net: Understanding the Crucial Role of Free Clinics in Cardiovascular Care

Lucas Zellmer, MD; Sanjoyita Mallick, DO; Jason Larsen, MBA; Gautam R. Shroff, MBBS; Maarya Pasha, MD

Free clinics are overlooked but important components of the United States' safety-net health care system. Unlike traditional safety-net hospitals and clinics, free clinics are predominantly volunteer run and rely on inconsistent funding streams, including time-limited grants and community-based donations. Despite these challenges, free clinics are tasked with addressing both upstream and downstream determinants of chronic disease care.

Meanwhile, the clinical and economic burdens of cardiovascular disease continue to be staggering, despite significant therapeutic advancements in acute and chronic care management. There are ongoing disparities affecting access to appropriate care at the appropriate time, and recent literature underlines the fundamental concept that addressing patients' social needs directly impacts cardiovascular disease outcomes.

The purpose of this commentary is threefold: to briefly describe current disparities in cardiovascular care, to discuss the role of free clinics in addressing social determinants of cardiovascular disease, and to highlight one free clinic's approach to comprehensive chronic disease management.

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Social Determinants of Cardiovascular Disease

Social determinants of health (SDoH) are the conditions in which people are born, grow, work, live, and age and the wider set of forces and systems shaping the conditions of daily life.[1] These factors are often the primary drivers of the tangible social needs faced by patients, such as housing, food, and education.

SDoH directly affect health outcomes; roughly 80% of health outcomes are attributed to factors beyond direct clinical care.[2] To this end, numerous professional groups and societies have published statements regarding social needs screening, intervention, and financing. In 2015, the American Heart Association (AHA) proposed the consideration of SDoH to improve population-level cardiovascular health and reduce associated deaths.[3] An updated 2020 Scientific Statement released by the AHA further outlined the importance of addressing SDoH for patients with heart failure. This call to action encouraged working towards a better understanding of the impact of SDoH, emphasizing data collection, implementing interprofessional care teams to bolster cross-sector navigation, and conducting research aimed at addressing SDoH.[3]

> Free clinics are currently an underrepresented component of the health care safety net and have great potential for future cardiovascular research—especially quality improvement interventions.

Cardiovascular disease is a leading cause of morbidity and mortality in the US, with roughly 1 in every 5 deaths attributed to heart disease. Modifiable risk factors for developing cardiovascular disease include hypertension, hyperlipidemia, diabetes, and other lifestyle factors. Significant disparities exist within the population distribution regarding control of these risk factors; this is directly affected by access to preventive cardiovascular care. Recent data suggest that housing insecurity,[4] lower socioeconomic status, and being Black[5] are associated with a greater risk of both developing cardiovascular disease and poorer clinical outcomes.

Uncontrolled hypertension is a leading risk factor for cardiovascular disease development. Certain social factors, including living environ-

ment, supportive relationships, and access to quality education and health care, continue to drive the disparity in clinical outcomes among patients with hypertension. For example, an increased risk of hypertension among individuals with low socioeconomic status has been described,[6] with decreased access to health care associated with poorer blood pressure control.[7] Moreover, racial/ethnic variations become apparent; nearly 32% of non-Hispanic White adults with hypertension have well-controlled blood pressure compared to 25% of both non-Hispanic Black adults and Hispanic adults.[8] The presence of these disparities necessitates an in-depth look into drivers of cardiovascular disease outcomes in underserved populations.

Free Clinics in the US – A Safety Net for the Safety Net

There are roughly 1400 free and charitable clinics in the US tasked with providing care for over 30 million uninsured individuals.[9] Despite low operating budgets – most commonly less than $500,000 per year – free clinics are charged with providing quality care to uninsured or underinsured patients. These clinics fill a significant gap in care for the uninsured by providing medications to manage acute and chronic diseases, as well as subsequent disease monitoring.[9] Historically, free clinics offer chronic disease management and primary care for the nation's most underserved patients; however, challenges with funding, staffing, and overall research infrastructure challenge the critical evaluation and dissemination of free clinic interventions.

Emphasizing Research and Community to Improve Cardiovascular Care

Opportunities to improve cardiovascular care should begin with the most vulnerable patients. Patients enrolled in large, practice-changing randomized clinical trials often fail to represent the collective diversity of patients seen in safety-net health care settings.[10] Coupled with the burden of adverse social needs in underserved populations, a discrepancy exists in the ability to generalize findings from large clinical trials to the cardiovascular care of patients receiving care at free clinics. In contrast to traditional research studies that often do not engage underserved communities, quality improvement (QI) methodologies can assess disease disparities through root cause analysis, revealing many patient-level SDoH factors and nonmedical barriers to care. Previous QI initiatives have revealed SDoH factors, such as lack of transportation, lack of social support, and self-management strategies, as causes for poor blood pressure control among patients seen in safety-net clinics.[11] Given limited staffing and resources in free clinics, QI can highlight care gaps and provide streamlined workflows that integrate SDoH screenings into clinic visits, thereby providing clinicians important information on the real-life social burdens that affect cardiovascular disease risk – information that is vital to help modify and reduce cardiovascular disease risk in this population.

The Centers for Disease Control and Prevention and the Community Preventive Services Task Force both support team-based approaches to cardiovascular care.[12] Embracing "ancillary" professionals has shown benefit in addressing determinants of cardiovascular outcomes beyond medications and procedures. Community health workers (CHW) or frontline public health professionals who have a deep understanding of the communities they serve, have proven beneficial in hypertension management of ethnic minority populations.[13] Interventions by CHW also show a reduction in emergency department visits and subsequent hospital admissions in patients with heart failure.[14] While free clinics are well positioned for community-based interventions, time-limited grants, staffing, and program assessment infrastructure represent barriers to initiation.

Case Example - St. Clare Health Mission

St Clare Health Mission (SCHM) is a volunteer-run free clinic located in La Crosse, Wisconsin. Founded in 1993 by a local Catholic nun, the clinic initially served as a screening clinic for incoming Hmong refugees. In 1997, SCHM broadened its scope to include addressing the general health needs of area low-income, uninsured individuals. This change prompted a significant increase in patient numbers, costs, and disease complexity. Through buy-in from local health systems and relationships with community-based organizations, SCHM continues to play an integral role in the care of underserved community members.

The passage of the Affordable Care Act[15] in 2010 ensured access to health insurance for millions of Americans. Despite the state of Wisconsin opting against Medicaid expansion, a significant proportion of SCHM's patient population then was able to receive care from one of two nearby health systems. The resultant decrease in the number of patients prompted a shift in strategy to include community-minded, population-level interventions. To this end, SCHM invested its resources into establishing a CHW program, developing a Community Pathways HUB, and establishing a mobile medical clinic aimed at providing care where patients live, work, and play.

SCHM also identified two specific disease processes that disproportionately affected its patient population: type 2 diabetes and hypertension. After the initiation of simple QI measures aimed at standardizing diabetes care with input from physicians, nurses, clinic management, and community health workers, SCHM saw significant improvement in A1c and appropriate prescribing practices. Additionally, SCHM recently sought to characterize the burden of adverse social needs in patients with hypertension and found significant transportation and food insecurity; these findings will guide further QI interventions.

Conclusions

Effective, equitable cardiovascular care involves clinics, hospitals, and extension into the community. Free clinics are uniquely positioned to impact the most vulnerable patients in the most meaningful way, despite staffing and budget constraints. As highlighted above, free clinics are currently an underrepresented component of the health care safety net and have great potential for future cardiovascular research – especially quality improvement interventions.

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References continued on page 4

Advanced Practice Providers' Wellness Essential for Health Care Organizations

Ashley Choudoir, MSN, APNP, NP-C; Fahad Aziz, MD

In the United States, the first case of COVID-19 infection was announced in early 2020. Soon after, the COVID-19 pandemic profoundly affected frontline health care workers, including advanced practice providers (APP). Despite limited resources, hospitals were filled with patients. Nonclinical staff adjusted to remote work, causing a delay in elective surgeries and widening the gap for social distancing. In this new situation, medical professionals faced the challenge of constantly changing treatment protocols against an unknown enemy. Despite the difficulties, they remained dedicated and worked tirelessly in short-staffed wards, risking their own health and personal sacrifices with unwavering determination.

Equipped with a broad set of skills adaptable to inpatient and outpatient settings, APPs were deployed across the country to address acute staffing shortages and manage COVID-19 cases from frontline positions, including urgent care, emergency departments, and critical care units. Hospitalists, including APPs and physicians, comprised the primary providers treating patients hospitalized with COVID-19.

A multicenter study showed that these frontline workers also faced several psychological conditions, including depression, anxiety, guilt, fear, and insomnia. It's worth noting that APPs had lower overall well-being compared to physicians, and there was significantly less focus on the well-being of APPs compared to physicians and nurses.[1] As a result, six in 10 APPs reported being burned out, and four in 10 reported being depressed.[2]

APPs played a critical role during the pandemic and are essential to the health care workforce. It's important for us to recognize the factors that cause APP burnout and support their overall well-being.

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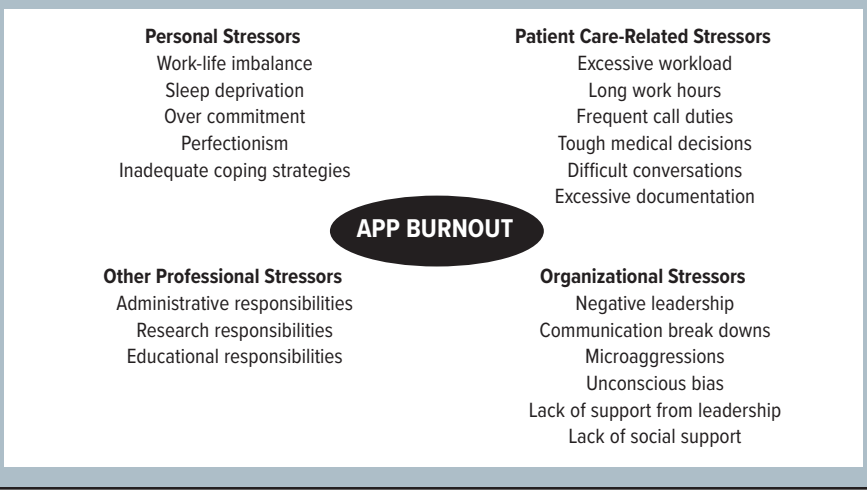
Figure 1. Stressors Leading to Advance Practice Provider Burnout



Factors Associated With APP Burnout

Just like physicians and nurses, APPs also experience many stressors in their everyday lives that can lead to burnout, especially during the pandemic. These stressors can be divided into four main categories: personal stressors, patient-related stressors, organizational stressors, and other professional stressors (Figure 1).

Understanding APP Wellness

Striking a balance between APP workload and feeling supported is necessary to cultivate APP wellness, and that support can be broken down into the following areas:

1. **Organizational support:** Organizational support is essential and includes:
   - Sufficient resources for medical practice, such as medical equipment, pagers, computers, and phones.
   - Sufficient training in electronic medical records.

- Appropriate support for technical issues.
- Sufficient time to meet work demands.
- Appropriate compensation.

2. **A culture of wellness:** Creating a wellness culture relies on fostering organizational values, attitudes, and behaviors that support self-care, and personal and professional development.
3. **Developing resilience:** Being resilient means being able to handle stressful situations in a positive and adaptive manner. Medical professionals who are more resilient have the ability to quickly recover from stressful situations and become even stronger. Resilience is based on three factors:
   - **Self-awareness:** Knowing and understanding one's weaknesses and emotions are key to self-awareness.
   - **Self-limitation:** Recognizing personal limits is key to building resilience. APPs, as medical professionals, are accustomed to handling challenging duties. Yet, it's vital to acknowledge our human boundaries and seek assistance from colleagues or supervisors when necessary.
   - **Public awareness:** APPs play a crucial role in any medical organization. However, their importance is often not fully recognized by the public, especially when compared to nurses and physicians. It is important to have a better understanding of the crucial roles that APPs play in order to foster healthy relationships between patients and APPs. This is also a significant factor in promoting APPs' well-being.

Figure 2. Advance Practice Provider (APP) Wellness Model

The well-being of APPs is a complex issue that depends not only on their own resilience, but also on the support and culture of health care organizations. It's important for these organizations to recognize that APPs, while highly skilled and adaptable, still face challenges in their demanding roles. To truly support their wellness, health care institutions must create an environment that actively promotes the mental, emotional, and physical health of these valuable team members. This goes beyond just acknowledging their struggles and involves investing in substantial support systems, such as mental health resources, professional development opportunities, and a workplace culture that encourages balance and self-care. The commitment to APP wellness should be deeply ingrained in the organization's values and practices, ensuring that APPs feel appreciated and supported as they navigate the complexities of patient care.

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Feasibility Study of a Low-Carbohydrate/ Time-Restricted Eating Protocol for Insulin-Using Type 2 Diabetic Patients

Philip N. Zimmermann, MD; Linda M. Baier Manwell, MS; Fauzia Osman, MPH; David Feldstein, MD

ABSTRACT

Introduction: Low-carbohydrate diets and time-restricted eating are methods to improve hemoglobin A1C in patients with type 2 diabetes. However, insulin-using patients are often counseled against these practices due to hypoglycemia concerns. This observational study evaluated a protocol utilizing both methods coupled with proactive insulin titration.

Objectives: To evaluate the safety and feasibility of a timed eating protocol for insulin-using patients and to assess its impact on outcomes, including insulin use and hemoglobin A1C.

Methods: Participants included insulin-using adults ages 49 to 77 years with type 2 diabetes. They were counseled to eat 2 meals per day in a 6- to 8-hour window of their choosing, with a goal intake of ≤30 grams of carbohydrates per day. Glucose was closely monitored, and insulin was adjusted per study protocol. Primary outcomes included hypoglycemic events and compliance with timed eating. Insulin use, hemoglobin A1C, body mass index, blood pressure, and quality of life also were measured.

Results: Nineteen of the 20 participants completed the 6-month study. No hypoglycemic events requiring urgent medical care occurred. Symptomatic episodes with glucose between 47 and 80 mg/dl were reported by 37% (7/19) of participants. Average daily insulin use decreased by 62.2 U ($P < 0.001$) and insulin was discontinued for 14 participants. Average hemoglobin A1C remained unchanged. Average body mass index decreased by 4.0 ($P = 0.01$), systolic blood pressure decreased by 9.9 mm Hg ($P = 0.02$), and diabetes-related quality-of-life metrics improved significantly.

Conclusions: These results demonstrate that a time-restricted eating protocol is feasible and safe for insulin-using patients with type 2 diabetes when paired with a proactive insulin titration.

INTRODUCTION

Type 2 diabetes is a major contributor to morbidity and mortality in the United States.1 Its pathophysiology is interwoven with obesity and contributes to comorbidities, including vision loss, kidney failure, lower extremity amputation, and cardiovascular disease.2 Major improvements in type 2 diabetes treatment have occurred over the past 2 decades, including novel pharmaceuticals such as sodium-glucose transport protein 2 (SGLT-2) inhibitors and glucagon-like peptide 1 (GLP-1) agonists. However, incidence has continued to increase, and over 37 million American adults currently live with this disease.3 The combination of rising incidence and increasingly expensive medication continues to accelerate type 2 diabetes-related health care expenditures.4 The prevailing paradigm of type 2 diabetes care does not appear to offer the potential for reversing these trends in costs or disease burden. However, development of more effective lifestyle interventions potentially could make an impact.

Observations from routine clinical practice show that periods of fasting tend to lower blood sugar and insulin requirements. Patients with type 2 diabetes who are required to fast for common medical procedures, such as colonoscopy, require substantial insulin reductions to maintain euglycemia during the periprocedural period. A dietary routine can be organized around such fasting intervals with the goal of reducing insulin requirements. This practice is often referred to as "time

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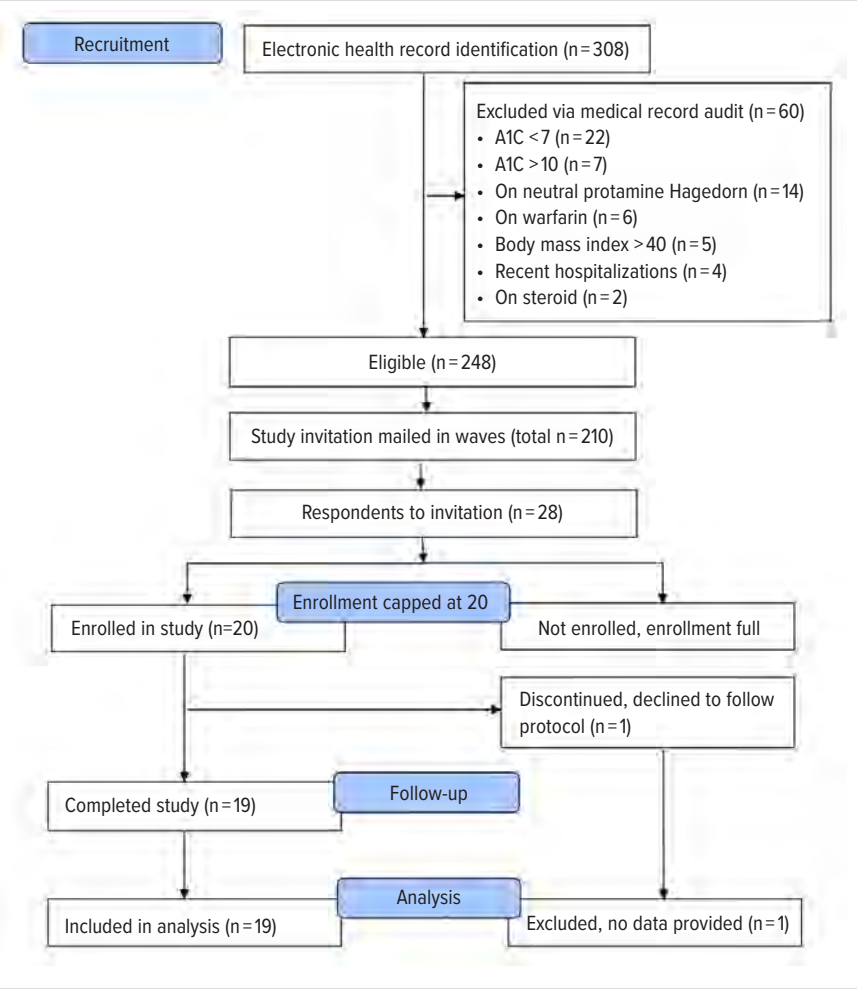
restricted eating" (TRE) and usually consists of a window of 6 to 10 hours where food is consumed followed by a 14- to 18-hour food-free interval.

Multiple studies report improved insulin sensitivity in nondiabetic populations who practice TRE compared to standard meal timing.[5-7] Further, TRE increases insulin sensitivity in non-insulin-using patients with type 2 diabetes[8] and improves insulin sensitivity in patients with prediabetes independent of weight loss.[9] There is also evidence that lower-carbohydrate diets can improve insulin sensitivity with superior hemoglobin A1C control compared to a low-fat diet.[10]

Although lower-carbohydrate (LC) diets and TRE have been shown independently to have positive effects on insulin sensitivity, no studies have been reported that combined these modalities to treat insulin-using patients with type 2 diabetes as part of a comprehensive insulin reduction program. Indeed, insulin-using patients often are counseled to refrain from these practices out of concern for hypoglycemia. We performed a study of a LC/TRE regimen with patients who have type 2 diabetes and use insulin to determine whether this population could safely use these methods when paired with a proactive insulin titration. We also sought to assess the regimen's impact on their insulin needs, hemoglobin A1C, body mass index (BMI), blood pressure, and quality of life.

Figure 1. CONSORT Flow Diagram



METHODS

This prospective cohort study evaluated the feasibility, safety, and efficacy of a LC/TRE protocol for patients with type 2 diabetes who use insulin. The study took place from February 2021 through January 2022 at 3 university-based general internal medicine clinics. Participants were followed for 6 months. The study was approved by the university's Institutional Review Board.

Participants

An electronic health record (EHR) data tool identified 308 insulin-using patients with type 2 diabetes who were medically homed at 3 general internal medicine clinics; 248 patients met inclusion and exclusion criteria. Letters were sent to 210 individuals in rolling fashion until the goal of 20 participants was met (Figure 1). Patients provided written informed consent at their first study visit. The initial recruitment plan called for flyers to be posted in study clinics, but COVID protocols halted clinic visits for routine care. This initiated the switch to direct mail. Participants were offered up to $285 for completing all study procedures.

Inclusion criteria included type 2 diabetes diagnosis, using once daily basal insulin, age 18 to 80 years, self-administering insulin, most recent A1C of 7% to 10%, stable diabetes medication regimen for > 3 months, demonstrated reliability with glucose monitoring and A1C checks, and BMI of 25 to 40.

Exclusion criteria included type 1 diabetes, using concentrated insulin or neutral protamine Hagedorn (NPH), living in a skilled nursing facility, unwilling or unable to do blood glucose checks 3 times per day, estimated glomerular filtration rate (eGFR) < 30 mL/min, taking steroids or warfarin, hospitalized within the past 3 months, symptomatic heart failure, weight loss > 10% in last 6 months, history of organ transplantation, pregnant or trying to become pregnant, and breastfeeding.

Study Visits

The protocol included 5 in-person visits over the course of 6 months. Participants met with the study physician at study initia-

tion, the start of month 4, and the 6-month conclusion. Intervening visits with the registered dietician occurred at the beginning of months 2 and 5 (Appendix).

Physician Visit 1 at Study Initiation: Participants were counseled to consume all calories in 2 meals within a 6- to 8-hour window of their choosing and educated on a lower carbohydrate diet with a goal intake of ≤30g of carbohydrates per day. Recommended meal plans featured meats, eggs, nuts, seeds, vegetables, and berries. Participants were encouraged to complete a food log and walk at least 20 minutes daily. They also received instructions on the insulin titration protocol and safety procedures, including a discussion of hypoglycemia symptoms and management.

Registered Nurse (RN) Phone Protocol: Participants started the protocol on a Monday to facilitate easy contact over a full 5-day work week. Daily contact continued until a stable insulin dose was reached. RN communications were reduced to weekly thereafter if the participant was still taking insulin or monthly once insulin was discontinued. Formal nurse calls also were scheduled at the beginning of months 3 and 6.

Registered Dietitian Visits 1 and 2 at Months 2 and 5: In-depth dietary counseling included a discussion of meal planning and expanded lower carbohydrate food options. A 3-day carbohydrate consumption food inventory was completed at each visit.

Figure 2. Total Insulin Use (Units/Day)

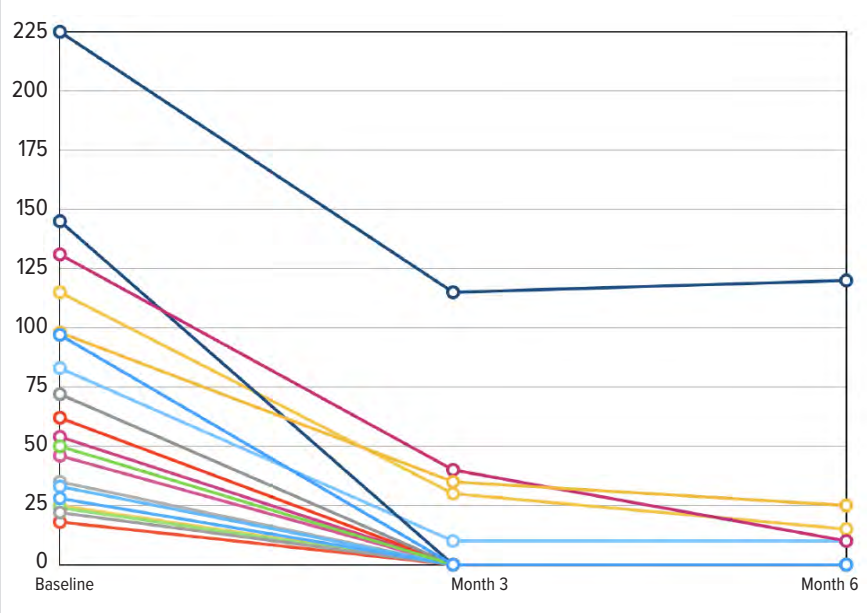


Table 1. Patient Characteristics and Outcomes (n = 19)

	Baseline	3 months	6 months	*P* value
Age, mean (SD), years	64.7 (8.3)			
Sex, N (%)				
Male	10 (52.6)			
Female	9 (47.4)			
Weight, mean (SD), pounds	227.7 (42.3)	205.7 (39.9)	201.2 (39.5)	0.11
Body mass index, mean (SD), kg/m^2	34.5 (4.30)	31.2 (4.27)	30.5 (4.17)	0.01[a]
Diastolic blood pressure, mean (SD), mmHg	80.5 (6.95)	77.7 (5.00)	72.8 (7.10)	0.002[a]
Systolic blood pressure, mean (SD), mmHg	134.5 (14.58)	129.1 (7.89)	124.6 (7.14)	0.02[a]
Hemoglobin A1C, mean % (SD)	7.8 (1.01)	7.9 (1.46)	7.8 (1.16)	0.99
Average time on insulin, years	9			
Short-acting insulin, mean (SD), units[a]	30.9 (37.63)	8.4 (20.62)	4.7 (12.18)	0.006[a]
Long-acting insulin, mean (SD), units[a]	40.8 (22.37)	3.68 (11.03)	5.0 (16.75)	<0.001[a]
Total insulin, mean (SD), units[a]	71.7 (53.66)	12.1 (28.15)	9.5 (27.63)	<0.001[a]

[a]Mean includes all study participants whether on insulin or not at that time point.

Physician Visit 2 at Month 4: Food logs, insulin use, blood sugar readings, and dietitian assessments were reviewed. Depending on insulin status, the discussion focused on either areas to improve adherence with the regimen or maintenance.

Physician Visit 3 After 6 Months: Protocol results were reviewed and final insulin and dietary recommendations were provided. The study physician communicated with each participant's primary physician regarding the participant's study progress and current medications.

Outcome Measures

At physician visits 1, 2, and 3, participant weight, height, and blood pressure were recorded. Diabetic medications were documented by the study physician, and hemoglobin A1Cs were drawn. Participants completed the 7-item Appraisal of Diabetes Scale (ADS) assessing psychological well-being, social well-being, role activities, and personal constructs on a 5-point Likert-like scale (Appendix). ADS scores can range from 7 to 35; a lower score corresponds with improved quality of life and decreased impact from diabetes.[11]

At physician visits 1 and 2, participants were given three monthly food logs (Appendix) to record the time of first and last eating each day and symptoms of hypoglycemia. These were returned by mail monthly to study personnel or brought to the next visit. Participants also received instructions regarding comple-

Table 2. Patient Compliance with Time-Restricted Eating (n = 19)

	Month 1, N = 16 (480 log entries[a])	Month 2, N = 16 (480 log entries[a])	Month 3, N = 16 (458 log entries[a])	Month 4, N = 13 (390 log entries[a])	Month 5, N = 13 (373 log entries[a])	Month 6, N = 11 (298 log entries[a])
Average time of eating (SD), hours	5.76 (1.9)	5.58 (1.9)	5.89 (2.0)	5.45 (2.2)	5.54 (2.0)	5.48 (2.2)
Range	0.15 – 13.3	0.1 – 13.3	0.3 – 2.4	0.2 – 13.3	0.2 – 11.0	0.0 – 14.0
< 8 hours 100% of time (%)	75%	56.3%	43.8%	30.8%	46.2%	54.5%
< 8 hours > 90% of time (%)	93.8%	100%	68.8%	84.6%	76.9%	72.7%
< 8 hours > 75% of time (%)	93.8%	100%	93.8%	100%	84.6%	92.3%
< 8 hours > 50% of time (%)	100%	100%	100%	100%	100%	100%[a]

[a]Entries = Monthly total of daily entries in subjects' food tracking logs.

tion of a 3-day food inventory documenting exact carbohydrate intake for all food consumed over a 3-day period.

At physician visits 2 and 3, participants were given a satisfaction survey where they rated, on a scale of 1=not at all to 5 = extremely, the likelihood of continuing the feeding protocol after study completion.

At registered dietitian visits 1 and 2, the 3-day food inventory was reviewed and carbohydrate counts were calculated. Incomplete data were discussed and food modeling provided best estimates of carbohydrate intake. This information was entered into the EHR. Food inventories have been shown to be an accurate assessment of patient food intake.[12]

Hypoglycemia Mitigation Protocol

Basal insulin was reduced by 50% on the day prior to protocol initiation and all short-acting doses were eliminated during the fasting interval. The 2 remaining short-acting insulin doses were left unchanged at study start for the 11 patients using mealtime insulin. Further insulin adjustments were made on a daily basis based on a predetermined titration protocol that reduced the insulin dose any time glucose dropped under 120 mg/dL (Appendix). This protocol preferentially titrated off long-acting insulin first to minimize its effect during the fasting window. Transient hyperglycemia up to 300 was tolerated during the first week in order to further minimize hypoglycemic risk. Participants were told to immediately inform study personnel of any severe hypoglycemic episodes defined as glucose < 50 and/or requiring medical assistance. Mild hypoglycemic episodes were recorded on the monthly food logs.

Data Collection

Participant sociodemographic data, A1C, weight, BMI, insulin dose, and average carbohydrate counts were extracted from the EHR by a member of the study team and entered in an Excel (Microsoft Corporation, 2018) spreadsheet on the study's secure server. Paper food logs and ADS results were copied into an Excel spreadsheet.

Statistical Methodology

We compared differences between the 3 different survey periods (baseline, 3 months, 6 months) using chi-square tests for categorical variables and the analysis of variance (ANOVA) for continuous variables. Similarly, we compared differences between the baseline and 6-month periods using a paired t test. Likert scale responses were examined individually using Fisher exact tests. Overall ADS scoring was assessed using a general linear mixed model analysis. We used a logistic regression model to find the odds of discontinuing insulin and 95% confidence intervals. All P values ≤ 0.05 were considered statistically significant. We conducted these analyses using SAS version 9.4M7 (SAS Institute Inc, Cary, North Carolina, 2020) and STATA version 17 (STATACorp LP, College Station, Texas, 2021).

Table 3. Appraisal of Diabetes Scale Results

Time Administered	Mean Score	Mean Difference (CI) vs Baseline	*P* value (from baseline)
Baseline	18.42		
3 months	15.68	-2.74 (-4.26 to -1.21)	< 0.001
6 months	15.42	-3.00 (-4.53 to -1.47)	< 0.001

No statistically significant difference between months 3 and 6.

RESULTS

Twenty participants were recruited and 19 completed the study. One declined further participation shortly after enrollment and provided no data to include in the analyses. The average age was 64.7, and nearly half of the participants were female (47.4%). The mean BMI was 34.5, and the average duration of insulin use was 9 years. All 19 participants attended the 3 physician visits and 15 completed both of the registered dietician visits (4 missed the second registered dietician visit).

Safety

Participants made no emergency or urgent care visits related to hypoglycemia over the course of the study. Symptomatic hypoglycemic episodes with readings between 47 and 80 were reported by 37% (7/19) of participants in 12 separate occurrences. Five of these episodes occurred within the first month of the study. Two participants experienced hypoglycemia in the third and fourth month. In all occurrences, hypoglycemia was associated with insu-

lin use. No participants experienced hypoglycemia once their insulin was stopped.

Insulin Use and Glycemic Control

Insulin use was stopped in 14 of the 19 (74%) participants by the end of the study (Figure 2). The titration process took less than 2 weeks for 12 of these. The other two stopped at 3 and 6 weeks, respectively. Five patients also stopped or reduced non-insulin diabetes medications outside of our protocol. The 5 participants who continued to use insulin were able to reduce their total insulin dose by 72%. Four of the 5 participants who continued basal insulin also continued short-acting insulin. Importantly, participants were able to achieve these changes in medication without worsening their A1C. Average A1C was 7.8% at the beginning and end of the study (Table 1).

BMI and Blood Pressure

Participants experienced statistically significant and clinically relevant improvements in both BMI and blood pressure (Table 1). Average BMI dropped from 34.5 at the beginning of the study to 30.5 by study end. This corresponded with an average weight loss of 26.5 pounds. Participants also experienced improvements in both systolic and diastolic blood pressure control. Average systolic pressure dropped from 134.5 mm Hg to 124.6 mm Hg. Three participants discontinued antihypertensive medications during the study due to significantly improved readings.

TRE and Carbohydrate Compliance

Most participants had a high degree of compliance with TRE (Table 2). Eleven of 19 provided the full 6 months of monthly food logs, 5 provided at least 3 months of data, and 3 did not provide any dietary data. The average time of documented eating was consistently under 6 hours throughout the study.

Carbohydrate counts performed during the dietitian appointments revealed that, in general, adherence was better for TRE than for carbohydrate restriction: 36.8% of participants were compliant with the <30g carbohydrate restriction at the 2-month mark, and this dropped to 26.7% by month 5 (Appendix). Additional participants met the less stringent 30 g to 60 g secondary target. At the time of the second dietitian appointment, the average carbohydrate intake per day was 61.7 g. Eight of the participants were in the > 60 g category; the top 3 reported carbohydrate intake values in this latter group were 90, 100, and 125 g per day. Of note, these are significantly lower than the recommended standard dietary intake of 225-325 g carbohydrates per day for a person who consumes 2000 calories daily.[13]

We had intended to perform a multivariate analysis to gain insight into whether compliance with TRE or the carbohydrate restriction predicted participants' ability to get off insulin. However, univariate analysis of the data did not find compliance with the discrete measures themselves to be independently predictive (Appendix).

Quality of Life and Satisfaction with the Study

Participants reported statistically significant improvements in their quality of life as measured by the ADS (Table 3). Scores improved significantly over the first 3 months, then continued to improve until study end. All areas assessed by the screening tool showed improvement; the most substantial changes resulted from improved coping with the diagnosis of type 2 diabetes and a decrease in type 2 diabetes impeding their life goals (Appendix).

At 6 months, participants were asked to respond to a question querying their intent to continue the LC/TRE protocol after conclusion of the study. The average response was 4.47 on a scale of 1 to 5. Thus, most participants reported a strong desire to continue.

DISCUSSION

We conducted a prospective study of a LC/TRE protocol with a cohort of insulin-using individuals with type 2 diabetes. Our results demonstrate that this protocol can be safely implemented in a primary care setting if it is done in concert with a proactive insulin titration. We also showed significant reductions in insulin use, weight, and blood pressure with these methods. These were accomplished while maintaining hemoglobin A1C. The overall improvement in quality-of-life scores demonstrates the potential of this protocol to improve an important outcome: helping participants feel in control of their type 2 diabetes management.

While the average hemoglobin A1C was still above goal in the setting of significant weight loss, this is not surprising since the mean daily insulin dose decreased by 62 units and no other medications were added. Our goal was to stop insulin, and we did not attempt to address non-insulin type 2 diabetes medications during the study as we wanted to isolate the effect on insulin use. An A1C of 7.8%, while unchanged, could still be improved. Clinically, participants could be further optimized on non-insulin-based treatments while working on further weight loss. Future studies could implement non-insulin medication titration along with this protocol.

This study builds upon previous research into the impact of TRE and LC regimens on type 2 diabetes in a novel way by combining the two methods and implementing them in an insulin-using population. Our results are congruent with glucose control findings from a randomized controlled trial by Che et al that was conducted in a population with obesity and type 2 diabetes.[14] Che found improvements in blood sugar control and weight loss with a 10-hour TRE regimen without carbohydrate restriction. They also documented significant reduction in diabetic medication use in the intervention group; however, they prioritized elimination of oral hypoglycemics over changes in insulin.

Our weight loss findings are also consistent with randomized controlled trial results from Jamshed et al.[15] They demonstrated that an eating window of less than 8 hours was superior for weight loss compared to a ≥12-hour window for patients without dia-

betes. Our time restriction was narrower and our study participants consumed significantly fewer carbohydrates on average (62 g v 135 g), potentially contributing to the greater weight loss we observed.

The specific intake of food within the TRE window is an additional difference in our approach. Most TRE-based interventions utilize an ad libitum food intake during the time-restricted period, and some have shown negative results.[16-17] We specifically gave directions for 2 discrete meals per day and advised against snacking unless necessary for hypoglycemia mitigation. This created a hypocaloric regimen on its own, eliminating most of the need for calorie-specific counseling. Perhaps more importantly, it created a consistency for participants that allowed all food intake to be appropriately covered with short-acting insulin around mealtime. Consistency can improve the ability to predict blood sugars in the short-term, allowing for a smoother insulin titration. It also helps establish a routine, which is essential for a process to feel normal and thus sustainable.

Many studies have focused on early TRE protocols, suggesting that early food intake has preferential metabolic effects compared to eating later in the day.[18] Although this may well be the case, we chose to explain the rationale for early TRE to our participants but made no effort to convince them to follow it. We instead encouraged them to choose a TRE window that felt most comfortable for them with the hope they would continue it in the long term. All 19 participants, left to their own choice, chose a late TRE window with food consumed at lunch/brunch and dinner. We observed that people value a structure that allows them to eat normal meals at socially conforming times and hypothesized that doing so would facilitate longer-term satisfaction.

Limitations

This was a small study without a control group, and we cannot be sure what the natural history of disease would have been for these participants. However, they were taking insulin for an average of 9 years prior to study initiation and there is little reason to expect that they would have been able to stop or decrease insulin use without this protocol. Only 3 clinical providers were involved in this study (1 physician, 1 registered dietician, and 1 registered nurse) and participants were seen in a single medical clinic. This limits generalizability as clinician qualities may have had a major role in the success of the protocol. Participant compliance with tracking daily food intake times fell to 58% in the final month of the study, so we do not have a complete picture of compliance across the entire study period. Additionally, the study duration of 6 months does not allow assessment of participants' ability to maintain this practice long term.

CONCLUSIONS

Fasting-based and carbohydrate-restricted diets have traditionally been viewed as a liability for insulin-using patients with type 2 diabetes due to fears of hypoglycemia. However, insulin-using patients may have the most to gain from these methods. This study demonstrated the potential of a LC/TRE protocol to safely lower insulin requirements. Randomized controlled trials are needed to compare this process to the current standard of care and to identify which components of this protocol are most important.

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Appendix: Available at www.wmjonline.org.

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Are Symptoms of Obstructive Sleep Apnea During Pregnancy Associated With Autism Spectrum Disorder in Children: A Case-Control Study

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ABSTRACT

Background: Obstructive sleep apnea complicates 10% to 32% or greater of pregnancies, however, reports on long-term effects on the children of pregnancies affected by obstructive sleep apnea are limited.

Objective: We sought to test the hypothesis that the children of pregnant people with symptoms of obstructive sleep apnea during pregnancy have an increased incidence of autism spectrum disorder.

Methods: This was a case-control study comparing the pregnancies of people whose children were later diagnosed with autism spectrum disorder without a known associated genetic condition to those whose children were diagnosed with autism spectrum disorder with a known associated genetic condition.

Results: Of the 51 total parents who were eligible and consented to participate, 4 had a child with autism associated with a known genetic condition, and 47 had a child with autism with no known genetic condition. The prevalence of any snoring (50.0% and 36.2%, respectively) and daytime tiredness (75.0% and 89.4%, respectively) were similar between both groups.

Conclusions: In this study, the prevalence of any snoring and falling asleep while driving during pregnancy was higher in the sampled population than typically reported in pregnant people. While the sample size for this study was small, our preliminary results suggest that parents of children with autism have a high prevalence of sleep-related concerns during their pregnancies, which indicates the need for further investigation – especially for obstructive sleep apnea. Future studies exploring the neurodevelopmental outcomes of children of a cohort of pregnant people with known presence or absence of obstructive sleep apnea during pregnancy is warranted.

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BACKGROUND

Obstructive sleep apnea (OSA) complicates 10% to 32% or greater of pregnancies, with a pooled worldwide prevalence of at least 15% (95% CI, 12%-18%) in a recent meta-analysis.[1–3] Some physiologic changes of pregnancy, namely increased oxygen consumption and decreased functional residual capacity, can lead to low maternal oxygen reserves and result in rapid oxygen desaturation if apnea or hypopnea events occur.[4] OSA is characterized by recurrent partial or complete airway collapse during sleep, which results in varying degrees of oxygen desaturation and microarousals and associated catecholamine release.[5] Recurrent desaturations cause increased release of reactive oxygen species, which act together to increase inflammation, dysregulate endothelial function, and increase blood pressure.[5] However, despite these known pathophysiologic pathways, OSA that both predates and which is incident during pregnancy remains underdiagnosed.[2,5] Two pregnancy-specific screening tools have been generated that boast high sensitivity and specificity for predicting OSA in pregnancy.[2,6] Both incorporate a combination of body mass index (BMI), maternal age, and snoring into their model, with less emphasis on sleepiness or other symptoms that are generally more common and less specific for sleep apnea during pregnancy.[1,2,6]

When OSA is diagnosed, systematic reviews and meta-analyses have demonstrated an increased risk of adverse pregnancy outcomes, namely hypertensive disorders of pregnancy,[4,5,7] gestational

diabetes, fetal growth restriction, and preterm birth.[5,7,8] However, reports on long-term effects on the children of pregnancies affected by OSA are more limited.

Emerging animal models suggest that gestational intermittent hypoxia (aiming to simulate recurrent desaturations typical of OSA) is associated with neuroinflammation in offspring.[9] Neuroinflammation and microglia or astrocyte dysfunction are associated with neurodevelopmental disorders, including autism spectrum disorder (ASD).[10,11]

In humans, one small prospective study and one population-based study have queried the association between OSA and aberrant behavioral development in offspring. The population-based study found that maternal OSA during pregnancy was associated with developmental vulnerability in male (but not female) children, defined as scoring below the 10th percentile in one or more assessment domains, including social competence, language and cognitive skills, communicative skills, and general knowledge.[12] A small prospective study showed that participants with confirmed OSA during pregnancy who lacked any other known pregnancy complications were statistically more likely (2.5-fold increased risk) to have children with low scores on social assessments at 1 year of age compared to participants with normal gestational sleep evaluations.[13] The mechanism for these neurobehavioral changes in the children resulting from these pregnancies may be related to OSA-induced sleep microfragmentation and macrofragmentation, which could manifest as daytime tiredness or fatigue during pregnancy. It also may be that cumulative hypoxia due to recurrent desaturations with OSA during pregnancy leads to neuroinflammation as the animal studies suggest. In general, ASD is conceptualized to be multifactorial in nature with both genetic and environmental contributing factors, and the role of OSA during pregnancy is one possible environmental factor worth exploring.

The purpose of this project was to evaluate whether the children of pregnant people at risk of OSA during pregnancy have an increased incidence of ASD. A case-control design was chosen, with cases representing children with ASD resulting from no known or identified genetic etiology and controls representing children with ASD associated with known genetic conditions to minimize recall bias. Our hypothesis was that more of the birthing parents of children with ASD without a known genetic etiology would be at risk of OSA during pregnancy than the birthing parents of children with ASD with a known genetic etiology.

METHODS

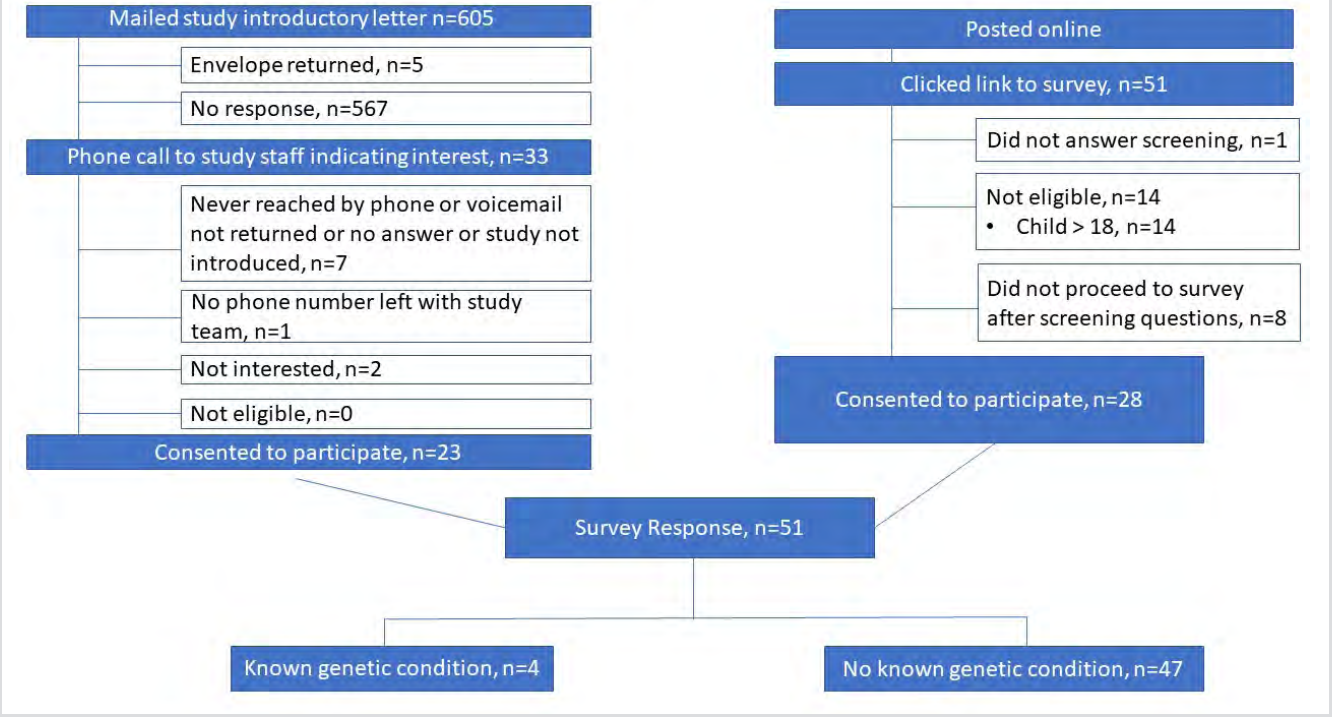
This study was reviewed by the Institutional Review Board (IRB) at the University of Wisconsin School of Medicine and Public Health (IRB 2021-1042). This survey study was initially designed to be administered via telephone to the parent who had been pregnant with a child who was later diagnosed with ASD. This survey was later adapted to an online format to allow wider participation.

Initially, people whose children were enrolled in a research registry at the Waisman Center at the University of Wisconsin-Madison with a diagnosis of ASD were mailed an introductory letter and printed informed consent information. Those who were interested were instructed to call the telephone number for study participation. If the study staff were not directly reached, a voicemail message requested that those interested in participating in the study record their name, contact phone number, and preferred time for a return call. A researcher (JN) then called the parent at the parent's preferred time and conducted the survey via telephone. The survey consisted of screening questions to confirm eligibility and questions about snoring, tiredness, and suspicion for sleep apnea during pregnancy. We also asked demographic questions about age, BMI, and the presence of comorbidities. The symptom of snoring was queried because it is a predictor of OSA and is included in most screening questionnaires for OSA used during pregnancy[6,14] and in the general population.[15–18] Snoring also has been used as a pseudo-surrogate for OSA in some studies.[19–22] Similarly, BMI, or obesity, is a predictor of OSA and is included in screening questionnaires.[6,15–18] Tiredness also is included in some, but not all, questionnaires used to screen for OSA.[15–17] While we could not retrospectively test those surveyed for the presence of OSA during their pregnancy since their pregnancies were all completed, these clinical measures and symptoms were queried because they are well-established risk factors for OSA.

When the response rate was low, the IRB protocol was amended to allow us to reach out to all parents of children who were patients of the Autism and Developmental Disabilities Clinic at the Waisman Center at the University of Wisconsin-Madison with a diagnosis of ASD. These parents were invited to participate via a mailed introductory letter and printed informed consent document. A list of children under 18 was generated by the clinic, and the letter was mailed to the listed parent of these children. Parents were specifically invited to participate as this project sought to interview the individual who was pregnant with the child who was later diagnosed with ASD. Those interested in participating were invited to call the study staff at a listed number. Their calls were returned by a researcher (JN) in same manner as noted above.

Due to low recruitment, the study protocol was modified to allow recruitment of survey responses from online communities for parents of children with ASD. Accordingly, the survey was modified slightly to allow it to be completed online via a survey format rather than as a study form, and a link to the survey was posted on social media sites inviting the parents of children with ASD to participate. Specifically, an invitation to participate and a survey link were posted on the UW Obstetrics and Gynecology's Twitter and Facebook page, Waisman Center Facebook page, Physician Mom Group Facebook page, Madison Mom Facebook page, Reddit, and a University of Wisconsin research email listserv.

Figure. Recruitment and Participation



Study fliers with a quick-response (QR) code link to the survey also were posted at the Waisman Center's clinic and the University of Wisconsin's pediatric neurology clinic. The online survey allowed participants to complete the entire survey online. Both the telephone survey and online survey were hosted on the University of Wisconsin Institute for Clinical and Translational Research's REDCap server.[23,24] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies that also hosts and allows electronic distribution of online surveys.[23,24]

The population surveyed were biological parents who had been pregnant with a child who was later diagnosed with ASD. Cases were selected as those whose children did not have an identified genetic condition associated with ASD. Controls were those whose children had an identified genetic condition associated with ASD. This population was selected as controls because their lived experiences since birth would overall be as similar as possible to the cases with the intention of minimizing recall bias. Specific genetic etiologies considered to represent genetic conditions associated with ASD or similar neurobehavioral changes included the following: MeCP2 genetic variant/Rett syndrome; LIS1, GRIN2B, and COL4A mutations; fragile X syndrome; and other microarray findings consistent with known genetic conditions associated with ASD based upon review by a trained pediatric neurologist and developmental pediatrician (KS and KK). The presence or absence of a genetic condition was assessed by the clinical team rather than as part of participation in this study, and genetic testing was not offered. Other inclusion criteria included parental age of 18 or greater at the time of participation in the survey. Exclusion criteria included neonatal history of intraventricular hemorrhage, hypoxic ischemic encephalopathy, neonatal sepsis, known perinatal stroke, or death of the child.

Table 1. Characteristics of the Pregnant Parent at the Time of the Index Pregnancy

	ASD Not Related to Known Genetic Cause N = 47	ASD Related to Known Genetic Cause N = 4	*P* value[a]
Age, mean (SD)	30.6 (6.3)	29.0 (7.0)	0.621
BMI, median (IQR)			
Prepregnancy	26.7 (22.1 – 33.6)	28.8 (26.4 – 34.4)	0.323
During pregnancy	30.8 (27.0 – 38.1)	36.4 (33.2 – 41.5)	0.153
Chronic hypertension, n (%)	1 (2.2)[b]	0 (0)	1.00
Diabetes, n (%)	1 (2.1)	1 (25.0)	0.221

Abbreviation: ASD, autism spectrum disorder; BMI, body mass index.

[a] *t* test for age, Wilcoxon rank sum test for BMI, Fisher exact test for chronic hypertension and diabetes.

[b] One person did not answer this question.

For statistical analysis, Fisher exact test, *t* test, and Wilcoxon rank-sum were performed where appropriate. Given the paucity of data and unknown effect size, an a priori sample size was not performed. All statistical analyses were performed using Stata

(16.1, StataCorp LLC, College Station, Texas).

RESULTS

From November 11, 2021 through November 29, 2021, 60 letters of introduction were mailed to registry participants introducing this study. From March 22, 2022 through April 7, 2022, 545 letters of introduction were sent to parents of clinic patients. Of 605 letters of introduction mailed to potential participants, 5 envelopes were returned due to changes of address, and we received 33 telephone calls indicating interest. One person did not leave a telephone number on the voicemail, thus could not be reached. Seven interested people were never reached by telephone. Following a verbal description of the study, 2 people were not interested in participating and 23 consented to participate. On May 24, 2022, the online survey was approved for use, and social media posts were approved on June 14, 2022. The survey was then made available via online links and posted on social media, shared via email correspondence, and available by scanning a QR code on recruitment posters. Fifty-one potential participants clicked on the survey link. Following a written introduction, 1 person did not respond to the screening questions, 14 people were not eligible due to their child being over 18 years old, 8 did not proceed to the survey itself after reviewing the screening questions, and 28 consented to participate. No respondents were excluded due to not having been pregnant with their child themselves or due to the presence of hypoxic ischemic encephalopathy or other exclusion criteria.

Of the 51 completed survey responses, 4 were from the parent of a child whose diagnosis was associated with a known genetic condition and 47 were from the parent of a child whose diagnosis was not known to be associated with a known genetic condition (Figure).

As shown in Table 1, demographic characteristics of the parents who had been pregnant with children with ASD with or without associated genetic conditions were similar. Symptoms of OSA, such as snoring, daytime tiredness, and falling asleep while driving, also were similar (Table 2). Snoring was reported by 36.2% of parents whose child with autism did not have a known genetic cause and 50.0% of parents whose child with autism did have a known genetic cause ($P = 1.00$). None of the parents whose child with autism was associated with a known genetic condition fell asleep while driving, compared to 6.4% of those whose child with autism was not associated with a known genetic condition ($P = 1.00$). One person whose child with autism did not have a known genetic condition had a confirmed diagnosis of OSA during their pregnancy; in her case, her diagnosis was made prior to pregnancy. The number of participants and the number of participants whose children have ASD with an associated genetic condition were low, precluding more detailed statistical analysis.

Table 2. Sleep Characteristics at the Time of the Index Pregnancy

	ASD Not Related to Known Genetic Cause N = 47	ASD Related to Known Genetic Cause N = 4	*P* value[a]
Any snoring during pregnancy, n (%)[b]	17 (36.2)	2 (50.0)	1.00
Loud snoring	7 (41.2)	1 (50.0)	1.00
Snoring 3 or more times per week	9 (52.9)	1 (50.0)	1.00
Cessation of breathing during sleep, n (%)[c]	1 (2.8)	0 (0)	1.00
Daytime tiredness, n (%)[d]	42 (89.4)	3 (75.0)	0.404
Fell asleep while driving, n (%)[e]	3 (6.4)	0 (0.0)	1.00
Ever diagnosed with sleep apnea, n (%)[e]	9 (19.1)	1 (25.0)	1.00
Diagnosed with sleep apnea before pregnancy[f]	1 (16.7)	0 (0)	1.00
Diagnosed with sleep apnea during pregnancy	0 (0)	0 (0)	N/A
Parent-suspected sleep apnea, n (%)[g]	4 (8.5)	0 (0)	0.152

Abbreviation: ASD, autism spectrum disorder.

[a]Fisher exact test used for all *P* values.

[b]Nine people in the nongenetic group did not recall; percent with loud snoring and frequent snoring only reported for those who snored at all. Three in the nongenetic group did not know whether they snored loudly. Five in the nongenetic group and 1 in the genetic group did not know whether they snored frequently.

[c]Two people in the nongenetic group did not recall and 11 did not answer. Two in the genetic group did not answer.

[d]Two people in the nongenetic group did not recall or did not know.

[e]One person in the nongenetic group did not recall.

[f]Three in the nongenetic group did not respond.

[g]Twelve people in the nongenetic group did not recall, 3 people in the genetic group did not recall.

DISCUSSION

The number of participants in this survey study was low, which precluded meaningful statistical analysis of this case-control study as intended. In this small sample, we found that the prevalence of the exposure of snoring and tiredness were similar between the birthing parent of children with ASD with a known genetic etiology and those without a known genetic etiology.

One unexpected finding was that the prevalence of any snoring during pregnancy in our population was overall higher than expected at 36.2% to 50%. Snoring is estimated to affect 1.2% to 35% of pregnancies.[19,25–27] While our overall numbers are small, the prevalence of snoring is higher than in reports in the general population and also higher than in pregnant people later diagnosed with OSA.[19,25-27] While snoring is not equivalent to a diagnosis of OSA, it is a clinical finding indicative of increased upper airway resistance and included in screening tools used for pregnant[2,6] and nonpregnant people.[15,16,18] The high prevalence of snoring is an important finding that merits future validation in larger populations and, ideally, corroboration with objective testing for OSA during pregnancy.

In this sample, we also found that 6.4% of the parents whose child with autism was not associated with a known genetic condition fell asleep while driving during their pregnancy. This is a dangerous occurrence, and the prevalence in this small sample is higher than reported in the general population. While the general prevalence of falling asleep while driving during pregnancy is not known, 4% of people in the US in general report having fallen asleep while driving in the prior 30 days,[28] and 4.26% of one pregnant population reported falling asleep while driving.[29] However, the sample size in our study was small; thus, this finding may represent random variation.

Our study has many limitations. First, analysis was limited by our sample size, which led to this analysis being underpowered. We attempted to increase recruitment by reaching out to a registry in addition to our local patients. We also transitioned the survey to an online format, posted links on social media, shared via an email listserv of individuals who may be interested in participating in research, and posted signs locally at the pediatric neurology clinic. A second limitation was that only one of the participants had a confirmed diagnosis of OSA during their pregnancy, which limits our ability to discern any impact of diagnosed OSA. Accordingly, and because we expected this based upon the low prevalence of screening and diagnostic testing for OSA during pregnancy, we used surrogates for OSA, such as snoring and tiredness, which can be indicators of OSA but do not constitute diagnostic criteria alone. Third, our retrospective design is limited by recall and susceptible to recall bias. Participants in this survey knew that the survey was evaluating prenatal sleep-related exposures that may relate to autism in the offspring. This may have affected who chose to participate at all and the responses of those who did participate.

This study raises an interesting finding regarding the higher-than-expected prevalence of snoring. While it is likely related to participation bias, it builds the case for further investigation into potential relationships between OSA during pregnancy and ASD in the children of these pregnancies. In particular, it would be helpful to query cohorts of pregnant people with or without known diagnoses of OSA during pregnancy for neurobehavioral outcomes in their offspring. As above, confirmation of OSA diagnosis through objective testing could also bring considerable value, by allowing phenotyping and endotyping of gestational pathophysiology with possible contributions to offspring ASD and point to downstream mechanistic pathways of interest for translational diagnostic and therapeutic studies. A coordinated effort to screen, test, and treat pregnant people for OSA, particularly if risk factors such as obesity and hypertension exist, may aid these efforts.

CONCLUSIONS

While the sample size for this study was small, our preliminary results suggest that parents of children with autism have a high prevalence of sleep-related concerns during their pregnancies, which indicates the need for further investigation – especially for OSA. Future studies exploring the neurodevelopmental outcomes of children of a cohort of pregnant people with known presence or absence of OSA during pregnancy is warranted.

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Postoperative Prescribing Practices Following Gynecologic Surgery

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ABSTRACT

Background: Opioids prescribed for postoperative pain have exceeded patient need in the United States, playing a significant role in the opioid epidemic. In the preintervention phase of this project (September 2018 – March 2019), a chart review and patient survey revealed that patients were prescribed double the number of opioids they consumed following gynecologic surgery.

Objective: To ascertain whether an educational intervention recommending opiate prescriptions based on postoperative opioid use decreases gynecologic surgeons' opiate prescriptions.

Methods: An educational intervention implemented in January 2021 communicated the discrepancy between patient need and medications prescribed and made prescribing recommendations for common gynecologic procedures. A postintervention (February 2021 – April 2021) retrospective chart review ascertained postoperative opioid prescribing practices. Residents were surveyed about their prescribing practices in June 2021. Descriptive statistics compared each phase.

Results: For laparoscopic hysterectomy, the median morphine milligram equivalent (MME) was 150 (IQR 112.5-166.9) for preintervention and 150 (IQR 112.5-150) postintervention. For vaginal hysterectomy, median MME declined from 150 (IQR 112.5-225) to 112.5 (IQR 112.5-150). For laparoscopic surgery without hysterectomy, the median MME was 75 for both preintervention (IQR 75-120) and postintervention (IQR 60-80). For vaginal surgery without hysterectomy median MME went from 75 (IQR 75-142.5) to 54 (IQR 22.5-112.5). Median MME for hysteroscopy and dilation and curettage was 0 for both phases. When surveyed, residents reported prescribing lower amounts than actual prescribing practices.

Conclusions: Despite education informing gynecologic surgeons that their opioid prescribing exceeded patient need, prescribing practices did not change. The difference between actual and resident-reported prescribing practices warrants further investigation.

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BACKGROUND

Now in its third decade, the opioid epidemic continues to be a major public health crisis. Since 1999, there have been more than 600 000 opioid overdose deaths in the United States, with more than 1 death every 13 minutes on average.[1,2] Though synthetic opioids play an increasingly large role, prescription opioids were still involved in approximately 24% of all fatal overdoses in 2020.[3] Thus, it is imperative that health institutions and clinicians improve narcotic prescribing practices to balance adequate pain control with responsible opioid stewardship.

Postoperative pain management has been identified as an area for improvement in surgical specialties. Between 67% and 92% of patients have unused opioids after surgery, which creates possible opportunities for misuse or diversion.[4] Within gynecological surgery, it has been reported that surgeons provide approximately twice the number of opioids used by most patients following hysterectomies.[5,6]

We adapted and implemented a survey-intervene-survey study design previously shown to be effective in general surgery.[7,8] We assessed and compared narcotic prescriptions and patient consumption following common gynecologic surgeries and generated prescribing recommendations to align with actual patient use. An educational intervention communicated these recommendations to clinicians. We then reassessed prescribing patterns postintervention to ascertain the impact of the intervention.

METHODS

Preintervention

Our Institutional Review Board deemed this quality improvement study exempt. Preintervention data were collected from patients undergoing benign gynecologic surgery at our large academic institution during a 3-month period prior to the COVID-19 pandemic. Patient discharge instructions included information about this quality improvement project, how to dispose of unused opioids, and how to opt out of participation. Patients who did not opt out were sent invitations via text message 7 and 14 days postoperatively to complete brief electronic surveys about postoperative pain medication use and satisfaction. Patients were asked about the number of tablets taken for both opioid and nonopioid pain medications. Satisfaction or dissatisfaction with pain control was queried using a 5-point Likert scale from 1 (very dissatisfied) to 5 (very satisfied). For those patients who responded to the survey, data were abstracted from the electronic health record regarding demographics, surgical details, and medications prescribed for postoperative pain.

Procedures were categorized into 6 groups: (1) hysterectomy (laparoscopic or robotic), (2) hysterectomy (vaginal), (3) laparoscopic or robotic gynecologic procedure without hysterectomy, (4) vaginal surgery without hysterectomy, (5) hysteroscopy (operative or diagnostic), (6) suction dilation and curettage (D&C). Surgeries that did not fall into one of these categories were excluded.

Opioid prescriptions and patient consumption data were converted to median morphine milligram equivalents (MME) to allow for comparisons across different opioid medications. Descriptive analyses characterized patient satisfaction with pain control and identified median MME and interquartile ranges prescribed for each procedure. Extreme outliers (n = 2), defined as falling outside the highest and lowest quartiles plus 1.5 times the interquartile range, were excluded. MMEs prescribed and consumed were compared, and prescribing recommendations that aligned with patient consumption for each surgery category were ascertained.

Intervention

Similar to the methods used by Hill et al in their general surgery intervention, we identified the MME value that would meet the needs of 80% of patients undergoing each of the 6 types of surgery and calculated the corresponding number of tablets of oxycodone or hydrocodone.[7,8]

The educational intervention for prescribers was a 15-minute live presentation delivered virtually during two protected educational times for the Department of Obstetrics and Gynecology: (1) Grand Rounds attended by faculty, staff, and trainees; and (2) mandatory resident didactic time.

Descriptive data from the preintervention phase, including differences between our opioid prescribing practices and patient consumption, as well as recommendations based on patient need, were included in the educational intervention. The slides and link to the Grand Rounds recorded presentation also were disseminated to the department via email following the live presentations.

Table 1. Sample Description Stratified by Intervention Phase

Variable	Preintervention (N = 146) % (n)	Postintervention (N = 500) % (n)	*P* value
Age (years)[a]	39 (32 – 49)	41 (34 – 51)	0.360
Body mass index (kg/m^2)[a]	28 (24 – 34)	29 (24 – 35)	0.837
Race and ethnicity			
Hispanic, multiracial, or other	1 (1)	5 (26)	0.011
Asian or Pacific Islander	3 2 (4)	5 (24)	
Black or African American	4 (6)	6 (32)	
Non-Hispanic White	92 93 (135)	84 (418)	
Surgery category			
Hysterectomy: laparoscopic/robotic	14 (20)	12 (61)	< 0.001
Hysterectomy: vaginal	9 (13)	4 (21)	
Laparoscopic/robotic surgery	25 (37)	19 (97)	
Vaginal surgery	16 (23)	8 (41)	
Hysteroscopy (diagnostic or operative)	27 (40)	42 (210)	
Suction dilation and curettage	9 (14)	14 (70)	

Abbreviations: kg, kilogram; m, meters.
[a]Data are median (IQR).

Postintervention

The same data abstracted from the electronic health record during the preintervention phase were abstracted for the 3 months following the intervention. No patient-reported data were collected.

To ascertain the impact of our intervention on prescribing practices, descriptive analyses compared the preintervention and postintervention samples using *t* testing for continuous variables that were normally distributed, Mann-Whitney U testing for other continuous variables, and chi-square testing for categorical variables. Mann-Whitney U testing compared MMEs prescribed preintervention and postintervention. A *P* value less than 0.05 indicated statistical significance, using SPSS Statistics 26.

Based on findings, a follow-up brief electronic survey queried obstetrics and gynecology resident physicians about the number of opioids, if any, they would prescribe for specific surgical categories.

RESULTS

During the preintervention phase, responses were received for 20.5% (172/840) of electronic surveys sent to patients. Electronic health records were reviewed for those 172 procedures preintervention, of which 151 (88%) were eligible for inclusion. During the postintervention phase, charts were reviewed for 602 patients undergoing gynecologic procedures, of which 514 (85%) were eligible for inclusion. After outliers and nonsensical survey responses were removed, 146 records were included in preintervention analysis and 500 were included in postintervention analysis. Median

Table 2. Opioids Prescribed Versus Consumed, Refills Required, and Patient-Reported Satisfaction With Pain Control

Surgery Category (N = 146)	MME Prescribed Median (IQR)	MME Consumed Median (IQR)	Difference	*P* value	Refill Required % (n)	Satisfied With Pain % (n)
Hysterectomy: Laparoscopic/Robotic (n = 20)	150 (112.5 – 166.9)	53.75 (15 – 138.8)	96.25	0.006	10 (2)	80 (16)
Hysterectomy: Vaginal (n = 13)	150 (112.5 – 225)	37.5 (0 – 75)	112.5	0.010	15 (2)	77 (10)
Laparoscopic/Robotic surgery (n = 37)	75 (75 – 120)	45 (0 – 105)	30	< 0.001	8 (3)	89 (33)
Vaginal Surgery (n = 22)	75 (75 – 142.5)	7.5 (0 – 71.3)	67.5	< 0.001	14 (3)	91 (20)
Hysteroscopy (n = 40)	0 (0 – 0)	0 (0 – 0)	0	0.734	0 (0)	98 (39)
Suction Dilation and Curettage (n = 14)	0 (0 – 0)	0 (0 – 0)	0	0.380	0 (0)	86 (12)

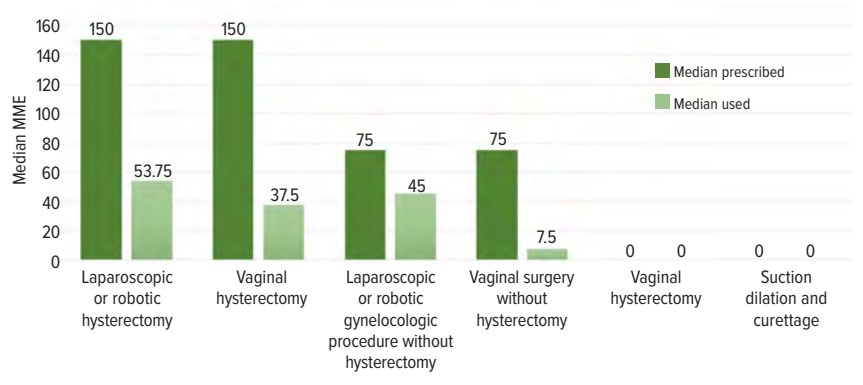
MME: morphine milligram equivalents.

age (39 – 41 years old) and body mass index (28 – 29 kg/m2) were similar in boyh samples (Table 1). The most common surgical categories in both samples were hysteroscopy and laparoscopy without hysterectomy. The preintervention sample had significantly more patients who identified as non-Hispanic White and a higher proportion of patients who underwent a vaginal hysterectomy, hysteroscopy, or vaginal surgery without hysterectomy (Table 1).

For the preintervention analysis, the largest quantities of opioids were prescribed for hysterectomy procedures and the smallest for suction D&C or hysteroscopy procedures. The median MME prescribed for both laparoscopic/robotic hysterectomy and vaginal hysterectomy was 150, which is equivalent to 30 tabs containing 5 mg hydrocodone, 20 tabs containing 5 mg oxycodone, or 19 tabs containing 2 mg hydromorphone. Opioids prescribed significantly exceeded opioids consumed for all surgical categories except suction D&C and hysteroscopy (Table 2), with unused opioids ranging from 30 MMEs (4 tabs of oxycodone 5 mg) for laparoscopic or robotic surgery without hysterectomy to 112.5 MMEs (15 tabs of oxycodone 5 mg) for vaginal hysterectomy. The largest differences between MMEs prescribed and consumed were for laparoscopic/robotic hysterectomy and vaginal hysterectomy (Figure 1).

During the preintervention phase, there were 5 opioid prescriptions among 40 hysteroscopy procedures (12.5%) for 37.5 to 50 MMEs, of which 3 patients (60%) took between 7.5 and 15 MMEs

Figure 1. Preintervention Median Number of Opioids Prescribed vs Used by Patients



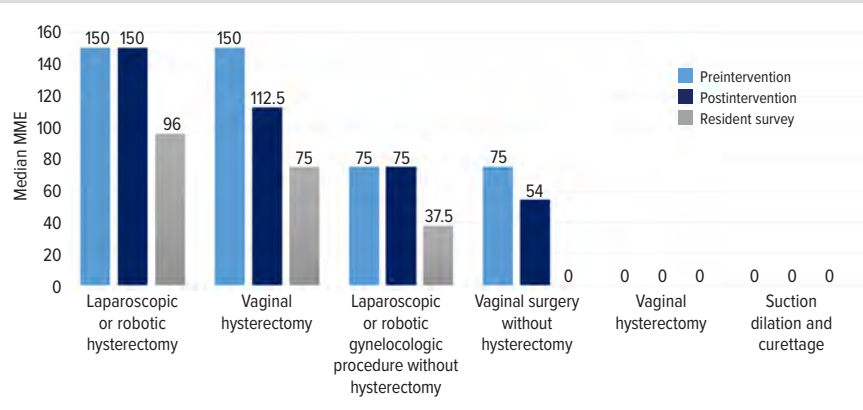
Abbreviation: MME, morphine milligram equivalents.

Table 3. Opioids Prescribed Preintervention and Postintervention in Morphine Milligram Equivalents

Surgery Category	Preintervention	Postintervention	Difference	*P* value
Hysterectomy: laparoscopic/robotic	150 (112.5 – 166.9)	150 (112.5 – 150)	0	0.405
Hysterectomy: vaginal	150 (112.5 – 225)	112.5 (112.5 – 150)	-37.5	0.059
Laparoscopic/robotic surgery	75 (75 – 120)	75 (60 – 80)	0	0.001
Vaginal surgery	75 (75 – 142.5)	54 (22.5 – 112.5)	-21	0.020
Hysteroscopy	0 (0 – 0)	0 (0 – 0)	0	N/A
Suction dilation and curettage	0 (0 – 0)	0 (0 – 0)	0	N/A

Data are reported as median (IQR).

Figure 2. Median Morphine Milligram Equivalents Prescribed Preintervention, Postintervention, and Reported on Resident Survey



of their given prescription. For suction D&C, there were 2 opioid prescriptions (37.5 and 75 MMEs) and 1 patient consumed 30 MMEs. Overall, 12% of patients undergoing surgery for which opioids are commonly prescribed required a refill (10/92, excluding hysteroscopy and D&C). Patient-reported satisfaction with pain control was high overall (89%) and ranged from 77% following a vaginal hysterectomy to 98% following hysteroscopy (Table 2).

During the 3 months postintervention, median MMEs prescribed were similar to preintervention levels for all surgical categories. There was a statistically significant decline in prescribing for vaginal surgery without hysterectomy and laparoscopic or robotic surgery without hysterectomy (Table 3, Figure 2). Though the median MME was similar preintervention and postintervention for laparoscopic or robotic surgery without hysterectomy, the spread in the IQR was detected as statistically significant due to the use of the Mann-Whitney U test. During this postintervention phase, there were 9 non-zero opioid prescriptions among 210 hysteroscopy procedures (4%), ranging from 30 MMEs to 225 MMEs. For suction D&C, there were 5 opioid prescriptions out of 70 procedures (7%), ranging from 37.5 MMEs to 150 MMEs.

Based on an observed pattern in our data that prescribing practices varied in correlation with resident rotation changes, we sought to ascertain additional information from residents specifically. In June 2021, 21 out of 27 (77.8%) obstetrics and gynecology residents from all 4 postgraduate years responded to the electronic survey regarding prescribing practices. The median opioid prescription residents reported they would prescribe was 96 (IQR 75–112.5) for laparoscopic or robotic hysterectomy, 75 (IQR 75–112.5) for vaginal hysterectomy, and 37.5 (IQR 37.5–75) for laparoscopic surgery. The median actual opioid prescription for both the preintervention phase (September 2018-March 2019) and postintervention phase (February 2021 – April 2021) was greater than what residents reported they would prescribe, except for hysteroscopy and D&C. Residents responded that they would not prescribe any opioids following a hysteroscopy or D&C. Overall prescribing amounts reported by residents were even lower than the recommendations from the educational intervention (Figure 2).

DISCUSSION

In this quality improvement study, we found significantly higher amounts of opioids prescribed than patients consumed for the 4 categories of gynecologic surgery (laparoscopic hysterectomy, vaginal hysterectomy, laparoscopy without hysterectomy, and vaginal surgery without hysterectomy) where opioids are routinely prescribed. Opioid prescribing was low overall for hysteroscopy and D&C and aligned with patient need. The vast majority of patients were satisfied with their pain control following all surgeries.

Following the educational intervention, we saw significant reductions in opioids prescribed for laparoscopy without hysterectomy and vaginal surgery without hysterectomy but not for laparoscopic or vaginal hysterectomies. Although the increased operative time, tissue dissection, and overall surgical complexity of a hysterectomy likely contributes to the increased need for opioids following these procedures, compared to similar routes not involving a hysterectomy, these results differ from a study conducted by Hill et al. In Hill et al's prior work, their educational intervention demonstrating misalignment between prescribing practices and patient need and recommending ideal opioid prescription rates significantly changed prescribing practices for all types of procedures. This difference may be due to our educational intervention not having surgeons distribute a survey form to patients at the time opioids were prescribed, whereas Hill et al had surgeons distribute a 1-page survey when prescribing opiates to patients, which may have served as a reminder to the surgeon of both the study being conducted and the recommended number of opiates to prescribe.

Interestingly, in our subsequent electronic survey of residents, they reported they would prescribe opioid amounts that were even lower than those recommended in the educational intervention and lower than the actual amounts prescribed. This difference warrants further investigation to better understand the factors that influence clinician prescribing.

Of note, the initial prescribing recommendations presented with the January 2021 educational intervention were set to meet 80% of patient need, as calculated based on preintervention patient survey response. These values may exceed emerging best practices in opioid prescribing and were later revised downward.[9,10] For example, based on the preintervention data, the 80th percentile of patient need for vaginal hysterectomy was approximately 120 MME or 16 tablets of oxycodone 5 mg. In comparison, evidence-based guidelines from Michigan's Opioid Prescribing and Engagement Network recommends no more than 10 tablets of oxycodone 5 mg for hysterectomies of any kind, and the Philadelphia Department of Public Health guidelines advise 5 of 5 mg oxycodone with a range of zero to 10 pills.[9,10]

An important factor that influenced our quality improvement initiative was the transition of almost all gynecologic surgery to outpatient as a result of the COVID-19 pandemic. The preintervention phase of this project took place prior to the pandemic when many patients undergoing hysterectomies stayed overnight postoperatively. During the postintervention phase, most patients went home the same day as their hysterectomy, which may have increased the MMEs prescribed by surgeons.

Limitations of our study include the low response rate of the patient survey and the overall small number of surgeries included in the preintervention phase. Voluntary participation could create response bias and alter our outcomes, as responders might be more likely to be those at the extremes of high or low opioid use, but using patient responses enabled us to tailor recommendations

for our patient population. Strengths of this study include the evaluation of opioid prescribing patterns for several major types of gynecological surgery beyond hysterectomies alone, as has been previously studied.[5,6]

We expected larger decreases in MMEs prescribed following our educational intervention, highlighting an opportunity for improvement within our institution and also reflecting a nationwide challenge. In subsequent work, we plan to identify factors that influence prescribing, evaluate the use of nonopioid pain control strategies and their impact on opioid use and patient satisfaction, incorporate data into an Enhanced Recovery After Surgery protocol, and develop and implement more robust interventions to limit opioid prescriptions to align with best practices.

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An Interprofessional Initiative to Address Tests Pending at Discharge for Hospitalized Pediatric Patients

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ABSTRACT

Introduction: Pediatric hospitalized patients often are discharged before all lab tests are completed. Given the risk of medical errors related to inadequate test follow-up, we piloted a collaborative initiative to address tests pending at discharge (TPAD) within our pediatric hospital medicine section. Our objectives were to delineate the responsibilities of case managers and pediatric hospital medicine clinicians in addressing these tests and to establish a communication process.

Methods: We formed an interprofessional team and performed a current state assessment, including a survey to pediatric hospital medicine clinicians to assess time spent following up TPAD and confidence that results were followed up in a timely and appropriate manner. We obtained a list of 1450 individual TPAD for the previous 9 months using an electronic health record data query, from which a list of 26 common and straightforward labs were identified for case manager follow-up. A shared case manager Epic Inbasket for TPAD was created and was checked twice daily. We developed a phased approach to establish a workflow for follow-up.

Discussion: The case manager partnership was launched in 4 phases for the duration of the 6-month pilot. However, due to duplication of work and less value of case managers addressing straightforward labs, the pilot was stopped. A more effective and mutually beneficial role for pediatric hospital medicine attendings and case managers may be to have the case managers address complex TPAD and communicate with primary care clinicians and families.

INTRODUCTION

Pediatric hospitalized patients often are discharged before all laboratory tests obtained during the hospitalization are completed. Although the percentage of pediatric patients with results pending at discharge is not published, it is estimated that up to 41% of adult hospitalized patients have tests pending at discharge (TPAD) and that almost half of these patients experience medical errors related to inadequate follow-up of these tests.[1-3] Successful follow-up of TPAD is a multistep process, including, but not limited to, identification and documentation of the tests, notification of person responsible for follow-up, and recognition and execution of the appropriate follow-up actions. A failure in any of these steps can result in inadequate follow-up. This leads to suboptimal care for patients with incomplete transitions of care from inpatient to outpatient clinicians. Poor management of TPAD can lead to duplication of efforts, delay of care, patient dissatisfaction, adverse events, and even litigation.[3-6]

A body of adult-based literature focuses on the issues around TPAD, from the discrepancies in how physicians perceive the actionability of the these test results to systematic reviews of interventions to improve TPAD follow-up.[7-10] In today's health care environment, patient care is intertwined with the electronic health record (EHR). Not surprisingly, multiple efforts have, therefore, focused on implementation of EHR-based tools, including automated result notifications and prompts within the discharge summary to enforce documentation of tests with pending results.[1,7,8,10-16] Other technological solutions have been utilized as well, such as automated email notification systems embedded within the health system's integrated clinical information systems.[11-13,17] Systematic reviews of the various interventions found that individual education and tools, such as health information technology-based tools, can improve awareness of TPAD, but solutions must be multifaceted.[7,8,10]

The same potential safety risks of TPAD exist in the hospitalized pediatric population, with the added complexity of commu-

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nication to caregivers, as well as patients, to provide continued patient- and family-centered care. Similar to adult hospital medicine, there is no best practice for how to most effectively handle TPAD in pediatric hospital medicine (PHM). Follow-up and notification of families and outpatient clinicians of certain results (ie, negative or normal results) are within nursing scope of practice and would not need to be completed by the discharging clinician. As hospitalists at an academic institution who work in 1-week clinical blocks and are heavily involved in other academic efforts, we potentially may not access the EHR for several weeks in between clinical activities, unless we are intentionally waiting for specific lab results. For this reason, there was concern for clinician variability in addressing TPAD. Additionally, depending on the nature of the result, TPAD follow-up can also be time-intensive, and we proposed it may be done more efficiently through a collaboration with other health care team professionals.

At our institution, nurse case managers have been champions of safe discharge and transitions of care to home. Thus, we proposed an expansion of the case manager role to address labs that are completed after discharge and to help direct communication with primary care clinicians and families. Our objectives were to establish a process for (1) defining which test results case managers would follow up, (2) establishing case manager workflow for addressing TPAD, and (3) communicating between case managers and the discharging clinician.

Box. Tests Pending at Discharge Included in the Pilot Project

Blood Culture	Adenovirus NAAT
Cerebrospinal fluid smear and culture	Enterovirus and parechovirus NAAT
Fungal culture	*Neisseria gonorrhoeae* DNA
Anaerobic/aerobic bacterial smear and culture	*Chlamydia trachomatis* DNA
Mycobacterium smear and culture	*Bartonella* Ab IgG and IgM with reflex titer
Respiratory syncytial virus NAAT	Cytomegalovirus IgG and IgM
Influenza A and B NAAT	Basic metabolic panel
Human metapneumovirus NAAT	Comprehensive metabolic panel
Rhinovirus NAAT	Complete blood cell count
Parainfluenza NAAT	Complete blood cell count with differential
Coronavirus NAAT	Cerebrospinal fluid profile

Abbreviation: NAAT, nucleic acid amplification test.

Table. Details of Phased Approach with Progressive Levels of Responsibility for Case Managers

Phase	Duration	Description	Purpose
1	11/19/18 – 1/1/19	CM and PHM attending receive negative/normal results for labs included in the pilot (Box) in shared InBasket. CMs write result note	Introduce CM to process of checking InBasket, documenting results in Epic
2	1/2/19 – 2/24/19	CMs receive negative/normal results. PHM attendings no longer receive negative/normal results	Remove results from PHM attendings InBaskets since CMs able to check results and document result note
3	2/25/19 – 4/21/19	CMs receive positive/abnormal results. PHM attendings continue to see positive/abnormal results.	Identify processes needed for CMs to triage positive/abnormal result
4	4/22/19 – 5/28/19	CMs receive positive/abnormal results. PHM attendings no longer receive positive/abnormal results.	CMs able to address both negative/normal results and positive/abnormal results

Abbreviations: CM, case managers; PHM, pediatric hospital medicine.

METHODS

We performed this work at a freestanding tertiary care pediatric hospital with 306 beds, 16 321 admissions per year, and an average daily census of 208 patients. Our PHM service has an average daily census of 36, and PHM attendings are clinically active for 7 consecutive days. We have 30 PHM attendings with 19 clinical full-time equivalents and 9 advanced practice providers. We have attending coverage 24 hours a day, 7 days a week, with a nocturnist present every night. Our case manager group has 34 members and 25 full-time equivalents that support all inpatient teams during weekdays with in-hospital coverage from 6 AM to 11 PM. Our hospital EHR is Epic (Epic Systems Corporation, Verona, Wisconsin).

We formed an interprofessional team, called the Discharge Follow-up Workgroup, consisting of hospitalists, acute care nursing leadership, information technology support, data analysts, and case managers. First, the team confirmed the preexisting process for communicating TPAD results. This process included automatic routing to the primary care clinician the following information after discharge: (1) discharge event notice with components of the patients' after visit summary, (2) discharge summary, (3) labs results completed after discharge. Primary care clinicians could choose fax or Epic InBasket as their preferred communication. Additionally, the discharging hospitalist also was routed test results finalized after discharge to their Epic InBasket.

During the information gathering phase of the project, we queried two pediatric hospital medicine listservs (pediatric hospital medicine division directors and pediatric hospital medicine Listserv) regarding TPAD practices. These resulted in responses from two institutions. One institution reported utilizing advanced practice providers for TPAD; the other stated that individual clinicians follow up on TPAD, similar to our institution's practice.

To assess the preexisting hospitalist workflow (prior to our PHM/case manager partnership), we surveyed the PHM attendings to assess the following: time spent after a service week fol-

lowing up TPAD (<30 minutes, 30-59 minutes, 1-2 hours, >2 hours) and confidence (using a 1-5 Likert scale) that TPAD from patients they care for were followed up in a "timely and appropriate manner."

We obtained a list of TPAD during the 9 months prior to our start date using a data query within our EHR (See Box). We selected laboratory results for case managers to manage based on frequency and feasibility (ie, those with a binary result), with the plan for expansion into more complex labs and responsibility over time. We sought to evaluate the time lapse between test completion and time reviewed but were unable to consistently determine when a result was reviewed by a clinician due to limitations within our EHR.

A shared case manager Epic Inbasket for TPAD for PHM patients was created. We developed a phased approach with progressive levels of responsibility and autonomy for case managers (Table) to establish a workflow for TPAD follow-up, documentation, and communication between case managers and PHM clinicians. We communicated with the PHM faculty prior to the beginning of each phase to reinforce the new changes. Throughout these phases, we tracked the time spent on TPAD follow-up by case managers, had regular team meetings with our core group, and had intermittent discussion and feedback sessions with the PHM faculty. The case managers were provided with information on changes to the workflow as we progressed through the phases. If they had any questions about how to address a particular result, they would email the core Discharge Follow-up Workgroup team for guidance, and we would use those examples for education and process development if needed.

The shared Epic Inbasket was checked by case managers twice daily, initially 5 days per week, increasing to 7 days per week by phase 3. They would review the result and write a brief note—regardless of whether the result was positive/abnormal or negative/normal—with the following as an example: "Lab result is normal/negative. Reviewed by CM (case manager)." A "tip sheet" was created for the case managers to use as a guide to review and document the result. If the result was positive, the case manager also would contact the discharging clinician via page or an email message, depending on the result. Email was used instead of the Epic messaging functionality based on feedback that PHM faculty did not check their Epic InBaskets regularly if they were not clinically active. One of the Discharge Follow-up Workgroup PHM attendings was always on call for the case managers if they were unable to contact the discharging clinician or had any urgent questions.

RESULTS

PHM Faculty Survey Results

Fourteen out of 30 PHM faculty responded to the survey question assessing time spent following up TPAD, on average, after a service week. Fourteen percent (2/14) of respondents spent less than 30 minutes, 43% (6/14) spent 1 to 2 hours, and 43% (6/14) spent more than 2 hours (Figure 1). Nine PHM faculty responded to the survey regarding confidence that TPAD were being addressed in a "timely and appropriate manner." See Figure 2 for results.

Figure 1. Hospitalists' Time Spent After Clinical Service Week Addressing Tests Pending at Discharge, N = 14

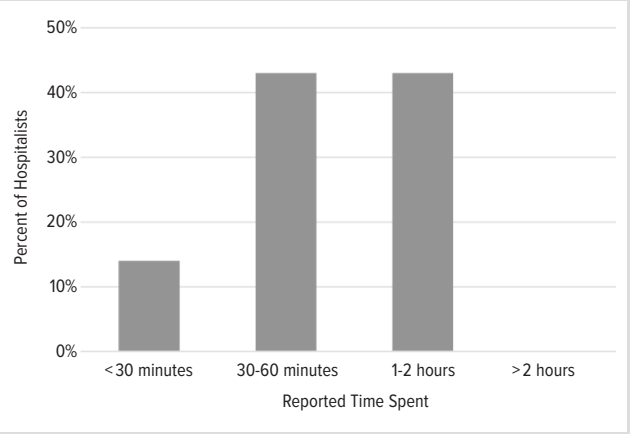
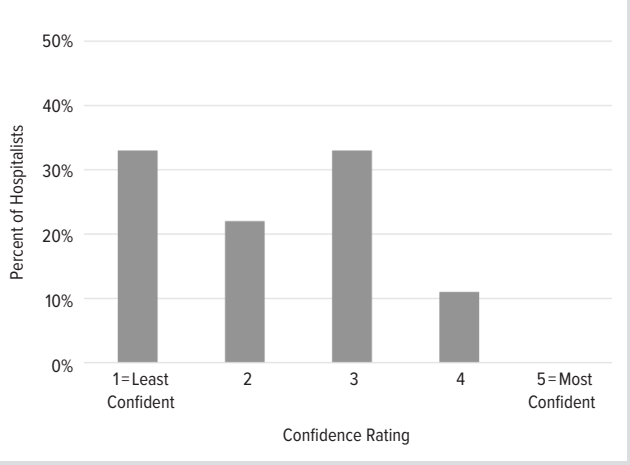


Figure 2. Hospitalists' Confidence Tests Pending at Discharge Were Being Appropriately Addressed, N = 9



TPAD Inclusion

Review of all TPAD over the 9 months prior to our start date resulted in 1450 individual tests. From these individual tests, we performed a frequency analysis; 22 initial laboratory results were identified as feasible for case managers to manage based upon the following: (1) binary nature of result and lack of ambiguity if positive or negative, and (2) nonurgent results (ie, a positive result would not have clinical impact if not seen for 24 hours). The laboratory values that required knowledge of the patients' clinical course or discussion with subspecialists or primary care clinicians remained the primary responsibility of the PHM clinicians. Originally, we planned to expand the scope of laboratory results covered by case managers to include more complex results;

however, this did not occur due to the discontinuation of the pilot work.

Establishing Workflow for Addressing TPAD

The PHM/case manager partnership was launched in phases, with each phase being 1 to 2 months, for the duration of the pilot, which lasted approximately 6 months (193 days). The case manager responsibilities and autonomy increased with the progression of phases. Thirteen case managers were trained on the process of checking the labs during this partnership, with 5 primary case managers reviewing the labs. Case managers checked the InBasket twice daily. Overall, there were 1102 results that generated a total of 1567 InBasket messages. (Some labs, such as culture results, are updated daily until final, resulting in multiple messages per lab result.) An average of 8.1 results were addressed per day. The time spent per day was 20 to 30 minutes, which included documentation and notifying the attending physician via email.

Communication Between Case Managers and the Discharging Clinician

A detailed protocol was developed for the case managers to address positive/abnormal results (Appendix 1). During our interprofessional monthly check-in meetings, case managers reported that the majority of TPAD were already addressed by PHM clinicians prior to them viewing the results. Informal feedback from our PHM attendings was also consistent with the case manager feedback – most of the time, the PHM attendings had seen the results before the case managers addressed them.

DISCUSSION

A process for case managers to address TPAD from patients discharged from the PHM service was established. We achieved our objectives of defining laboratory results for case managers to follow up and establishing a workflow for them to address those tests and communicate with the discharging clinician. However, during our work to establish a process for TPAD follow-up, we realized it lacked efficiency and was not sustainable, so we discontinued the pilot after 6 months. The major barriers we encountered included duplication of work between case managers and PHM attendings, no perceived benefit to PHM attendings in shifting TPAD follow-up responsibilities to case managers, and lack of ability to expand addressing TPAD due to case managers' bandwidth. Despite discontinuing the pilot, we learned several lessons that may be of use to other hospital medicine groups seeking to implement a similar process around timely TPAD follow-up.

Despite involvement of the case managers, PHM attendings continued to frequently check lab results, leading to duplication of efforts. At our institution, PHM attendings work a 7-day clinical service week, and attendings were often still on clinical service when the results of the TPAD were returned on their discharged patients. As a result of their frequent interface with the EHR throughout the day, they often viewed the results before case managers since the case manager InBasket was checked only twice daily. Even in phase 4 when TPAD results were not coming to their Epic InBaskets, many PHM attendings still followed TPAD results through EMR patient lists. Thus, there was duplication of work between the case managers and PHM attendings as both groups often were following up on results simultaneously. After the pilot ended, debriefing with the hospitalist group revealed that many hospitalists continued to feel obligated to follow all TPAD despite case manager involvement – especially since many complex labs remained the responsibility of the PHM attending.

As mentioned, part of our work included a survey to our faculty assessing time spent following up TPAD results after clinical service weeks and whether they were confident that TPAD were being addressed in a timely and appropriate manner. We had a low response rate to both questions, as less than 50% of the faculty completed the survey, which we assumed was due to survey fatigue. However, it is possible that some faculty did not feel process improvement was needed in this area, for various reasons. Retrospectively, we could have considered including a direct question of whether faculty thought we should work to improve the current TPAD follow-up process or had an open discussion with the faculty prior to starting the project.

By design, the TPAD included in the pilot also were noted to be easily addressed by PHM attendings. Therefore, having these tests addressed by case managers did not lead to a significant efficiency benefit for the clinicians. Planned next steps included having case managers follow up more complex TPAD, such as those that may require primary care clinician or subspecialist discussion. However, due to other competing responsibilities and with seasonal fluctuations in hospital census, the case managers could not commit to taking on a larger role to address TPAD. Since there was lack of benefit to the PHM attendings and low likelihood of expanding the case manager role, our interprofessional team decided to discontinue the pilot and return to the previous workflow of having the PHM attendings follow up on the TPAD.

Although our PHM/case manager partnership for following up TPAD was discontinued, the work was still beneficial for both groups. As we prepared for the partnership, PHM attendings had the opportunity to reflect on existing processes for handling lab results, raising awareness of the importance of TPAD responsibility. This may have led some attendings to be more diligent regarding responsibility for TPAD. We also identified a gap of clinician coverage during vacation or family or medical leave, and our section developed an internal process to cover our partners during these times. The case managers working with our interprofessional teams developed an even more intimate understanding of the problems associated with TPAD. We believe they can use the knowledge developed during our work to enhance discharge plan-

ning by working with the care team to delegate TPAD responsibility prior to discharge.

We believe the description and dissemination of our work will benefit other PHM sections who face similar issues with TPAD. At our institution, given their regular daily full caseload, case managers did not appear to be the correct fit for assisting with TPAD. Regardless of who assumes responsibility for these tests, they need the appropriate time and resources to become fully accountable for the process, and delegation should take into consideration current workloads. Smaller teams or groups with fewer TPAD still may be able to successfully incorporate case managers into the TPAD process. However, in our group, a team of 30 PHM attendings and 5 core case managers may have been too large to develop appropriate trust to allow for the most efficient processes. Without such trust, changing physicians' personal preferences and habits for following TPAD can be difficult.

Other PHM sections also may benefit from our efforts involving our EHR. The process we built could be replicated and implemented by other institutions that use Epic, as routing and Epic InBaskets are available within standard Epic operating systems.

As PHM attendings, we still believe there is a gap in how TPAD are addressed and remain concerned about related safety issues. Future interventions to address this gap could include a dedicated PHM registered nurse with the primary responsibility of addressing TPAD and communicating with specialists, primary care clinicians, and families. Ideally, this role would be integrated into our team and would receive additional training on specific and complex TPAD and how to communicate with specialists and primary care clinicians. With a more dedicated role, it would be easier to build trust between PHM attendings and the TPAD follow-up specialist, allowing for follow-up of both simple and more complex TPAD.

CONCLUSIONS

Overall, after performing this work, our conclusions regarding TPAD are similar to the ideas and concerns we had at the beginning of our pilot: TPAD pose a significant safety issue to our patients, there is variability in how they are addressed, and there does not seem to be a simple solution or one-size-fits-all approach to address them. We also acknowledge that the 21st Century Cures Act,[18] implemented nationally in 2021, adds additional complexity to TPAD. As a result of this legislation, an increasing number of patients and families have access to their electronic health records and test results, and families may have questions about the results without an easily accessible care clinician. Thus, it is essential that clinicians communicate with patients and families about the results of TPAD.

Future solutions for addressing TPAD need to be efficient in maximizing the scope of involved team members, systematic, inclusive of all TPAD to ensure safe follow-up, and trusted by all members of the team.

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Appendix: Available at www.wmjonline.org

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Eyes on the Future: Inspiring Latino Middle School Youth to Pursue Careers in STEM Through Early Interactive Science Programming

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ABSTRACT

Background: Given the need for a diverse health care workforce, efforts must be made early in their education to support underrepresented minorities in medicine and the science, technology, engineering, and mathematics (STEM) fields.

Methods: The Eyes on the Future program introduces underrepresented minority 8th grade students to science and medicine via interactive science-based programming and mentorship by medical and graduate students. Program impact was evaluated using pre- and post-program surveys.

Results: Of 25 participating students, 24 and 22 responded to pre- and post-program surveys, respectively. Students showed strong interest in science concepts and STEM careers, with high, positively correlated, and statistically similar pre- and post-program survey responses.

Discussion: The Eyes on the Future program was well-received and represents a step towards addressing barriers to STEM careers faced by underrepresented minority students.

BACKGROUND

Given the racial and ethnic makeup of the United States and health disparities present, the need for a diverse health care workforce is imperative.[1] Physicians from groups underrepresented in medicine play an important role in caring for underserved populations and may be key to addressing health disparities. In 2020, Hispanic and Latino individuals made up 18.7% of the US population but in 2018 only accounted for 5% of the physician workforce and 6.2% of medical school matriculants.[2,3] Similarly, stark gaps can be found across other underrepresented minority (URM) racial and ethnic groups.

To create a more diverse health care workforce, efforts are needed to support URM students in medicine and the science, technology, engineering, and mathematics (STEM) fields early in their education. Although URM teens express interest in STEM careers at the same rate as White teens, URM students face a range of barriers while navigating a path to medicine, including cost, lack of guidance and role models, and challenges with professional identity development.[4-7] Professional identity development—ie, the process that teaches individuals how to think, act, and feel like a professional in the STEM fields—can be especially challenging for URM students who are learning how to navigate their intersectional identities.[5-6] Furthermore, a student's perceived enjoyment in the sciences—across all races—significantly decreases between the 4th and 8th grades, which suggests a critical timepoint to engage students in STEM.[4]

In this report, we describe the structure and content of the Eyes on the Future (EOTF) program, an early, interactive, science-based program implemented in a single school in Milwaukee, Wisconsin. We provide a preliminary assessment of its impact in influencing student attitudes about science and STEM careers and discuss its value to both middle school students and medical and graduate students, as well as suggestions for future directions. We hope the information from this study will be utilized to expand such programs for URM students in Wisconsin and beyond.

METHODS

EOTF Curriculum: Development, Goals, and Content

The EOTF program has been held yearly since 2014 and supports 25 students at a single school in Milwaukee, Wisconsin. In 2014, the Association of American Medical Colleges Diversity Policy and Programs unit held a ProjectMED video competition, which called

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for initiatives targeting K-12 students to increase the diversity of future physicians and scientists. The initial EOTF team submitted a video detailing the program and was awarded seed funding to support the program. The program aims to introduce URM 8th grade students, primarily of Latino background, to science and medicine via interactive science-based programming and mentorship by Medical College of Wisconsin (MCW) medical and graduate students. A key component to the success and continuity of this program has been the ongoing partnership between middle school staff, the MCW Department of Ophthalmology and Visual Sciences, and MCW's Latino Medical Student Association chapter.

This report focuses on the 2022 program, which consisted of 5 events: (1) an interactive presentation on eye anatomy and eye health conditions and creation of human eye models (Appendix 1); (2) cow eye dissections; (3) a medical simulation experience at the MCW Standardized Teaching Assessment Resource Center, where students listened to heart and lung sounds and practiced on a patient model who was a smoker with chronic obstructive pulmonary disease; (4) a visit to the Discovery World Science and Technology Museum; and (5) an information session on STEM careers, MCW pipeline programs, and preparation for graduate education. Students were selected for participation based on the science teacher's perception of the student's high baseline science interests. A focus on eye anatomy and health was chosen given that the US Hispanic and Latino population has some of the highest rates of vision loss and blindness caused by eye diseases, in addition to the existing collaboration with the MCW Department of Ophthalmology and Visual Sciences.[8]

Assessment and Evaluation Methods

Students completed a voluntary, anonymous survey before and after the EOTF program using the online Qualtrics survey tool. The survey was developed using questions adapted from previously published surveys.[9,10] Parents and students participating received an informational letter before the program and could choose to opt out of data collection. Questions focused on assessing student attitudes about the sciences and future career goals using a 5-point Likert scale (Appendix 2). Higher scores indicated more positive attitudes, except for the question "Boys generally do better in the sciences than girls," where higher values indicated agreement with the statement.

Data analyses were performed using R, version 4.1.0 (R Foundation). Responses to Likert-scale survey questions were analyzed within and across gender and question domain categories. Median ranks for each question were compared using the Mann-Whitney U test. Dependent *t* tests were used to compare mean pre- and post-program responses for question pairs. Cronbach's alpha reliability coefficients were calculated, with 95% confidence intervals determined by the Feldt method. A threshold of 0.7 was selected to indicate reliability. Spearman correlation coefficients were used for correlative analysis of pre- and post-program responses. Statistical significance was defined as $P < 0.05$. The MCW Institutional Review Board approved the study of this program.

Table 1. Demographics of Middle School Students

Variables	Pre-Program Count (N = 24)	Post-Program Count (N = 22)
Sex		
Boys	13 (54%)	12 (55%)
Girls	11 (46%)	10 (45%)
Race and Ethnicity[a]		
Hispanic or Latino/a	24 (100%)	22 (100%)
White	3 (13%)	3 (14%)
I plan to attend _____ after high school		
4-year college	20 (83%)	16 (73%)
2-year college	1 (4%)	1 (5%)
Technical school, apprenticeship, or trade school	0 (0%)	0 (0%)
Get a full-time job	0 (0%)	1 (5%)
Not sure	3 (13%)	4 (18%)

[a]Some students identified with more than one race or ethnicity category.

RESULTS

Twenty-five students participated in the 2022 program. Of these, 24 (96%; 13 boys, 11 girls) completed the pre-program survey and 22 (88%; 12 boys, 10 girls) completed the post-program survey. Student demographics are shown in Table 1. All respondents identified as Hispanic or Latino/a, and 3 respondents in both the pre- and post-surveys also identified as White. Students attended, on average, 4.7 of 5 events.

Pre- and post-program survey responses to questions in the science interest and STEM career domains were high for both boys and girls. Responses were above neutral for every question (Tables 2 and 3).

Comparison of pre- and post-program responses to individual questions using the Mann-Whitney U test revealed a statistically significant decrease in the median score for boys answering, "I like hearing science presentations." None of the remaining comparisons were statistically significant for any combination of gender and question domain (Table 3).

Comparison of average Likert scores between pre- and post-program responses with the dependent *t* test revealed no statistically significant differences for any combination of gender and question domain (Table 3).

Cronbach's alpha reliability coefficients were generally high. However, confidence intervals overlapped the threshold of 0.7 for every combination of gender and question domain (Appendix 3).

Correlative analysis of average Likert scores for each question showed a strong, positive correlation between pre- and post-program scores. Spearman correlation coefficients were statistically significant for every combination of gender and question domain (Appendix 4).

Table 2. Results of Science Attitudes Questions – Counts and Percentages

	Total		Boys		Girls	
Science Interest Questions[a]	**Pre-Program (N = 24)**	**Post-Program (N = 22)**	**Pre-Program (N = 13)**	**Post-Program (N = 12)**	**Pre-Program (N = 11)**	**Post-Program (N = 10)**
Science is interesting.	23 (96%)	21 (95%)	13 (100%)	12 (100%)	10 (91%)	9 (90%)
I like hearing science presentations.	19 (79%)	13 (59%)	11 (85%)	7 (58%)	8 (73%)	6 (60%)
I like talking about science with others.	15 (63%)	15 (68%)	10 (77%)	8 (67%)	5 (45%)	7 (70%)
I like asking questions.	12 (50%)	11 (52%)	6 (46%)	6 (50%)	6 (55%)	5 (50%)
I want to take more classes in science.	22 (92%)	18 (82%)	13 (100%)	9 (75%)	9 (82%)	9 (90%)
I understand science.	17 (71%)	17 (77%)	12 (92%)	10 (83%)	5 (45%)	7 (70%)
I feel I will get a good grade in science.	22 (92%)	21 (95%)	13 (100%)	12 (100%)	9 (82%)	9 (90%)
Science is useful to the world.	24 (100%)	22 (100%)	13 (100%)	12 (100%)	11 (100%)	10 (100%)
Science will affect me throughout my life.	23 (96%)	21 (95%)	12 (92%)	11 (92%)	11 (100%)	10 (100%)
STEM Career Questions[a]	**(N = 24)**	**(N = 22)**	**(N = 13)**	**(N = 12)**	**(N = 11)**	**(N = 10)**
I want to have a job in science and medicine in the future.	19 (79%)	17 (77%)	9 (69%)	9 (75%)	10 (91%)	8 (80%)
I am smart enough to pursue a job in science and medicine.	19 (79%)	19 (86%)	10 (77%)	11 (92%)	9 (82%)	8 (80%)
A job in science and medicine is cool.	24 (100%)	21 (95%)	13 (100%)	11 (92%)	11 (100%)	10 (100%)
Anyone can have a job in science and medicine.	19 (79%)	18 (82%)	10 (77%)	10 (83%)	9 (82%)	8 (80%)
Going to college is very important to me.	23 (96%)	20 (91%)	13 (100%)	11 (92%)	10 (91%)	9 (90%)
Going to college is very important to my family.	24 (100%)	21 (95%)	13 (100%)	11 (92%)	11 (100%)	10 (100%)
I feel like I will have adequate resources and support to apply to college in the future.	22 (92%)	22 (100%)	12 (92%)	12 (100%)	10 (91%)	10 (100%)

Abbreviation: STEM, science, technology, engineering, and mathematics.

[a]Likert scale response options: Strongly disagree (1 point), disagree (2 points), neither agree nor disagree (3 points), agree (4 points), strongly agree (5 points). The values are given as the number of respondents who responded with "agree" (4 points) or "strongly agree" (5 points) on the 5-point Likert scale, with the percentage in parentheses.

When asked about level of agreement with the statement, "Boys generally do better in the sciences than girls," 67% of students disagreed or strongly disagreed before the program, while 77% disagreed after the program. No students agreed or strongly agreed with this statement at either time point (Appendix 5).

DISCUSSION

This report describes an early science-based program for URM students in the 8th grade and provides a preliminary assessment on influencing student attitudes about science and STEM careers. Overall, the program exposed students to a variety of STEM careers, provided information on pipeline programs, connected participants with local medical and graduate school contacts, increased their knowledge on eye health conditions, and encouraged professional identity development. Additional benefits included providing medical and graduate students an opportunity to give back to the local community and to develop communication skills. The development of such skills is essential for future physicians and scientists as they educate the public and disseminate information.[9]

Unique features of the EOTF program include the strong partnership with the middle school and leadership from the Latino Medical Student Association, which promoted student mentorship. Priority was placed on recruiting a diverse group of MCW student volunteers to share their experiences navigating their academic journey, including the challenges they faced along the way, and to model URM student professional identity development. These mentors also taught students about eye and health conditions affecting the Latino community, hopefully enabling them to raise awareness and become early health advocates within their families and community. Furthermore, many middle school students were introduced to local medical and science institutions, such as the Medical College of Wisconsin and the Discovery World Science and Technology Museum.

Despite students' subjectively positive response to the program, statistical analyses of Likert survey data were generally equivocal. In univariate comparison of mean pre- and post-program survey scores, the only statistically significant difference was a decrease in boys' response to "I like hearing science presentations." This finding may represent either a true decrease in boys' interest in hearing science presentations or a false-positive error in the setting of multiple comparisons. Pairwise comparisons within and across question domains revealed no statistically significant differences. Wide confidence intervals for Cronbach's alpha reliability coefficients suggested that modifications to survey design or sample size may result in a more reliable measure of attitudes. Finally, pre- and post-program survey scores showed a strong positive correlation, indicating that students' positive attitudes before the EOTF program were maintained afterward.

The rationale for these equivocal changes pre- and post-

Table 3. Results of Science Attitudes Questions – Averages and *P* values

	Total			Boys			Girls		
	Pre-Program Avg (N = 24)	Post-Program Avg (N = 22)	*P* value	Pre-Program Avg (N = 13)	Post-Program Avg (N = 12)	*P* value	Pre-Program Avg (N = 11)	Post-Program Avg (N = 10)	*P* value
Science Interest Questions[a]									
Science is interesting.	4.29	4.23	0.95[b]	4.54	4.42	0.70[b]	4.00	4.00	0.42[b]
I like hearing science presentations.	4.08	3.73	0.10[b]	4.38	3.67	0.03[b]	3.73	3.80	>0.99[b]
I like talking about science with others.	3.63	3.73	0.65[b]	3.85	3.75	0.70[b]	3.36	3.70	0.32[b]
I like asking questions.	3.46	3.62	0.69[b]	3.46	3.64	0.64[b]	3.45	3.60	0.95[b]
I want to take more classes in science.	4.17	3.95	0.28[b]	4.38	4.00	0.21[b]	3.91	3.90	>0.99[b]
I understand science.	3.79	3.86	0.73[b]	4.15	4.00	0.71[b]	3.36	3.70	0.27[b]
I feel I will get a good grade in science.	4.04	4.09	0.53[b]	4.23	4.17	>0.99[b]	3.82	4.00	0.39[b]
Science is useful to the world.	4.79	4.82	>0.99[b]	4.77	4.92	0.59[b]	4.82	4.70	0.64[b]
Science will affect me throughout my life.	4.38	4.41	0.90[b]	4.38	4.42	>0.99[b]	4.36	4.40	>0.99[b]
Average Score	4.07	4.05	0.71[c]	4.24	4.11	0.20[c]	3.87	3.98	0.07[c]
STEM Career Questions[a]									
I want to have a job in science and medicine in the future.	4.17	4.18	>0.99[b]	4.15	4.25	>0.99[b]	4.18	4.10	0.99[b]
I am smart enough to pursue a job in science and medicine.	4.00	3.86	0.33[b]	4.15	4.00	0.46[b]	3.82	3.70	0.59[b]
A job in science and medicine is cool.	4.33	4.36	0.76[b]	4.38	4.42	0.85[b]	4.27	4.30	>0.99[b]
Anyone can have a job in science and medicine.	4.29	4.27	0.77[b]	4.15	4.25	>0.99[b]	4.45	4.30	0.73[b]
Going to college is very important to me.	4.75	4.59	0.44[b]	4.85	4.67	0.52[b]	4.64	4.50	0.71[b]
Going to college is very important to my family.	4.83	4.68	0.41[b]	4.77	4.83	0.59[b]	4.91	4.50	0.064[b]
I feel like I will have adequate resources and support to apply to college in the future.	4.29	4.36	0.84[b]	4.38	4.33	0.85[b]	4.18	4.40	0.53[b]
Average Score	4.38	4.33	0.21[c]	4.40	4.39	0.80[c]	4.35	4.26	0.25[c]

Abbreviation: STEM, science, technology, engineering, and mathematics.

[a]Likert scale response options: Strongly disagree (1 point), disagree (2 points), neither agree nor disagree (3 points), agree (4 points), strongly agree (5 points).

[b]Mann-Whitney test.

[c]Paired *t* test.

program is likely multifactorial but primarily related to study power. Students selected to participate in the program already had a positive attitude toward science. Therefore, the expected effect size was smaller, and more participants would be needed to appreciate differences with statistical significance. Alternatively, enrolling students with a lower baseline interest in science could leave greater room for improvement in response to the program, which might be measurable without a drastic increase in the number of participants. Finally, revisions to the survey may help evaluate student attitudes with greater precision, leading to a more powerful study.

In the future, we hope to increase our sample size and outreach by broadening inclusion criteria. Meanwhile, adding unique, anonymized survey codes would enable pairwise comparison of individual participants. Long-term goals include tracking longitudinal impact on career choice and utilizing focus groups to collect qualitative data on student attitudes toward the program.

Substantial systemic changes are needed to address the barriers faced by URM students interested in science and STEM careers. The EOTF program is one example of how community outreach can help children and adolescents confront some of these barriers through education and mentorship, support early professional identity development, and encourage a sense of inclusion and belonging for URM students in STEM. This early, low-cost outreach program also could be adapted for use in a variety of settings and populations.

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Appendices: Available at www.wmjonline.org.

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Utilization of Mental Health Services by Medical College of Wisconsin Trainees

Jenna T. Le, BS; Timothy McAuliffe, PhD, MS; Himanshu Agrawal, MD; David Cipriano, PhD, MS

ABSTRACT

Introduction: The goal of this study is to describe the change in utilization of mental health services by trainees at a private medical college in Wisconsin after specific interventions were instituted by the administration.

Methods: Multiphase interventions designed to increase access to care were instituted at the student behavioral health clinic. These interventions were based on the findings of online wellness surveys distributed to the Medical College of Wisconsin during the 2016-2017 school year. The authors collected annual utilization reports of student use of mental health services at the Medical College of Wisconsin and plotted them along a timeline of specific administrative interventions.

Results: Since the 2016-2017 academic year, medical students have used an average of 1274 mental health service visits per year compared to 637 visits annually during the academic years 2010-2011 through 2015-2016. The number of mental health visits increased significantly during 2016-2017 versus the average number of visits in previous years ($P < 001$; Cohen's $d = 4.39$).

Discussion: Similar to results shown worldwide, medical students in Wisconsin experience diminished mental health relative to their nonmedical peers. Recommendations have been made to provide additional administrative support to provide increased mental health resources to medical trainees. The findings in this report imply that incorporation of recommendations from the stakeholder medical trainees may be a key feature in the successful design and implementation of these supports.

BACKGROUND

A 2018 study reports that the rates of depression and suicidal ideation are higher among medical students than similarly aged nonmedical peers.[1] Nationally, the 12-month prevalence of a major depressive episode and serious suicidal ideation reported in 2016 were 10.9% and 8.8%, respectively, for 18 to 25 year olds and 7.4% and 4.2%, respectively, for 26 to 49 year olds.[2] A recent meta-analysis reported a depression rate of 27.2% and an alarming 11.1% prevalence of suicidal ideation among medical students. Burnout rates are also significantly higher among medical students than the general population, and studies suggest that this may be the origin of future physician burnout.[3-5] High rates of depression, suicide, and burnout also have been reported among residents[6] and physicians.[7,8] In addition to adverse effects on academic performance, the consequences of poor mental health and burnout among medical students may extend into patient care. Medical student psychological distress has been associated with unprofessional behaviors and decreased empathy. Decreased empathy and burnout among residents and physicians have been correlated with increased rates of medical errors and lower quality care.[6,7] Although there is growing literature on medical student wellness at the national and international levels,[9,10] data at the state level still remain relatively lacking.

In 2017, a survey was conducted to assess medical student mental health and wellness at the Medical College of Wisconsin (MCW). It found that 3 most commonly endorsed stressors in medical school were "general lack of time," "volume of academic material," and "lack of time for self-care."[1] Nearly 12% of respondents screened positive for severe depression, and 7.4% acknowledged having had thoughts of being better off dead or of harming themselves in the last 2 weeks. Forty-three percent of respondents

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stated that while they felt they needed mental health services, they did not pursue them."[1] The survey revealed that many students do not utilize available mental health services due to lack of time, limited access, and concerns over confidentiality and stigma. This is consistent with other studies that have reported low utilization rates for mental health services by depressed medical students.[4,10,11]

This report describes the utilization rates of mental health services at the MCW student behavioral health clinic, in the context of specific interventions implemented by the institution to address perceived barriers to care, including lack of time, limited access to mental health services, stigma, and concerns about confidentiality.

Table 1. Timeline of Targeted Changes to Address Mental Health Resources for MCW Students

Timeline	Intervention	Barrier Targeted
2010	Appointment of director of student and resident behavioral health (SRBH)	—
2011	Financially supported clinic visits reduced from 8 to 5	—
2017	Change in director of SRBH	—
February 2017	Mental health survey distributed to MCW medical students	—
June, 2017	Improving session on mental health services during orientation week for medical students	Stigma, confidentiality concerns
July, 2017	Launch of Thursday afternoon clinic to coincide with protected time offered to medical students	Limited access, lack of time
2019	Relaunch of student and resident behavioral health website www.mcw.edu/thrive	Stigma, confidentiality concerns, limited access
2020	Financially supported clinic visits increased from 5 to 10; MCW starts offering SilverCloud online psychotherapy modules; Wellbeing didactic sessions added to clerkship rotations (designed and delivered by office of SRBH); Growth Mindset slides for lecturers to use (in place or in addition to wellness slides); SRBH designs supportive email template for faculty to send students following unsatisfactory grades	Stigma, confidentiality concerns, limited access

METHODS

Student Mental Health Interventions Initiated

Multiphase interventions designed to increase access to care were instituted at the student behavioral health clinic on the following timeline (See Table 1).

- February 2017: The first mental health climate survey was conducted among MCW students. It incorporated not only mental health screening items, but questions about utilization and perceived barriers to care.
- June 2017: The session on student mental health held during orientation week for the incoming class was increased from 15 minutes to 1 hour, incorporating data on heightened risk for medical trainees and wellness information. The session also featured the addition of "lived experience" presentations during which current students were asked to share stories about their own mental health struggles and how they overcame them.
- July 2017: A new medical student behavioral health clinic was developed with dedicated appointment times for students on Thursday afternoons, when students have more flexibility due to the absence of scheduled courses during this time.
- August 2019: The website for student and resident behavioral health was revamped and relaunched with easy-to-use information about intake procedures and well-being resources.
- March 2020: SilverCloud, an online self-help program based in cognitive-behavioral therapy, was launched and offered free to students.
- July 2020: The school increased from 5 to 10 the number of unbilled visits available to students. At the same time, a student assistance program was introduced to offer students more options for care. This program offered a network of mental health providers across the state as well as legal, financial, and wellness consultations.
- Early 2021: A culturally inclusive well-being tab was added to the website featuring links to culturally inclusive health care/healing, spiritual, professional networking, entertainment, and fellowship resources in the wider community.

Statistical Analysis Methods

Data used for this study were drawn from annual utilization reports of mental health services at the MCW medical student behavioral health clinic for academic years 2010-2011 through 2021-2022. This anonymized data consist of student use of mental health services on campus or with contracted providers. It is compiled by school (medicine, pharmacy, graduate) and campus (Milwaukee, Central Wisconsin, and Green Bay).

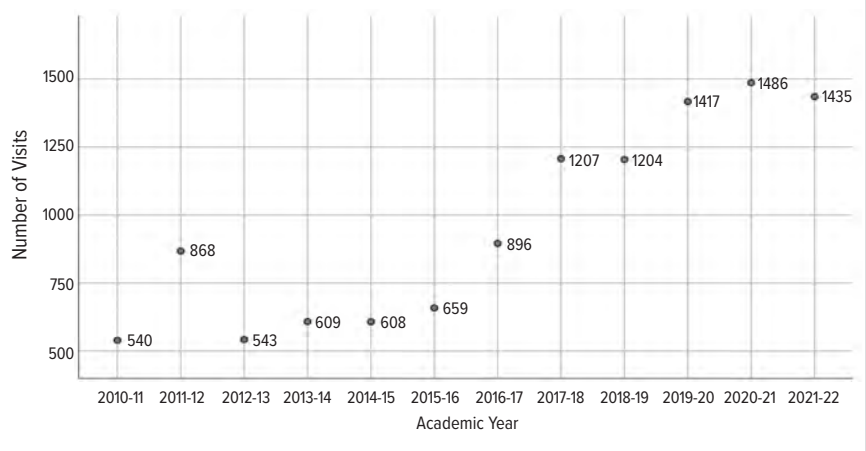
Annual utilization data were plotted along a timeline of the specific interventions (Figure). The utilization reports summarize the total number of clinic visits for mental health services from July 1 through June 30 of each academic year. Because data are available only for the number of visits and not for the number of unique student patients served during this period, we used the annual total number of visits for mental health services as the outcome.

To examine the change in utilization of mental health services visits after 2016-2017, we used Poisson regression, with the dependent variable of annual number of mental health services visits for academic years 2010-2011 through 2021-2022 and an independent variable designating pre-2016–2017 and post-2016–2017. The summary statistics for the mean annual number of visits for the academic periods 2010-2011 through 2015-2016 and 2016-2017 through 2021-2022 are calculated based on the Poisson regression results.

RESULTS

There were notable increases in medical student visits to mental health professionals within 12 months of implementing several separate interventions. These include the distribution of the focused mental health survey for medical students at MCW, increasing the duration and quality of the session on mental health services during orientation week, adjusting the availability of mental health professionals to coincide with protected time for medical students, an increase in the number of unbilled clinic visits from 5 to 10, and the upgrade and relaunch of the trainee behavioral health website.

Figure. Student Mental Health Visits per Year



Medical students used an average of 1274 mental health service visits per year from 2016-2017 through 2021-2022 compared to 637 per year during 2010-2011 through 2015-2016, a significant increase ($P < 0.001$; Cohen's $d = 4.39$). Table 2 shows summary statistics for the mean annual number of visits per academic year for 2010-2011 through 2015-2016 and for 2016-2017 through 2021-2022.

Table 2. Summary Statistics for Mental Health Services Utilization per Academic Year

	Mean	SE	*P* value	95% CI
No. of visits per year			< 0.001	
2010-11 through 2015-16	637.83	57.10		522.48 – 778.64
2016-17 through 2021-22	1274.17	80.71		1106.45 – 1467.31

DISCUSSION

This is the first report to our knowledge that describes the effect of targeted infrastructural changes at a medical school on the utilization of mental health services by medical students in Wisconsin. Prior research utilizing wellness surveys at the University of Wisconsin School of Medicine and Public Health and MCW demonstrated that Wisconsin medical students experience depression and suicidal ideation at rates greater than those reported in the general population but similar to rates found among medical students more broadly.[1] The initiation and implementation of systemic interventions designed to increase access to care coincided with a steady increase in utilization of mental health services, including clear upward spikes in utilization that coincided with the following specific interventions.

Curriculum changes designed to address stigma and educate medical students about measures to protect confidentiality: The session related to mental health services during orientation week for medical students was improved with respect to content and delivery, and the duration was increased from 15 minutes to 1 hour. The addition of powerful discussions during which current students shared their own lived experiences aimed to reduce stigma around mental health. Additionally, the director of student and resident behavioral health collaborated with psychiatry residents to design and deliver to each psychiatry clerkship cohort a monthly 1-hour didactic session related to student behavioral health, available resources, and students' rights to confidentiality. Institutional leadership supported this effort by identifying protected time for these sessions. We recommend that other institutions consider implementing similar interventions targeted at specific junctures in students' training, such as periods of high stress and times when students are already immersed in learning about mental health.

Specific measures aimed at increasing access to mental health services: Institutional leadership designated Thursday afternoons as protected time for all medical students. At the same time, there was an intentional and focused overhaul of staffing and infrastructure at the student behavior health clinic combined in addition to the introduction of a student assistance program, which offered students more options for care, more scheduling flexibility, and a more diverse provider panel. We recommend that other institutions consider implementing similar interventions, which enable synchronization of protected student time and availability of mental health resources, including outpatient psychotherapy and medication management sessions.

It is also worth noting that when the number of unbilled clinic sessions per student was increased from 5 to 10, utilization of mental health services increased. It does not appear that this increase is due to increased distress among MCW learners, rather we suggest that students may be particularly vulnerable to discontinuing treatment if they are required to pay for it themselves. One measure of acuity is the Interactive Screening Program, an anonymous self-assessment instrument from the American Foundation for Suicide Prevention.[12] While it is voluntary and a relatively small number of students elect to participate (typically less than 10%),

acuity data is available for several years, including 2014-2016 and 2017-2019. The average level of acuity for all respondents (on a scale of 1 to 3, with 1 representing the highest acuity) for the years 2014-2016 was 2.28. The average level of acuity for 2017-2019 (covering the largest increases in utilization over the previous 3-year period) is 2.20.

Study Limitations

This study has several limitations. Potential confounding factors to consider include the establishment of specific curricula aimed at reducing stigma and bolstering self-care (eg, the REACH curricula in 2018[13]) and direct and indirect effects of the COVID pandemic. Future research may include studies that measure sustainability of such interventions, replicating this study at other institutions, and ongoing collection and analysis of stakeholder information to ensure the continuing evolution of such services.

CONCLUSIONS

Overall, the timeline reported in this study suggests that there was a direct correlation between the utilization of behavioral health services and specific interventions, namely enhancement of the introduction to mental health services during orientation week, including discussion of lived experience; opening appointment times to align with protected time for students; raising awareness through the website, surveys, and other digital resources; addressing stigma and confidentiality concerns through information campaigns; and increasing the number of clinic sessions offered at no cost to students.

Apart from the tangible intervention of increasing the number of unbilled sessions, the rest of the initiatives have to do with increasing access through scheduling ease and reducing barriers to care by addressing stigma and confidentiality concerns. Our findings highlight the value of integrating mental health interventions at an institutional level and their impact on the utilization of mental health services.

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A Case of Doxycycline-Induced Pancreatitis

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ABSTRACT

Introduction: Acute pancreatitis is a common cause of hospitalizations in the United States, causing approximately 230 000 to 275 000 annual admissions We present the case of a patient with acute pancreatitis likely due to doxycycline.

Case Presentation: A 64-year-old male was admitted after developing acute epigastric pain radiating to his back, a lipase of 6611 (units/L), and a computed tomography scan showing moderate peripancreatic inflammation. He had no recent alcohol use, his gallbladder was surgically absent, and he had no gallbladder pathology on evaluation; however, he had been started on doxycycline 10 days prior. While hospitalized, he was treated with pain medications, fluids, and antibiotics for aspiration pneumonia. His acute symptoms resolved, except for minor intermittent abdominal pain 2 months after discharge.

Discussion: Doxycycline-induced pancreatitis has been reported within 3 to 17 days of medication initiation. Given the temporal correlation and lack of other inciting etiologies, we determined the most likely etiology was doxycycline.

Conclusions: Further study is needed to understand the pathophysiology and incidence of doxycycline-induced pancreatitis.

INTRODUCTION

Acute pancreatitis is a common reason for hospitalizations in the United States, causing approximately 230 000 to 275 000 annual admissions.[1,2] Overall mortality estimates are between 5% and 30% in severe cases.[1,2] Alcohol use and gallstone disease are the most common causes, leading to 30%–35% and 30%–40% of cases, respectively.[1,2] Drug-induced pancreatitis (DIP) is likely an underreported and underrealized etiology of acute pancreatitis due to difficulty identifying and definitively proving a causal effect. Medications are estimated to cause between 0.1% and 2% of acute pancreatitis cases, but this is likely an underestimate as there are over 500 drugs reported to cause acute pancreatitis. Therefore, there is some concern that patients labeled with idiopathic pancreatitis may actually have DIP.[1-3]

The pancreas secretes inactive zymogens of digestive enzymes into the duodenum. The zymogens are activated by duodenal enterokinase cleaving trypsinogen into trypsin, which then activates the other pancreatic enzymes.[3] To prevent premature activation and autodigestion, the pancreas has several protective mechanisms.[3] These include trypsin inhibitor, which binds and reduces trypsin activity, autolysis of activated trypsin, and proteases, such as alpha-1-antitrypsin.[3] Acute pancreatitis occurs when these mechanisms are overwhelmed.[3]

Acute pancreatitis is the onset of pancreatic parenchymal and peripancreatic fat necrosis with inflammation. There are several systems used to characterize the severity of pancreatitis.[2] Regardless of classification, in mild pancreatitis, there is limited necrosis and/or organ failure. Comparatively, in severe pancreatitis, there is a considerable amount of pancreas necrosis. Comorbid intrapancreatic thrombosis, vascular disruption, intraparenchymal hemorrhage, and failure of one or more organ systems is present. It is believed that an inciting etiology, such as reflux by an obstructing gallstone, overwhelms the protective mechanisms leading to autodigestion of the pancreas causing an inflammatory response.[2,3]

Patients classically present with constant epigastric pain radiating to the back, with severity typically correlating to the severity of the pancreatitis.[2,3] Patients also may have associated jaundice,

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fevers, tachypnea, hypotension and/or hypoxia.[2,3] Grey Turner (flank ecchymosis) and Cullen (periumbilical ecchymosis) signs are often described in the literature; however, these are found only in approximately 3% of cases.[2,3] Complications can include pancreas necrosis, which can lead to late or recurrent infection. Pseudocysts – a walled off collection of fluid – can develop infections, hemorrhage, rupture, gastric outlet obstruction, splenic vein thrombosis/hemorrhage, and other complications.[2,3] Extrapancreatic manifestations affect numerous organ systems and can include cardiovascular (splanchnic vein thrombosis, pseudoaneurysm, worsening of chronic underlying coronary artery disease), abdominal (abdominal compartment syndrome), and pulmonary (worsening of underlying chronic lung disease). New severe complications are rare after 48 hours.[2,3]

Diagnosis of acute pancreatitis requires 2 of the following 3 findings: classic abdominal pain, lipase greater than 3 times the upper limit of normal, and characteristic imaging findings on appropriate imaging modalities (computed tomography [CT], magnetic resonance imaging [MRI], or ultrasonography).[3] DIP is harder to diagnose, as it involves ruling out common etiologies and performing an in-depth medication review and history.[2,3] Historical evaluation should consider prior episodes or other potential etiologies. Further evaluation with levels of liver enzymes, triglycerides, and calcium – as well as imaging evaluation with abdominal and endoscopic ultrasounds – should be completed. However, it is not recommended to perform endoscopic retrograde cholangiopancreatography (ERCP) if there is no evidence of choledocholithasis. If DIP is suspected, offending drugs should be discontinued or exchanged, if possible. A definitive diagnosis is difficult but is considered more likely if symptoms resolve with discontinuation of the drug of concern, especially if symptoms recur with medication challenge.[1-3]

Numerous classification systems have been defined over the years to determine the likelihood of a medication causing acute pancreatitis. One of the first systems reported was by Mallory and Kern, which defined the drug as a definite, probable, or possible cause of pancreatitis using the following criteria:[4]

1. Onset of pancreatitis had to occur while receiving treatment with the medication;
2. Disappearance of pancreatitis symptoms with discontinuation of the medication;
3. Exclusion of other causative etiologies; and
4. Symptom relapse with medication rechallenge.

Later classification systems by Trivedi and Pitchumoni revised stratifications to a 3-group system but concentrated on the frequency of cases and results of mediation rechallenge.[5] A third classification system has been proposed by Badalov et al, which focuses on the number of cases in the literature, whether there was a rechallenge, and the time between when the drug was initiated and pancreatitis occured.[6] The latency is classified as short (<24 hours), intermediate (1-30 days), or long (>30 days).[6] Badalov classifications are as follows:

- Class 1A: At least 1 case report with positive rechallenge, all other causes are excluded.
- Class 1B: At least 1 case report with positive rechallenge, other causes are not excluded.
- Class II: At least 4 cases in the literature, with at least 75% having consistent latency.
- Class III: At least 2 cases in the literature, no rechallenge, and no consistent latency.
- Class IV: Single case report without rechallenge, drug not fitting into other categories.[6]

Naranjo et al developed an Adverse Drug Reaction Probability scale to standardize evaluation of drug reactions (see Table 3).[7] The Naranjo scale and Badalov classification are similar; however, the Naranjo scale relies on more data points and is not designed specifically for DIP. The Naranjo scale relies on blood levels and placebo administration, while the Badalov classification relies heavily on case reports and the latency period. While the Naranjo scale initially was used for clinical research into drug-induced injury, it is not limited specifically to this purpose and is simple to utilize.[6,7]

Table 1. Past Medical History and Admission Lab Values

Past Medical History

- Severe peripheral artery disease with claudication
- Mesenteric ischemia
- Active smoker with 35 pack year history
- Coronary artery disease with prior myocardial infarction, status post 4 vessel coronary artery bypass
- Chronic pain syndrome with bilateral low back pain with sciatica
- Chronic obstructive pulmonary disease
- Stable angina
- Renal artery stenosis
- No history of pancreatitis
- Congestive heart failure with preserved ejection fraction
- Chronic kidney disease stage 3
- No history of alcohol abuse

Presenting Labs

- Complete blood cell count: WBC 15.9/uL, hemoglobin 15.5 g/dL, platelets 214/uL
- Electrolytes (in mmol/L): sodium 145, potassium 3.7, chloride 112, calcium 10.0
- Liver function tests: alkaline phosphatase 112 units/L, AST 13 units/L, ALT 21 units/L, total bilirubin 0.3 mg/dL
- Kidney function: BUN 27 mg/dL, creatinine 1.19 mg/dL, GFR 68 ml/min/1.73 m^2
- Other labs: carbon dioxide 23.0 mmol/L, albumin 3.3 g/dL, troponin 44 ng/L
- Cholesterol panel (in mg/dL): total 106, HDL 48, triglycerides 73, LDL 52

Abbreviations: WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein

CASE PRESENTATION

A 64-year-old man presented to our outpatient primary care clinic for an elliptical excision of a skin lesion of the left buttock. There were no immediate complications; however, 8 days after the pro-

Table 2. Patients' Medications, Treatment Duration, Risk of Pancreatitis, Reported Number and Timeline of Development of Pancreatitis

Medications	Evidence Behind Potential Pancreatitis	Patient Duration of Therapy/Literature Reported Time Before Pancreatitis	Number of Reported Cases
Acetaminophen	Case reports, typically with overdose;[5] retrospective cohort study of overdose patients[11]	>17 years/up to 1 year after overdose	13 cases, 1 with reexposure;[5] 2958 cohort and 11 832 controls, HR 2.4 (95% CI, 1.29-4.47)[11]
Albuterol	No reported cases	6 years/NA	N/A
Amlodipine	Case reports	6 years/time course not provided	<10 cases[5]
	FDA medication insert		Between 0.1% and 1%[13]
Aspirin	Case reports	6 years/time course not provided	<10 cases[5]
Atorvastatin	Reported cases; case control study	6 years/hours to years; OR 1.67 (95% CI, 1.18-2.38) if used within 7 days, OR 1.15(95% CI, 0.87-1.52) if used >7 days ago[10]	2 cases;[12,14] 5810 cases w 5733 controls;[10] <10 cases[5]
	FDA medication insert		Frequency not reported[13]
Cistazole	No reported cases	6 years/NA	N/A
Clonidine	Reported cases from 1977; patients had other risk factors including cholestasis and thiazide treatment	6 years/NA	3 cases[15]
Doxycycline	Retrospective cohort study, case studies	10 days/2 – 28 days;[1,8,9] 1 case 273 days (chronic use for acne)[1]	4 patients reported across 3 case reports
	FDA Medwatch		Frequency not defined[16]
Hydrocodone	No evidence for hydrocodone, population-based studies show increased risk of pancreatitis in people who undergo acetaminophen overdose	>17 years/timeline not provided[5]	N/A[5]
	FDA medication insert		Frequency not specified, monitoring patients with known biliary dysfunction is recommended due to concern of sphincter of Oddi spasm[14]
Ibuprofen	Case reports	>17 years/timeline not provided[5]	<10 cases[5]
	FDA medication insert		<1%[13]
Metoprolol succinate	No reported cases	5 years/NA	N/A
Morphine	Possible pancreatitis secondary to morphine overdose;[17] 1 case after routine dose;[18] cited literature for codeine and heroin[5]	6 years/within 24 hours of initiation[5,17]	2 case reports,[17,18] opiate case reports numbered at 42 with 5 rechallenged[5]
	FDA medication insert		Frequency not specified, monitoring patients with known biliary dysfunction is recommended due to concern of sphincter of Oddi spasm[13]
Nitroglycerin	No reported cases	6 years/NA	N/A
Omeprazole	Case reports	6 years/timeline not provided	<10 cases[5]
	FDA medication insert		<1%[13]
Paroxetine	No reported cases	>17 years/timeline not provided[5]	N/A
	FDA medication insert		Frequency not defined[13]
Pregabalin	No reported cases	3 years/NA	N/A

Note: Data found by searching PubMed for "medication" and "pancreatitis" and reviewing results for each reported medication as well as reviewing the prescription drug insert for each medication for pancreatitis on AcessFDA.com.[13]

cedure, he was found to have a surgical site infection. Initially, he was prescribed cephalexin (Keflex) 500 mg 3 times a day, which he took for 4 days prior to transitioning to doxycycline 12 days after the procedure due to an upset stomach.

The patient was admitted to the hospital 22 days after the procedure (day 10 of doxycycline) with acute onset of epigastric pain radiating to the back, lipase of 6611 units/L, and a CT showing moderate peripancreatic inflammation consistent with pancreatitis. His history revealed he had not consumed alcohol recently, and his baseline alcohol consumption was 1 to 2 drinks every other month. He took ibuprofen 800 mg intermittently; the last dose was within 1 week of admission. Doxycycline was last taken the afternoon prior to admission. He was diagnosed with pancreatitis and admitted.

On admission, omeprazole was changed to pantoprazole per hospital formulary. CT abdomen revealed moderate peripancreatic inflammation consistent with pancreatitis, multiple nonobstructive bilateral renal calculi with underlying moderate-

to-severe left renal atrophy, and mild sigmoid diverticulosis. Right upper quadrant abdominal ultrasound showed that the patient's gallbladder was surgically absent, his liver was normal in architecture with no biliary ductal dilation, and the common bile duct was unremarkable with a maximal width of 4 mm. The pancreas was poorly visualized due to overlying bowel gas, and his right kidney was unremarkable. Chest x-ray revealed chronic cardiomegaly with minimal congestion. Past medical history and admission labs are noted in Table 1; medications, duration of therapy, and potential for acute pancreatitis are noted in Table 2.

Table 3. Patient's Calculated Naranjo Score[7]

Question	Yes	No	Don't Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	-1
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
Total Score				4

Total scores range from -4 to +13. Reactions are considered doubtful if below 0, possible if between 1 and 4, probable if between 5 and 8, and definite if 9 or above. Scores for individual questions are calculated based on specific criteria for each question. See Naranjo et al for specific criteria.[7]

During his hospital course, the patient was allowed nothing by mouth and was treated with intravenous opioids and aggressive fluid resuscitation. His pain improved and he started a clear liquid diet on day 3 of hospitalization; aspirin and ibuprofen were discontinued. On hospital day 4, he was noted to have worsening dyspnea and increasing oxygen requirement. A chest x-ray showed a new right lower lobe infiltrate compared to his admission x-ray, and his white blood cell (WBC) count had increased to 17 400/uL. He was started on cefepime 1g twice daily and vancomycin dosed per pharmacy for aspiration pneumonia. Echocardiogram showed an ejection fraction above 55% and diastolic function with an A wave greater than the E wave. On day 5, supplemental oxygen needs decreased. On day 6, the patient started a fat-restricted diet and was given metronidazole 500 mg 3 times daily due to a persistently elevated WBC count and concern for abdominal infection. Repeat abdominal CT scan to evaluate for infection on day 7 showed mild pancreatitis, which was felt to be improving compared to admission CT. He experienced improvement on antibiotics and on a fat-restricted diet during the hospitalization.

On hospital day 9, the patient was discharged on cefdinir 600 mg daily for 7 days for hospital-acquired aspiration pneumonia. On follow-up about 8 weeks after discharge, his primary care clinician indicated he had weaned off his chronic opioids and had some mild, intermittent residual abdominal pain. A lipase checked at this time was normal. Unfortunately, the patient passed away from an acute myocardial infarction about 16 weeks after admission.

DISCUSSION

Doxycycline-induced pancreatitis is a seemingly rare, but previously documented event. Chadalavada et al performed a retrospective cohort study looking at 841 cases of acute pancreatitis and found 31 cases secondary to medications, including doxycycline.[1] Additionally, there are several reported probable cases of pancreatitis as a result of doxycycline treatment.[1,8,9]

In our case, more common etiologies, such as trauma, ethyl alcohol, hypertriglyceridemia, post ERCP, gallstone disease, and genetic disorders were ruled out via the patient's history. Evaluation for autoimmune and malignant etiologies of his pancreatitis was not pursued due to the lack of typical symptoms (eg, weight loss, jaundice, or pancreatic enlargement), and his clinical improvement. Similarly, viral infections were thought to be unlikely without a history of corresponding symptoms.

There was a possibility that the pancreatitis was related to longstanding vascular disease, aspirin, omeprazole, amlodipine, or atorvastatin. However, this was thought to be unlikely due to the temporal correlation of doxycycline treatment. The patient's only medication documented to cause pancreatitis after long-term use was atorvastatin, possibly through interactions with the CYP3A subsystem.[19] However, this appears to be a weak correlation, with an odds ratio of 1.67 (95% CI, 1.18-2.38).[10] Rather than directly causing pancreatitis, it is possible that atorvostatin decreases the threshold for pancreatitis, as it has been noted that DIP is more likely in patients with multiple comorbidities and polypharmacy.[11,19] This is certainly a possibility for our patient given his comorbidities and polypharmacy.

As in most idiopathic versus DIP cases, it would be difficult to definitively prove doxycycline as the cause without rechallenging, which has obvious ethical concerns. The patient's Naranjo score was calculated at 4, indicating a possible reaction (see Table 3).

Furthermore, the time course is within the timeframe of 3 to 15 days reported in several other studies.[1,8,9] Not all authors calculated a Naranjo score, so it is more difficult to quantify the likelihood of reaction.[1,8,9] We would argue that quantification should be recommended in all suspected cases, due to the difficulty identifying and subsequently diagnosing DIP. Therefore, we argue that with the addition of our case, the Badalov classification for doxycycline would increase to level II within the available literature.[6]

CONCLUSIONS

DIP is a rare etiology of acute pancreatitis, and doxycycline is a medication with case reports supporting it as an inciting etiology. Increasing knowledge of medications with the potential to cause acute pancreatitis will help with diagnostic clarity and therefore elucidate the true incidence and prevalence of drug-induced pancreatitis.

We present another case of possible doxycycline-induced pancreatitis to educate clinicians and add to the body of evidence of medications that can cause pancreatitis. Our intent is to increase clinicians' recognition of potential DIP and facilitate further investigation into the topic.

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Severe Thrombocytopenia in Decompensated Liver Disease: An Example of Accelerated Intravascular Coagulation and Fibrinolysis

Jesse Fletcher, BA; Brandon J. Calley, BS; Pinky Jha, MD, MPH

ABSTRACT

Introduction: Advanced liver disease can present with severe thrombocytopenia that can be difficult to delineate and manage. Here we describe a unique entity of accelerated intravascular coagulation and fibrinolysis (AICF) in a patient with decompensated liver disease.

Case Presentation: A 56-year-old male with a history of alcoholic cirrhosis was admitted for weakness, nausea, metabolic derangement, and acute kidney injury determined to be secondary to decompensated liver disease. During admission, his platelet count declined to <10 000/μL requiring 8 total platelet transfusions. Laboratory and clinical evaluation supported a diagnosis of AICF, and the patient gradually improved with supportive management.

Discussion: AICF can present similarly to disseminated intravascular coagulation, and careful evaluation of specific laboratory values is required for accurate diagnosis. Appropriate management minimizes the associated increased risk of bleeding and prevents delay in procedural intervention.

Conclusions: This case highlights the importance of early clinical and laboratory correlation, multidisciplinary care, and supportive treatment in the management of AICF.

INTRODUCTION

Advanced liver disease results in an imbalance between procoagulant and anticoagulant factors that can present as a variety of hematological abnormalities, including thrombocytopenia. Thrombocytopenia in liver disease is often multifactorial, with varying degrees of platelet sequestration in the spleen, decreased liver production of thrombopoietin, and accelerated fibrinolysis.[1-3] Approximately 75% of patients with chronic liver disease have mild thrombocytopenia (100 000-150 000/μL), and approximately 13% have moderate thrombocytopenia (50 000-100 000/μL).[1] Severe thrombocytopenia (<50 000/μL) in liver disease is rare and may represent a profile of hematologic abnormalities associated with decompensated liver disease referred to as accelerated intravascular coagulation and fibrinolysis (AICF).[4]

CASE DESCRIPTION

A 58-year-old man with a history of alcoholic cirrhosis, hypertension, and type 2 diabetes presented initially to a primary care clinic for evaluation of generalized weakness, nausea, and progressive lower extremity swelling. Further review of symptoms was negative for chest pain, shortness of breath, abdominal pain, hematuria, and weight loss. Physical examination was notable for worsening ascites and lower extremity edema. Laboratory evaluation revealed elevated blood urea nitrogen, elevated creatinine, hyponatremia, hyperkalemia, low albumin, and elevated bilirubin. He was subsequently recommended for admission, upon which hepatology and nephrology were consulted. His presentation was determined to be secondary to decompensated cirrhosis complicated by acute kidney injury with both pre-renal and hepatorenal components in the setting of recent diuretic use. He underwent paracentesis on hospital day 1 and 2, which yielded 8 total liters of serous, amber-colored fluid. Subsequent fluid studies were negative for spontaneous bacterial peritonitis and malignancy (Table 1). Albumin challenge was completed, and appropriate albumin supplementation was given. Kidney function improved on hospital day 6 with supportive treatment. Persistent hypoten-

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Table 1. Peritoneal Fluid Studies From Hospital Day 1

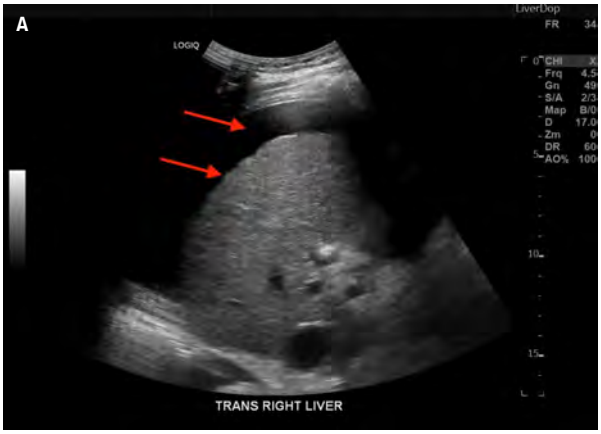
Peritoneal Fluid Studies	Hospital Day 1
Color	Yellow
Clarity	Cloudy
White blood cell count (/uL)	91
Lymphocyte (%)	71
Monocyte/macrophage (%)	29
Amylase (U/L)	7
Protein (g/dl)	1.4
Glucose (mg/dL)	223
Lactate dehydrogenase (U/L)	43
Aerobic/anaerobic culture with Gram stain	Negative 5 days

Table 2. Select Complete Blood Cell Count Results Throughout Hospital Admission

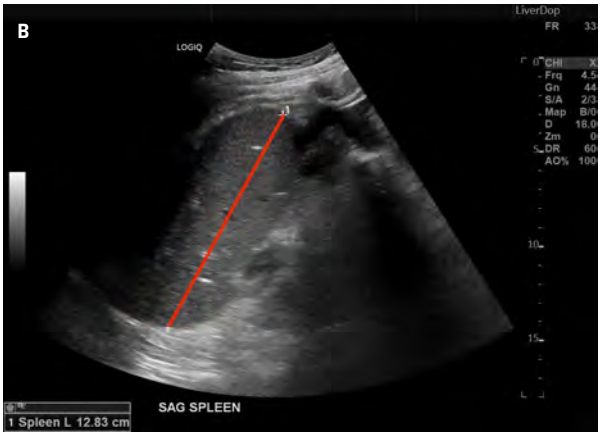
Complete Blood Cell Count	WBC Count (10e3/uL)	Hemoglobin (g/dL)	MCV (fl)	Platelet Count (10e3/uL)
Ref Ranges	**3.9 – 11.2**	**13.7 – 17.5**	**79 – 98**	**165 – 366**
Day 1	4.8	10.5	102	94
Day 2	2.8	8.2	101	60
Day 3	2.9	7.7	104	30
Day 4	3.5	8.0	106	19
Day 5	2.9	7.7	107	8
Day 6	3.1	7.8	106	10
Day 7	2.7	7.5	106	10
Day 8	2.9	7.8	108	30
Day 9	3.6	7.4	105	20
Day 10	3.5	7.4	106	10
Day 11	4.6	8.4	106	12
Day 12	3.8	8.2	105	22
Day 13	3.3	7.7	112	27
Day 14	3.2	8.6	109	13

Abbreviations: WBC, white blood cell; MCV, mean corpuscular volume; ref, reference.

Figure. Image From Ultrasound of Liver and Spleen



A. Arrows highligh nodular liver edge as evidence of cirrhosis, as well as surrounding ascites.



B. Line highlights spleen length of 12.83cm, indicative of minimal splenomegaly.

sion throughout admission required titration of midodrine up to 15 mg 3 times daily.

Platelet levels gradually declined from 94 000/μL on admission to 8000/μL on hospital day 5 (Table 2). Hematology was consulted and recommended platelet transfusion for platelet counts less than 10 000/μL. Thrombocytopenia persisted despite the transfusion of 8 total units of platelets from hospital day 5 to day 10. Thrombocytopenia initially was attributed to a combination of decreased liver production of thrombopoietin and possible splenic sequestration, both secondary to decompensated liver failure. Ultrasound of the liver and spleen was negative for thrombus and revealed minimal splenomegaly (Figure). On hospital day 8, physical exam was notable for scattered petechiae, oozing from an intravenous line site, and increasing ascites. Laboratory evaluation revealed increased prothrombin time (PT) (18.2 seconds) and partial thromboplastin time (pTT) (44.3 seconds), decreased fibrinogen (101 mg/dL), and elevated D-dimer (4.35 mg/L fibrinogen equivalent units), prompting concern for disseminated intravascular coagulation (DIC). Additional laboratory evaluation revealed factor VIII activity of 175%, within the normal reference range of 64% to 189%, which lessened suspicion for DIC and pointed towards hyperfibrinolysis secondary to decompensated liver disease. The patient did not meet the criteria for liver transplantation; thus, supportive care was favored by hematology and hepatology. Platelet levels remained low but gradually stabilized without any further evidence of bleeding. The patient was subsequently discharged on hospital day 10 with close outpatient follow-up.

DISCUSSION

AICF and DIC have similar clinical presentations that may include oozing of blood from venipuncture sites, thrombocytopenia, prolonged PT and pTT, decreased fibrinogen, and elevated D-dimer.[5] The exact cause of AICF is unknown, but elevated levels of tissue

plasminogen activator resulting from decreased hepatic clearance, as well as decreased levels of antifibrinolytic factors, have been hypothesized as potential contributors.[4,6] There is additional evidence that ascitic fluid has fibrinolytic properties, and its absorption through the thoracic duct also can contribute to the systemic accelerated fibrinolysis seen in advanced liver disease.[2]

While AICF can present similarly to DIC, they can be differentiated by evaluation of specific clotting factor activity levels. In DIC, the levels and, thus, activity of all clotting factors decrease due to their rapid systemic consumption. However, in AICF, low clotting factor activity is due to decreased clotting factor production in the liver; thus, only those factors produced in the liver will have low activity. Since clotting factor VIII is produced by endothelial cells systemically, its activity will be normal or slightly increased in AICF, allowing for the differentiation between AICF and DIC.[7] Additionally, increased level of factor VIII has been associated with cirrhosis, further aiding in the differentiation between AICF and DIC.[3,7]

The distinction between DIC and AICF is important as it directs the management of thrombocytopenia in advanced liver disease. The gold standard for management of DIC is treatment of the underlying condition.[7] While treatment of other causes of thrombocytopenia in advanced liver disease focuses on the correction of splenic sequestration and decreased thrombopoietin, the exact cause of AICF remains unknown and treatment is mainly supportive.[1] Antihyperfibrinolytic therapy including ε–aminocaproic acid and tranexamic acid have been used to combat hyperfibrinolysis in advanced liver disease, specifically to prevent blood loss during liver transplantation, but evidence of their efficacy is limited.[1] As with all hematologic abnormalities associated with advanced liver disease, the definitive treatment is liver transplantation.[8]

AICF and other hematological abnormalities associated with advanced liver disease often complicate clinical courses and delay procedural interventions due to increased risk of bleeding.[1,4] While the associated increased risk of bleeding is generally accepted, the extent to which thrombocytopenia and hyperfibrinolysis contribute to it is relatively unclear.[6] The use of conventional coagulation tests with evaluation of factor VIII activity are useful in the diagnosis of AICF but offer little insight on the risk of bleeding as they only evaluate procoagulant factors.[6,9] Accurate assessment of bleeding risk in patients with AICF may be accomplished with the use of thromboelastography, which offers a better assessment of the interactions between procoagulant and anticoagulant factors as well as platelets.[9] However, current use of thromboelastography is limited by availability and lack of standardization among test protocols.[9] Regardless, the early and precise management of AICF is important to minimize the risk of bleeding, specifically in patients with decompensated liver disease for whom recurrent paracenteses may be indicated.

CONCLUSIONS

This case highlights several significant considerations for clinicians, primarily the importance of clinical and laboratory correlation to determine the most appropriate cause of thrombocytopenia in patients with advanced liver disease. In this particular case, the distinction between DIC and AICF was made through normal clotting factor VIII levels. Further, multidisciplinary management leads to swifter diagnosis and implementation of an appropriate plan of care. This minimizes bleeding risk and prevents delay in procedural intervention. Lastly, given that AICF is a complication of advanced and irreversible liver disease, treatment is largely supportive unless clinically indicated for transplantation.

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Central Cord Syndrome After Fall From Inversion Table

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ABSTRACT

Introduction: Central cord syndrome, the most common incomplete traumatic spinal cord injury, often results in functional impairment with variable recovery.

Case Presentation: Central cord syndrome developed in a 64-year-old man during routine home use of an inversion table.

Discussion: The incidence of central cord syndrome, which occurs most frequently after a fall, is increasing among older persons. Age-related changes in the cervical spine may predispose the spinal cord to compression and injury during a fall. Evidence for lumbar traction as treatment of low back pain is limited.

Conclusions: This unusual case of spinal cord injury during inversion table use highlights the relationship between anatomical changes in the cervical spine and the mechanism of injury typical in central cord syndrome. The resulting increased risk of central cord syndrome for older adults should be discussed with patients in the context of activities that could lead to falls or cervical spine extension.

INTRODUCTION

Billions of dollars are spent annually by individuals and insurance plans on treatment of low back pain.[1] Although noninvasive and accessible options such as home inversion tables are commonly used, falls and serious injuries can occur during inversion table use. In general, falls are a leading cause of death and morbidity among older persons.[2] Specifically, spinal cord injury (SCI) due to a fall is more likely in older persons, in part because of degenerative changes that commonly alter spinal anatomy.[2] Central cord syndrome (CCS), the most common incomplete traumatic SCI, can cause considerable functional impairment.[2,3] Weakness affecting the legs more than the arms and bladder dysfunction are typical in CCS.[4] Among older persons, CCS most frequently occurs because of a fall.[3] As patients seek relief from pain thought to result from degenerative spinal processes, they may be more predisposed to falls and SCIs because of these same degenerative processes.

We present a case of CCS resulting from an injury during use of a common home lumbar traction device. In general, evidence supporting the efficacy of lumbar traction is limited.[5] We discuss how the conversation about lumbar traction changes as patients age and related anatomical changes occur; we review how CCS can affect an individual; and we highlight the importance of CCS in the population as a whole. Our case emphasizes the importance of considering the added risk from age-related changes, especially with the use of therapy for low back pain that has limited evidence.

CASE PRESENTATION

A 64-year-old retired male construction worker with a history of chronic low back pain arrived at the emergency department by ambulance after an injury at home. His wife, who had not seen him for 2 or 3 hours, found him after he had partially fallen from his home inversion table. He was conscious when she found him, but he could not remember the event. He described neck pain and weakness in his arms and legs. He could not stand and was bleeding from a wound on the back of his head. Emergency medical services was activated. In the emergency department, the Glasgow Coma Scale score was 14 because of lack of spontaneous eye opening. Grip strength was graded 1/5 bilaterally. Elbow

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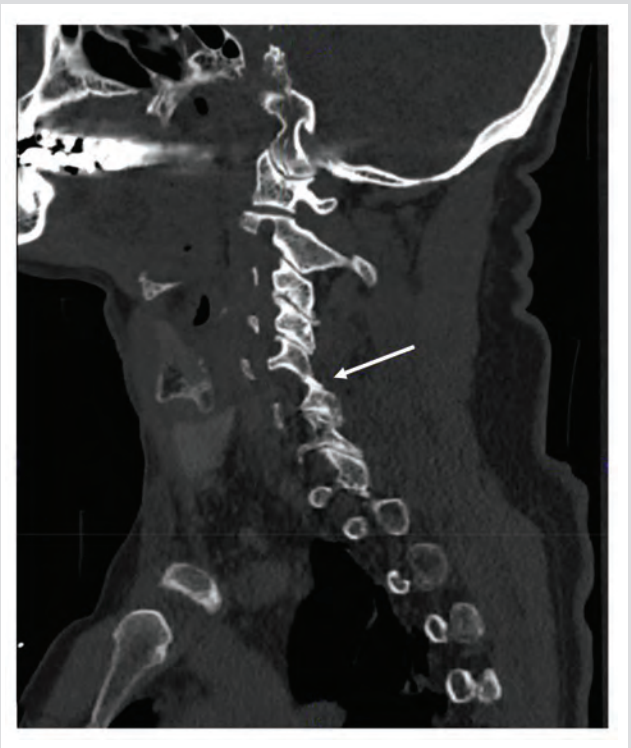
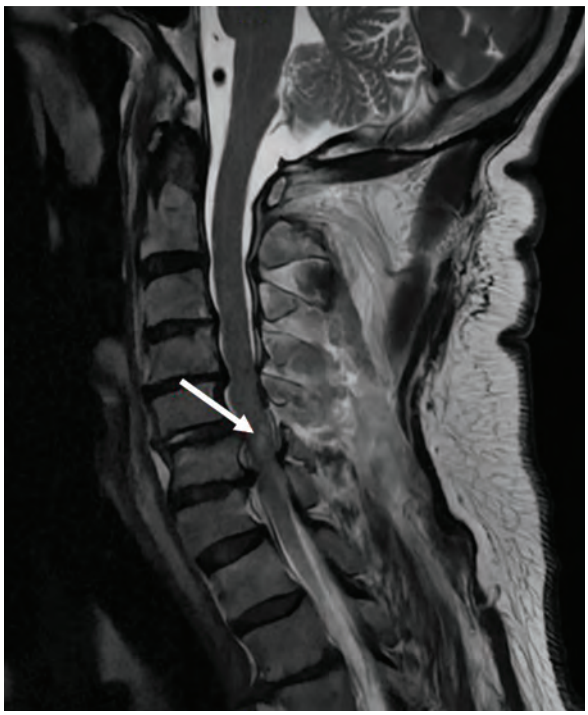
Figure 1. Computed Tomography of the Neck



Sagittal view shows right-sided perched facets at C5-6 (arrow).

Figure 2. Magnetic Resonance Imaging of the Neck



T2-weighted image shows spinal cord edema (arrow).

flexion and extension were graded 4/5 bilaterally. Ankle dorsiflexion, knee extension, and hip flexion were graded 4/5 on the left. The right lower extremity was strong. Sensory examination was not done initially, but results were normal during his hospital course. Computed tomography of the cervical spine showed perched facets at C5-6 on the right with marked anterolisthesis and severe central canal stenosis from C4 through C7 (Figures 1 and 2). Magnetic resonance imaging showed cord edema at C5-6. The neurosurgery service was consulted, and decompression and fusion were performed.

In the days immediately after surgery, the patient's markedly impaired hand function was a primary concern. An indwelling catheter remained in place because of urinary retention, and he had episodes of bowel incontinence. Orthostasis was treated with an abdominal binder, elastic bandage wraps, and midodrine. He ambulated 50 meters with a front-wheeled walker and contact guard assistance. He was discharged to an acute inpatient rehabilitation unit, where over the next 11 days the indwelling urinary catheter was removed and volitional voiding returned. Upper extremity function improved. At his discharge, finger flexion and abduction strength had increased to 4/5 bilaterally, and he could ambulate unlimited distances independently without a cane or walker. Use of midodrine was tapered and discontinued. He returned home to his wife and daughter and continued therapy as an outpatient.

At his 1-month follow-up in the rehabilitation clinic, the patient had normal bowel and bladder function. On examination, he had 4/5 finger abduction bilaterally and 4/5 finger flexion on the left only. He could perform a body-weight squat, heel walk, and toe walk. He described improving neuropathic pain in his upper extremities and no longer required pain medication. Overall, he was encouraged by his functional gains and had already returned to many of his previous household activities.

DISCUSSION

Low back pain is common, and the risks and benefits of the numerous treatments available for low back pain require ongoing discussion. The lifetime prevalence of low back pain is 75% to 84% in industrialized countries.[1] Patients and health plan providers spend billions of dollars annually on low back pain treatments with variable efficacy.[4] The independent use of devices to treat low back pain is commonly reported in our clinic and thought by many patients to be safe and effective. Lumbar traction has been used as a relatively inexpensive and noninvasive treatment option. Benefit theoretically results from decreased pressure on intervertebral discs and sensitized neural tissue.[6] Although patients often report therapeutic benefit, only limited evidence supports the effectiveness of lumbar traction for treatment of low back pain.[5,6] In a randomized controlled trial of 120 patients with low back pain, no benefit was observed between

those who received mechanical lumbar traction in addition to physical therapy and those who received physical therapy alone.[7] Specific patient subsets may be more likely to benefit from lumbar traction as an adjunctive treatment. A recent meta-analysis of the efficacy of mechanical traction for treatment of lumbar radiculopathy symptoms suggested possible short-term effectiveness of supine mechanical traction when used in combination with supervised physical therapy.[5] Adverse effects are infrequently described, although Thackeray et al[7] described aggravation of low back or leg pain in 44% of 61 patients who used lumbar traction. We could not find published articles that addressed the safety of lumbar traction devices specifically with older persons.

Lumbar traction can be applied in various ways. There is little if any standardization among health care professionals and individuals who use it. The type of device, method for securing oneself to the device, and duration of traction vary. Use of a home inversion table is perhaps the most common method of therapeutic lumbar traction for treatment of low back pain, and home inversion tables are readily available in retail stores and online. Inversion table therapy is often performed independently by securing one's feet to an adjustable platform and lying supine before using the device to gradually rotate into an inverted position and thereby exert traction on the lumbar spine. Typically, the body is positioned supine approximately 60 degrees below horizontal with the feet pointed upward and the head downward (Figure 3). The head is typically 3 to 6 inches above the ground. It has been theorized that when a person is in this position, some intervertebral separation occurs, relieving painful pressure on structures within the lumbar spine.[6] Relieving compressive forces on an intervertebral disc or spinal nerve is thought to lessen nociceptor activity, with the result that users of an inversion table may feel relief of low back pain.[5]

Medical literature specifically addressing the effectiveness of inversion table treatment is limited. In our review, we did not find discussions on the safe use of inversion tables. Injuries related to inversion table use have been reported but only sparingly. Jung et al[8] described 3 cases of cervical SCI during use of an inversion table in South Korea, where inversion tables are widely used and often are available in public spaces. In each of the 3 cases, the person's feet slipped from the inversion table harness and their head struck the ground. Of the 3 patients, 1 had a complete SCI and 2 had incomplete SCI; all 3 patients required decompression surgery and placement in long-term rehabilitation facilities.

The worldwide prevalence of traumatic SCI is bimodal, with 1 peak between the ages of 15 and 29 years and a second peak at ages older than 50 years.[3] The US often has the highest annual incidence of SCI among reporting countries and has an estimated 17 000 new cases annually.[7,9,10] CCS, which accounts for about 10% of SCIs in adults, also has a bimodal distribution.[3,9] In younger patients, CCS usually results from high-energy events (eg, motor vehicle accidents, assaults, and athletic injuries), but among patients older than 60 years, falls are the most common cause of CCS.[3] As the mean age of the US population has increased, the number of SCIs and the mean age of injured persons have increased.[9,10] Degenerative changes and spinal stenosis, which become more common with older age, generally predispose older persons to spinal cord compression.[4] In cervical stenosis, less space is available to accommodate the spinal cord in the central canal, so the spinal cord is more vulnerable to compression, especially on hyperextension.[4] These changes in both spinal morphology and mechanics most likely account for the age-related variation in injury patterns and the increasing incidence of CCS in the US.[2,4,6,9] Most SCIs now occur in older patients.[9] As the US population ages, CCS could account for more than half the SCIs by the end of the century.[9] Safe and appropriate use of treatments, such as home inversion tables, is increasingly important for CCS prevention.

Figure 3. Depiction of Inversion Table Use

Image from "sandalphonarts." Adobe stock image; used under extended license.)

The clinical description of CCS has remained relatively consistent since it originally was delineated in the 1950s.[4] Arm weakness with comparative preservation of leg strength is pathognomonic.[4] Bladder dysfunction and urinary retention are common.[4] Sensory impairment below the level of injury is variable.[4] A simplified definition of CCS has been proposed that allows for the variability often observed in clinical presentations and includes patients who have any posttraumatic sensory or motor deficits localized to the cervical spinal cord.[9] Prognosis varies, but patients generally have marked improvement—particularly if they are young and the motor deficits are moderate.[4] For most patients, the American Spinal Injury Association motor score doubles after 1 year.[4] In a systematic review of 12 articles evaluating prognosis in traumatic CCS secondary to extension of a stenotic cervical spine, patients had excellent recovery of hand function with preserved lower extremity function at presenta-

tion.[11] This is similar to our patient's presentation, although we have found limited information specifically on inversion table injuries and their mechanism. Age and degree of SCI are important prognostic factors, and older patients who have a stenotic spinal canal stenosis have poorer outcomes.[4] Decompressive surgery may be required, particularly for fracture and dislocation.[9] Neuropathic pain and functional impairments may persist, negatively affecting independence—especially among patients older than 50 years.[4]

Historically, the presumed pathogenesis of CCS has been based on spinal cord anatomy and the somatotopic organization of the corticospinal tracts.[9] Mechanical compression is thought to injure the central spinal cord, preferentially disrupting the medial corticospinal tracts that control upper extremity function while sparing the more lateral corticospinal tracts that control the lower extremities.[9] Postmortem studies have identified selective damage to white matter in the area of the corticospinal tracts. However, the exact influence of corticospinal tracts on motor function and the specific location of neuronal injury in CCS are topics of debate.[12] Wallerian degeneration has occurred in patients with acute traumatic CCS without a decrease in the number of motor neurons supplying the hand musculature.[12] Rostral injury to the corticospinal tracts as they decussate in the brainstem also has been postulated.[9] Many conclusions about the details of corticospinal tract anatomy come from observations in nonhuman primates; only a few human postmortem studies are available. Some investigators believe that the evolution of human corticospinal tracts has resulted in an innately greater role in upper extremity function.[9] The considerable variability in CCS pathophysiology reflects many factors, including injury severity.[9] However, clinical diagnosis of CCS is dependent on the neurologic examination.[9]

Our patient is part of the growing segment of the population with higher risk for CCS. Portions of the case presented here are classic for CCS in presentation and in course. The patient was a retired manual laborer who most likely had preexisting cervical spondylosis and then had an injury resulting in arm weakness greater than leg weakness; impaired bowel and bladder function recovered within days. Perched facets on imaging suggest flexion and distraction of the cervical spine rather than hyperextension as the mechanism of injury classically thought to occur in most cases of CCS.[13] At follow-up 1 month after his injury, the patient had only slight hand weakness and mild neuropathic pain, despite severe injury. This is consistent with other reported cases of CCS in which surgical intervention targeting a specific pathologic site was done shortly after presentation.[11]

Our patient's inciting traumatic event occurred during independent use of a home inversion table for the treatment of chronic low back pain. This mechanism of injury may be underreported given the prevalence of both low back pain and this treatment modality. The evidence for the efficacy of lumbar traction for relief of low back pain is minimal compared to the evidence for the efficacy of established treatments, such as therapeutic exercise. Information on how to safely use an inversion table is also limited. It may be helpful to ensure the safety of ankle-holding or harness mechanisms. Compared with independent use of an inversion table, the use of lumbar traction in a therapy office or with a spotter may decrease the risk of injury. Health care professionals must carefully consider a patient's specific risk factors when they consider options for treatment of low back pain.

CONCLUSIONS

The balance between risk and benefit is important to consider with treatment of any condition, including low back pain. Commonly available home medical devices should be included in the discussion. Challenges specific to inversion table use include limited safety guidance and the usual practice of independent use. Our case shows the potential for SCI—especially for patients at higher risk—as an important consideration in discussions of inversion table treatment. Although the prognosis is usually favorable, CCS can lead to serious long-term functional impairments. An understanding of how age-related anatomical changes contribute to common mechanisms of injury in CCS allows for more informed discussions of the risks and benefits of certain treatments, including lumbar traction. For some patients, these discussions may lead to the determination that the risk of severe injury outweighs the perceived benefit of inversion table use—particularly given the paucity of evidence for lumbar traction as an effective treatment of low back pain and the availability of proven techniques, such as therapeutic exercise.

Trauma prevention is primary in averting SCIs at a societal level. Limiting the occurrence of traumatic events can help mitigate morbidity and maximize quality of life in the growing older population. Accordingly, we advocate careful consideration before use of home medical devices such as inversion tables.

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A Case of Weak D Serologic Phenotype

Alice M. Boshoven, MD; Laura Verhagen, DO

ABSTRACT

Introduction: Rh D alloimmunization is the serologic response that occurs when Rh D-negative patients are exposed to Rh D-positive blood. Rh D blood typing is recommended in pregnancy to prevent alloimmunization.

Case Presentation: A 27-year-old gravida 3, para 2012 (G3P2012) previously Rh D-negative female presented with discordant and weakly positive Rh D blood typing results. Confirmatory genetic testing revealed weak D phenotype that can be treated clinically as Rh D-positive.

Discussion: Genetic variants of Rh D can cause varied blood typing results depending on the hospital reporting protocol utilized. If labeled as Rh D-negative, this could lead to unnecessary administration of Rh D immunoglobulin in pregnancy. Genetic variants should be suspected when patients are noted to have blood typing results that are discordant or weakly positive.

Conclusions: Rh D genotyping should be considered when discordant or weakly positive Rh D blood type results are noted in order to confirm and classify genetic subtype.

INTRODUCTION

Antigens on the surface of red blood cells determine blood type and are designated as ABO and Rh, with specific subtypes including Rh D. Patients with the Rh D antigen on the surface of their red blood cells are considered Rh D-positive. Patients without the Rh D antigen on the surface of their red blood cells are considered Rh D-negative. The US Preventive Services Task Force (USPSTF) recommends Rh D blood typing and antibody screening for all pregnant women during their first prenatal visit (Grade A recommendation).[1] Maternal antibody screening is an indirect antibody test evaluating for maternal antibodies to red blood cell antigens (indirect Coombs). Further, the USPSTF recommends repeat Rh D antibody screening at 24 to 28 weeks for Rh D-negative women unless the biological father is also Rh D-negative (Grade B recommendation).[1]

Evidence supports the USPSTF recommendations for performing routine blood typing during pregnancy in order to prevent maternal Rh D alloimmunization, which is an immune response resulting from exposure to foreign red blood cell antigens.[2] Antenatal bleeding, miscarriage, ectopic pregnancy, procedures including chorionic villus sampling, and delivery all can result in fetal-maternal hemorrhage.[2] During a fetal-maternal hemorrhage, small amounts of fetal blood cells can be introduced into maternal circulation. If the fetus is Rh D-positive, Rh D-negative mothers can subsequently form antibodies against fetal blood cells. Maternal IgG antibodies created to combat foreign red blood cell antigens can subsequently cross the placenta, attach to fetal red blood cell antigens, and cause destruction of the red blood cells by macrophages in the spleen.[3] This can have serious implications for fetal well-being, often resulting in hemolytic disease of the fetus and newborn (HDFN). This can be identified with direct antibody testing of the newborn, evaluating for maternal antibodies attached to the surface of neonatal red blood cells (direct Coombs). HDFN can lead to severe hemolysis, anemia, hydrops fetalis, stillbirth, postnatal jaundice, and multiorgan failure. More than 50 red blood cell antigens have been identified to cause HDFN; however, one of the most severe forms is caused by Rh D alloimmunization.[3,4]

Prophylactic use of passive Rh D (anti-D) immunoglobulin (RhIG) given to Rh D-negative women can prevent alloimmu-

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Table. Patient Blood Type Results

Specimen	Historical Red Cross Blood Type	May 2018 Status Post Spontaneous Abortion	July 2018 Prenatal Labs	Feb 2019 Delivery	Nov 2020 Prenatal Labs	June 2021 Delivery in New Hospital System
Blood Type	A Rh D-positive	A Rh D-negative	A Rh D-negative	A Rh D-negative	A Rh D-negative	A Rh D (weak positive)
Genotype						Weak D Serologic Phenotype with a Type 1 Allele

nization. In the United States, a dose is administered routinely at 28 weeks gestation to prevent alloimmunization during the third trimester prior to delivery. A second dose is given within 72 hours after delivery for Rh D-negative mothers with Rh D-positive babies.[2] Rh D-negative prevalence varies widely based on geographic location, with rates as high as 15% in North America and Europe, 5% in India, and 0.1% to 0.3% in Asia.[2] The prevention of sensitization and, thus, prevention of Rh HDFN has saved millions of lives, though inequitable access to screening and treatment globally contributes to ongoing disparities in perinatal morbidity and mortality.[3]

CASE PRESENTATION

A 27-year-old woman with no pertinent past medical history transferred to our family medicine clinic for prenatal care. Her first pregnancy in May 2018 resulted in early spontaneous abortion. She had no previous documentation of blood type in the electronic medical record; however, she had donated blood prior and had documentation from the Red Cross that her blood type was A Rh D-positive. At the time of her miscarriage, type and screen demonstrated A Rh D-negative with indirect Coombs negative. Due to the discordant results, the type and screen was repeated and confirmed. She subsequently received her first dose of RhIG.

Pregnancy was achieved shortly thereafter in July 2018. Her prenatal labs noted her to be A Rh D-negative with indirect Coombs negative. At approximately 28 weeks gestation, she received her second dose of RhIG. In February 2019, she delivered a term newborn via normal spontaneous vaginal delivery. RhIG evaluation after birth again noted blood type A Rh D-negative with indirect Coombs negative, and her newborn infant was similarly noted to be Rh D-negative with direct Coombs negative. She did not receive RhIG at that time.

In November 2020, she achieved pregnancy again and transferred care to our family medicine clinic. Prenatal labs demonstrated A Rh D-negative with indirect Coombs negative. She received her third dose of RhIG at approximately 28 weeks gestation. In June 2021, she delivered a term newborn via normal spontaneous vaginal delivery in a new hospital system with a different blood typing protocol. She developed a postpartum hemorrhage. A type and screen evaluation was obtained after birth with noted blood type A Rh D (weak positive) with indirect Coombs negative. Her newborn infant was noted to be A Rh D-positive, direct Coombs negative. Fetal cell stain was negative. Because of both discordant and weak positive testing, confirmatory genetic weak D testing was recommended by the blood bank. She received her fourth precautionary dose of RhIG while confirmatory genetic testing was pending.

Ultimately, the patient was found to have weak D serologic phenotype with a type 1 allele. She is not a candidate for RhIG in future pregnancies, and she can receive Rh D-positive blood should red blood cell transfusion be required in the future.

DISCUSSION

Weak D serologic phenotype is a genetic variant of the Rh D antigen most commonly affecting White patients at a rate of approximately 0.2% to 1% of the population. In many cases, one or more amino acid substitutions occur in the Rh D protein, which results in reduced antigen expression on the surface of red blood cells.[2,5] This results in weak or no reactivity to anti-D reagent initially but moderate or strong agglutination with antihuman globulin.[5] Clinically, some subtypes of weak D can be managed safely as Rh D-positive with minimal risk of alloimmunization and some cannot. Other Rh D antigen genetic variants beyond weak D exist as well but are beyond the scope of this case report.

Interestingly, serologic typing methods and Rh D interpretation vary by lab. In the case of patients with weak D phenotype, this can result in discordant findings. In addition, current standards for transfusion medicine require blood donors and newborns to undergo more thorough analysis and confirmation of weak D phenotype. Generally, this results in the inclusion of the weak D phenotype into an undifferentiated Rh D-positive category. This prevents administration of weak D phenotype blood to a Rh D-negative patient and ensures that a Rh D-negative mother appropriately receives RhIG after giving birth to an infant with weak D phenotype. While hospital protocols vary as noted in the case presented, more thorough testing often is not a requirement for transfusion recipients or pregnant women, and weak D phenotype patients in this case are generally categorized as Rh D-negative.[2,5] These management protocols aim to prevent alloimmunization but result in confusion for both patients and clinicians, as exemplified in the case presented. Prior to receiving care from our clinic, discordant blood typing results were noted, yet the patient was managed as Rh D-negative. She received RhIG several times before confirmatory genotyping occurred.

Testing for agglutination with antihuman globulin will identify

weak D phenotype; however, further delineation with genotyping is necessary to impact management decisions. Types 1, 2, and 3 weak D antigens do not form antibodies when exposed to Rh D-positive red blood cells, so they can be managed safely as Rh D-positive. These subtypes encompass approximately 80% of all weak D phenotypes identified. There has been alloimmunization demonstrated with some other weak D subtypes, thus demonstrating the value of genotyping.[5] The work group convened by Association for the Advancement of Blood and Biotherapies and College of American Pathologists estimates that if Rh D genotyping were performed in women with childbearing potential who are noted to have discordant blood typing results, approximately 24 700 doses of RhIG could be avoided annually in the United States.[5] Similarly, if transfusion recipients with discordant blood typing results underwent Rh D genotyping, 47 700 units of Rh D-negative red blood cells could be spared annually.[5]

The potential social impacts of routinely utilizing Rh D genotyping are vast. Rh D-negative blood type is less common than Rh D-positive blood type. Its prevalence varies based on geographic location but is less than or equal to 15% of the population.[2] Rh D-negative blood is utilized disproportionally when emergencies preclude the use of blood typing prior to red blood cell administration. This results in risk for a shortage of Rh D-negative blood, particularly in low resource areas of the world. Additionally, RhIG is manufactured by intentionally alloimmunizing Rh D-negative male donors (by injection of Rh D-positive red blood cells) and utilizing their plasma.[5] This poses theoretical risk to the donor who becomes alloimmunized through the process.[5] In the last 50 years, Rh disease-related morbidity and mortality have only dropped by approximately 50% despite the emergence of RhIG. While the specific burden of Rh disease in lower income countries is not well known, it is known that the biggest shortfalls occur in South Asia and sub-Saharan Africa where there is a high incidence of neonatal deaths due to complications of HDFN.[6] Shortages of RhIG play a role. Reducing the use of Rh D-negative blood and RhIG in situations where weak D genotyping deems it appropriate could mean more availability where shortages currently exist.

The work group supports performing Rh D genotyping for all discordant blood typing results.[5] The American College of Obstetricians and Gynecologists has identified that genotyping is a management option but recognizes that there is an overall lack of comprehensive cost-benefit data to strongly support a change in current recommendations.[2] However, a simulated financial analysis published in 2015 suggested that Rh D genotyping may provide clinical value without significantly increasing costs.[7]

CONCLUSIONS

Rh D genotyping should be considered when patients are found to have discordant or weakly positive Rh D blood typing results. Since blood type cannot change with time, discordant results should increase suspicion of Rh D variants, including weak D. Doing so could reduce risk to individuals by avoiding unnecessary medical interventions. Additionally, as we strive to better understand and address health care disparities, Rh D genotyping has the potential for social impacts on a larger scale by increasing availability of precious resources. Additional cost-benefit analysis of Rh D genotyping may be useful in better defining the role of Rh D genotyping in clinical care.

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Proceedings from the 2023 Medical College of Wisconsin Innovations in Healthcare Education Research Annual Conference

The following award-winning abstracts were presented during the 10th Annual Medical College of Wisconsin (MCW) Innovations in Healthcare Education Research (IHER) Annual Conference on September 19-21, 2023. Health care educators and researchers from MCW and other national institutions meet annually at IHER to present their research and innovative ideas and to learn from one another about the new and creative approaches to educating students and residents. The 3-day conference includes nationally recognized keynote speakers, panel sessions, workshops, roundtables, oral presentations, and posters which can be viewed at https://www.mcw.edu/IHER2023. Three hundred participants hailed from 22 states and 7 countries. The winning oral presentations and posters in the research and innovations categories are published below.

BEST ORAL PRESENTATION – INNOVATIONS

Development and Trial of a Low-Cost, Simulation-Based Abortion Skills Training

Emily Lambert, BS; Alenna Berosa, MS; Elisha Jaeke, BS; Julie Szczygielski, BS; Allison Linton, MD; Kathryn Dielentheis, MD

Problem Statement: Nearly 1 in 4 people capable of becoming pregnant will obtain an abortion in their lifetime. Thus, it is crucial that graduating medical trainees are equipped to provide abortion care. However, turbulent legal landscapes have limited access to adequate surgical abortion training. Efforts led by various organizations and providers have expanded access to abortion education, though there remains a necessity for supplemental training in the absence of direct patient care experiences. In addition, as learners travel for educational experiences, providing pre-rotation education is critical. The use of simulation training in medical education has shown improvement in skills acquisition, though abortion care simulations are limited by cost, realism, or widespread use. This project addresses these issues with a low-cost, procedurally realistic, and easily implementable task trainer.

Approach: Two board-certified Ob-Gyn physicians with extensive abortion care experience compiled a list of techniques necessary to teach resident trainees, which included paracervical block, cervical dilation, manual vacuum aspiration (MVA), dilation and curettage, and intrauterine device (IUD) placement post-abortion. A design matrix was used to evaluate fruits for use as the uterine model for first- and second-trimester abortion; dragon fruit and papaya were chosen, respectively. A preliminary model comprised of an anatomical pelvis, polyvinyl chloride (PVC) pipe, dance tights, hair ties, silicone, and fruit was created. A group of 14 Ob-Gyn residents evaluated the face validity of the task trainer. A survey was provided to each participant to assess their exposure to abortion education, confidence with abortion techniques, and feedback on the simulation. Resident feedback was compared with physician expertise to create the final model.

Lessons Learned: This low-cost 5-station model received favorable feedback from the Ob-Gyn residents. Feedback included that residents in the PGY-1 and 2 years would likely benefit most from this simulation. Junior residents demonstrated the greatest face validity improvements in perceived confidence performing an MVA and post-abortal IUD insertion, while senior residents demonstrated consistent confidence across the 5 procedures. Learners of all levels demonstrated consistent confidence performing a paracervical block and cervical dilation, likely due to previous direct patient-care interaction as these are two techniques not unique to surgical abortion. The materials for the model are readily available and affordable, making it accessible to a variety of training programs or individual learners.

Significance: This work illustrates the educational use of simulation abortion skills training. Additionally, it further demonstrates the feasibility of creating low-cost, medium-fidelity medical education simulations through the creative adaptation of everyday objects.

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BEST ORAL PRESENTATION – INNOVATIONS

Evaluation of a Health Equity Curriculum to Improve Cultural Competence With Asian American Native Hawaiian Pacific Islanders

Owen Bowie, BS; Anji Li, BSE/MSE; Iaong Vang, BS

Problem Statement: AANHPIs (Asian Americans, Native Hawaiians, and Pacific Islanders) represent 6.1% of the US population, with unique health disparities and social inequities that warrant consideration. However, there is currently limited education on AANHPI health and associated disparities within national health education. Because culturally sensitive training helps reduce health disparities and improve quality of care, our goal is to create a nationally established curriculum for health care trainees on AANHPI health.

Approach: The Health Advancement for Asian Pacific Islanders through Education (HAAPIE) curriculum was designed as the first comprehensive national curriculum on AANHPI health. It addresses AANHPI health issues through an integrative lens of history, intersectionality, and other social determinants of health. An online self-paced learning curriculum with 6 modules was developed and available to Medical College of Wisconsin affiliates. Participants completed an electronic pre- and post-survey that contained 5 domains and 69 items. The pre-survey questions were adapted from the Clinical Cultural Competency Questionnaire, a validated survey tool that measures cultural competency. Survey results were evaluated using paired t tests.

Lessons Learned: Out of 77 interested participants and pre-surveys, 60 enrolled in the curriculum (77.9%) and 22 completed post-surveys (28.6%). On a 5-point Likert scale, pre-survey results showed supportive attitudes towards the AANHPI population (mean = 4.17, SD = 0.99) and the importance of learning about this population and its health disparities (mean = 4.73, SD = 0.7). However, results also indicated a lack of training in cultural diversity (mean=1.9, SD = 1.17), little educational experience in AANHPI health (mean=2.62, SD=1.07), cultural awareness, knowledge (mean=2.98, SD=1.14), comfort in complex situations (mean=2.61, SD=1.22), and skills (mean=2.32, SD=1.08). Evaluation of the impact of the pilot curriculum showed statistically significant improvements in all fields ($P < 0.05$).

Significance: The HAAPIE initiative highlighted and addressed the need for training on AANHPI health. This novel curriculum improved attitudes, knowledge, and skills working with AANHPI populations. Future directions include analyzing the impact of curriculum modules and expanding HAAPIE across the nation.

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BEST ORAL PRESENTATION – RESEARCH

TikTok, Does it Have a Reliable Role in High Quality Nano-learning Within Medical Education?

Akua Asare, MBBS

Introduction: Nano-learning is the condensing of content into small units for learners to achieve an objective. At the forefront of this could be "TikTok." Currently, most medical students' source of information is from subscription websites like "Osmosis" and "Quesmed." These sites deliver high-quality visual information; however, it often can be lengthy and lack insight into patients' experiences. TikTok can be the free, patient-centered alternative, once its video content quality reaches that of its rivals. The aim is to elicit the ability of TikTok to advance the ways we deliver teaching or enhance self-directed learning within medical education.

Methods: Twelve peer-reviewed articles were analyzed to find common pros and cons of TikTok in regard to medical education delivery via a thematic analysis. Articles that used the DISCERN criteria (1-5 scale) for appraising the quality of consumer health videos were analyzed to produce scores quantifying the videos' informative quality.

Results: Four out of 12 studies used a form of the DISCERN criteria. Of these, scores ranged from 0.98 to 3.75 with a combined mean of 2.40, defined as poor quality educational videos. For content created by physicians, the DISCERN score was consistently higher than nonphysician-created videos. Upon thematic analysis, TikTok supports nano-learning strategies, enhances nano-activities with advanced features, and could be useful for medical students lacking patient exposure. However, videos were criticized for being superficial, the algorithm-driven timelines were a concern, and there were worries about misleading information.

Conclusions: Currently, there is "little" reliable role of nano-learning in formal learning environments in medical education as the information produced from informative medical education videos cannot be validated. Therefore, for now, nano-learning modalities--such as educational content on TikTok--are used mainly in informal learning environments. I suggest that future medical education content creators produce TikTok videos with caution and consult evidence-based resources whenever possible. Content developed for TikTok should fit the medium but also link to more in-depth learning, driving learners to more thorough, evidence-based resources grounded in educational theory.

Significance: This study provides a foundation for further research and development of TikTok as a tool for delivering high-quality medical education content.

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BEST POSTER PRESENTATION – RESEARCH

Promoting Health Literacy and Preventive Care: A Monthly Curriculum and Mobile Clinic Initiative

Manvita Mareboina, BS; Diana Orabueze, BS

Introduction: A strong foundation in health literacy is essential for individuals to make informed decisions about their health, par-

ticularly in underserved rural communities where access to health care may be limited. While this skill is built over a lifetime, it is particularly crucial to start developing it in childhood. The early years of cognitive development are an important time to introduce health literacy interventions that can establish health-related behaviors for life. Therefore, we established a partnership between the LION Mobile Health Clinic and the Centre Hall Library System to deliver a comprehensive health literacy workshop curriculum to children in the Centre County community.

Methods: The curriculum, which incorporated the health services provided by the LION Mobile Health Clinic and the reading time services offered by the Centre Hall Library, fulfilled the Pennsylvania Star Forward Program's requirements for public libraries by covering essential topics, such as sleep awareness, nutrition, exercise, and hygiene. During the implementation of the curriculum, the LION Mobile Health Clinic provided health services outside the Centre Hall Library. To assess the effectiveness of the program, pre- and post-surveys were administered to participants, which not only collected demographic information but also targeted health literacy questions.

Results: Findings suggest a significant impact of the Health Literacy Workshop curriculum on children's engagement levels. Results indicate that children remained engaged for up to two activities and were more likely to participate actively when encouraged by their parents. Moreover, surveys of parents indicated that children displayed a strong comprehension of the skills taught and effectively incorporated them into their daily routine. Participants reported enjoying the workshops and post-reading activities. Additionally, there was increased attendance and participation rates of both the Centre Hall Library system and the Pennsylvania State University College of Medicine's LION Mobile Clinic unit.

Conclusions: These findings demonstrate the efficacy of the curriculum and demonstrate the potential for public health interventions to make a meaningful impact on community health outcomes. The partnership between the mobile clinic unit and local libraries in Centre County enables us to leverage current events to boost participation and establish rapport with new communities. The participation of parents in their children's education enhances long-term retention and understanding. These tools enable us to continue refining our programs to better meet the needs of rural communities, with constant potential for collaboration between health care providers and public libraries to promote health literacy.

Significance: This innovative curriculum and approach can easily be adopted by other library systems and educational institutions to increase health literacy while making mobile care units more accessible.

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BEST POSTER PRESENTATION – INNOVATIONS

Closing the Loop: Implementing an Annual Survey to Gauge Student Feedback

Riya Shah, BS; Matthew Brennan, BS

Problem Statement: Wayne State University School of Medicine (WSUSOM) faculty and administration seek consistent, standardized feedback from students to address top student concerns. The Independent Student Analysis (ISA) survey is a comprehensive, student-led survey that provides evaluations of and recommendations for the medical education program at WSUSOM. This survey is conducted every 8 years. At the moment, there exists no regularly administered large-scale student feedback mechanism.

Approach: To establish a more consistent line of communication between students and administration, annual implementation of the ISA survey may better facilitate solutions to student concerns. Student leaders designed a shortened version of the ISA (38 questions) by determining the top priorities for student feedback. Budget allocations were determined with administration to incentivize student participation. Following survey distribution, the committee met to review and summarize the results, as well as brainstorm solutions to student concerns. The ISA Committee then compiled a summary presentation with survey results, analysis, and recommendations for administration. Following this presentation, the committee will continue to work alongside administration to tweak and implement the suggested solutions.

Lessons Learned: Nearly 80% (79.3%) of the student body responded to the ISA survey (n = 967). Of the 38 questions, students overall expressed low satisfaction (<70% combined satisfied and very satisfied) in 20 questions. The ISA Committee placed emphasis on finding solutions to the questions that received low satisfaction rates. By asking pointed free response questions, the team was able to pinpoint which areas students had the most concerns in and factor in student solutions into the final report. In general, the top 3 areas that received the most free-response comments were preclinical curriculum, communication, and clinical curriculum. As such, the team will encourage administration to focus its quality improvement measures on these priority areas. Annually gauging student satisfaction and feedback is vital to measuring the efficacy of the medical education program at WSUSOM.

Significance: There are many institutions that use student feedback surveys to maintain their quality improvement measures. However, WSUSOM is unique with this initiative being 100% student-led at our large, single-campus institution with more than 1200 students. Student feedback helps in identifying shortcomings and refining solutions.

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Sanjay Asthana, MD, FACP

Robert N. Golden, MD

Wisconsin Alzheimer's Disease Research Center—Notable Discoveries and Accomplishments in Dementia Research

Sanjay Asthana, MD, FACP; Robert N. Golden, MD

The population in the United States is aging rapidly. Currently, over 56 million Americans are older than 65, comprising 17% of the populace. By 2050, this number will increase to nearly 85 million. Much of this growth is due to the aging of Baby Boomers, who in 2030 will be aged 66 to 84—the "young old"—and will number 61 million people. At that time, those born prior to 1946—the "oldest old"—will amount to 9 million people. These individuals are vulnerable to multiple aging-associated diseases, including heart disease, cancer, stroke, dementia, and functional impairments that lead to higher morbidity and mortality compared to younger people. This will have a major impact on health care needs and expenditures.

Alzheimer's disease (AD) is the most common cause of dementia, afflicting more than 6.7 million Americans. The sixth leading cause of death in the nation, AD imposes devastating suffering and socioeconomic burdens on patients, their families, and society. The disease's neuropathologic hallmark is the deposition of amyloid and tau, two abnormally processed proteins that are deposited in parts of the brain and, over decades, lead to death of neurons and other pathologic changes that cause cognitive and functional deficits and eventual loss of life.

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Author Affiliations: Sanjay Asthana, MD, FACP, is the associate dean for gerontology; the Duncan G. and Lottie H. Ballantine Professor of Geriatrics; head of the Division of Geriatrics and Gerontology, Department of Medicine; and director of the Wisconsin Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health. Robert N. Golden, MD, is dean of the UW School of Medicine and Public Health and vice chancellor for medical affairs at UW-Madison.

The Division of Geriatrics and Gerontology in the University of Wisconsin School of Medicine and Public Health's (SMPH) Department of Medicine is renowned internationally for its innovative programs in aging and dementia research. The division is one of the largest of its kind in the United States.

The SMPH supports the National Institutes of Health (NIH)-funded Wisconsin Alzheimer's Disease Research Center (ADRC), the first geriatrics-based center of excellence in dementia research in the country. Funded continuously since 2009, the ADRC conducts state-of-the-art research across the full continuum of AD pathophysiology, including its molecular biology, epidemiology, neuroimaging and fluid biomarkers, clinical phenotype, treatment, prevention, and community-engaged and dissemination and implementation research. The ADRC also supports several cohorts involving over 1100 participants with or without dementia, and it collaborates extensively with the NIH-funded Wisconsin Registry for Alzheimer's Prevention (WRAP). Led by Sterling Johnson, PhD, professor of medicine and associate director of the ADRC, WRAP coordinates a cohort of more than 1700 participants who were cognitively unimpaired and in their early- to mid-50s when recruited to study the natural progression of AD over 20 years ago. Together, the Wisconsin ADRC and WRAP provide access to two of the largest and longest-followed cohorts of well-characterized, diverse participants, as well as datasets for cutting-edge research across the pathobiology of AD and related dementias. Findings from ADRC- and WRAP-supported studies provide novel insights into molecular mechanisms underlying AD and related dementias. These findings are directly relevant to improving patient care, enhancing quality of life, reducing caregiver stress, and decreasing health care costs.

Studies show that AD pathology starts decades before the first symptoms of the disease. This provides a unique opportunity to diagnose the disease when a person is asymptomatic and initiate treatments or prevention strategies to slow or stop progression. The Wisconsin ADRC is among the first centers in the country to identify novel brain imaging, cerebrospinal fluid (CSF), and cognitive and blood-based biomarkers of preclinical AD that could diagnose the disease early; identify patients eligible to receive newly approved, disease-modifying treatments; and help with risk prediction. Recent breakthrough AD biomarker findings from the ADRC and WRAP indicate that:

- brain white matter undergoes degeneration during preclinical stages of AD and relates to cognitive decline;
- the age of onset and duration of amyloid deposition in the brain can be estimated from PET brain imaging and blood AD biomarkers;
- presence of both amyloid and tau in the brain is associated with faster cognitive decline;
- CSF markers of neurodegeneration, such as neurogranin and neurofilament light, increase with disease severity and predict worse cognitive performance; and

- plasma levels of phosphorylated tau-217, an abnormal epitope of tau, are strongly correlated with amyloid and tau PET scans, are associated with worse cognitive trajectories, and could serve as a marker of response to treatment with emerging new therapies for AD.

AD biomarker research findings from the Wisconsin ADRC and WRAP have attracted widespread attention and noteworthy funding from the NIH. The NIH recently awarded a $150 million grant to Dr Johnson entitled "ADRC Consortium for Clarity in AD and Related Dementias Research through Imaging (CLARiTI)." The grant's overarching scientific goal is to identify multiple etiologies that commonly coexist in patients with dementia. The project will involve all 37 ADRCs across the nation and collect longitudinal magnetic resonance imaging and amyloid and tau PET brain imaging, cognitive and blood-based AD biomarker data, and consent for brain autopsies in 2000 ethnoculturally diverse participants with or without dementia. CLARiTI will provide access to extensive, leading-edge neuroimaging and biomarker data collected through harmonized protocols across the country. This will generate information concerning the heterogeneity of clinical presentations and pathology, as well as the role of coexisting pathologies in AD and related dementias.

Convincing evidence shows that health inequities and health care discrimination lead to a delay in diagnosis and treatment of AD in millions of people from underserved, underrepresented groups across the nation. Under the guidance of Carey Gleason, PhD, leader of the Inclusion of Underrepresented Groups Core, the Wisconsin ADRC is examining AD disparities through the establishment of two of the largest cohorts of African American and Native American participants in the United States. Following more than a decade of prospective study, these cohorts provide substantial research data and blood and CSF samples for collaborative research worldwide. These biospecimens and data will help examine the potential effects of race and ethnicity on AD biomarkers, cognition, and transition from presymptomatic to symptomatic stages of the disease. Preliminary findings from a National Institute on Aging-funded study (principal investigator: Carey Gleason), entitled "African Americans Fighting Alzheimer's in Midlife (AA-FAiM)," suggest that a lower plasma ratio of two abnormal forms of amyloid in African Americans is associated with cognitive decline during preclinical stages of AD.

Systematic research has provided evidence that exposure to various sociocultural, biological, and environmental factors over the life course affects risk of and resilience to AD and related dementias. Under the leadership of Amy Kind, MD, PhD, the UW Center for Health Disparities Research is among the first centers to underscore the significance of examining the potential relationship between social determinants of health—encompassing economic stability, education quality, health care access and quality, neighborhood and built environments, and social and community context—and the pathobiology of AD and related dementias. In June 2018, Dr Kind and her team published a landmark paper in the New England Journal of Medicine identifying an Area Deprivation Index (ADI) as a marker of neighborhood disadvantage and a major contributor to health inequities in the United States, including those related to AD and related dementias. Wisconsin ADRC-supported studies employing ADI suggest that:

- living in most disadvantaged neighborhoods is associated with cognitive decline and accelerated neuronal death in areas of the brain specifically affected by AD pathology;
- neighborhood disadvantage is related to the development of amyloid plaques and neurofibrillary tangles; and
- residing in poor neighborhoods is linked with lower cerebral and hippocampal volume in cognitively unimpaired people.

In 2018, under the leadership of Dr Asthana, director of the Wisconsin ADRC, the NIH funded a study entitled "Wisconsin Longitudinal Study—Initial Lifetime Impact on Alzheimer's Disease (WLS-ILIAD)." The study involves over 6000 Wisconsin high school graduates from 1957 who have been followed by the UW Department of Sociology for more than 60 years. The study's goal is to examine the potential effects of lifelong exposure to various social determinants of health on risk of and resilience to dementia. In May 2023, the study was renewed with a $50 million NIH grant to collect blood samples from 5000 participants and evaluate the possible relationship between blood-based AD biomarkers and the diagnosis of dementia, markers of disease progression, and risk of or resilience to AD and related dementias. The renewed WLS-ILIAD study is the first to evaluate the association between social determinants of health and AD and related dementias in a population-based cohort.

The foundational principle of community-engaged research is the active engagement of members of communities facing health inequities and the incorporation of their input across all stages of a study, including its design, outcome measures, recruitment, data collection, analysis, implementation, and dissemination. Under the leadership of Dr Gleason and Dorothy Edwards, PhD, the ADRC has successfully recruited large numbers of participants from underrepresented groups, fostered by the center's commitment to the principles of community-engaged research. The ADRC supports several community advisory boards, which include leaders and research participants from communities with higher prevalence, burden, and suffering from dementia. This approach has helped the ADRC design studies of direct relevance and interest to marginalized communities in Wisconsin.

The Wisconsin ADRC and its multiple affiliated studies conduct cutting-edge, impactful research across the full continuum of AD and related dementias with direct relevance to enhanced patient care. Breakthrough research from the ADRC is generating information that will expand our understanding of the molecular pathobiology and early diagnosis, treatment, and prevention of AD and related dementias, as well as the sociocultural and environmental effects on these illnesses.

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Working together, we can prevent prescription painkiller abuse in Wisconsin. Since 4 out of 5 heroin addicts start with prescription painkillers, we can also help to curb the statewide heroin epidemic. Go to DoseOfRealityWI.gov to learn what you can do to help.

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A message from Wisconsin Department of Justice, and the Wisconsin Department of Health Services

Wisconsin Department of Health Services

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