advancing the art & science of medicine in the midwest

WMJ

2026 • volume 125 • issue 3

advancing the art & science of medicine in the midwest

WMJ

CALL FOR PAPERS & REVIEWERS

Since 1903, the *Wisconsin Medical Journal—WMJ* (ISSN 2379-3961)—has served as a forum for professional communication and continuing education for physicians and other health professionals. This tradition continues today, but with a broader focus that extends across the country and even around the world.

Published six times per year through a partnership between the Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health, *WMJ* is a peer-reviewed, indexed scientific journal available electronically—free, full text online and through PubMed.

WMJ invites original research, case reports, review articles, brief reports, essays and letters to the editor about current medical and public health issues.

WMJ also seeks health care professionals who can be objective and insightful to add to our pool of highly qualified reviewers. To volunteer, sign up at www.wmjonline.org/for-reviewers/

www.wmjonline.org

Volume 125 • Issue 3 • 2026

WMJ

advancing the art & science of medicine in the midwest

COVER ART

The Weight Inside the Heart

Mubashra Waseem, MBBS

Watercolor on paper

Artist Statement:

This artwork represents the relationship between depression, poor mental health, and the heart. It also raises the question of how many diseases can take root in the heart due to poor mental health, and how deeply depression and sadness can invade it, causing significant damage.

See page 335 for information about the artist.

• • •

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

TThe *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, socio-economic, or organizational articles. All articles and artwork published herein, including commentaries, letters to the editor, and editorials represent the views of the authors, for which neither *WMJ* nor the publisher take responsibility, unless clearly stated. Advertising content is the responsibility of the advertiser and does not imply an endorsement or sponsorship by *WMJ* or the publsiher and its affiliates unless specified. *WMJ* is indexed in Index Medicus, Hospital Literature Index, and Cambridge Scientific Abstracts.

Submit manuscripts at www.wmjonline.org.

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

ISSN 1098-1861 • Established 1903

Published 6 times a year, beginning in March

When the Jar Keeps Growing

To the Editor:

Aziz and Jarjour's editorial, "When Everything Matters: Choosing What Truly Counts in Academic Medicine," offers thoughtful guidance for academic physicians navigating increasingly complex professional lives.[1] Their call for intentionality, prioritization, and aligning one's work with a deeper sense of purpose will resonate with many faculty members.

We agree that academic physicians benefit from clarity about their "big rocks." However, the essay largely frames the problem as one of individual choice. Many faculty are not overextended because they have failed to define what matters. The decision to pursue academic medicine reflects what matters most: generating and disseminating knowledge, educating future generations, and improving patient care.[2] Rather, many are overextended by institutional expectations that exceed the limits of time, energy, and human attention.

Patient care is a clear example. Academic physicians are increasingly expected to maintain clinical productivity comparable to private practice colleagues while simultaneously fulfilling academic responsibilities. Yet much of modern care occurs outside traditional productivity measures through documentation, inbox management, patient messages, and regulatory requirements. A hospital-wide survey found that academic physicians spent 24% of working hours on patient-related administrative duties, with two-thirds reporting negative effects on their ability to deliver high-quality care.[3] Much of this work remains difficult to measure but not difficult to feel.

The same is true for academic work. Teaching, mentorship, scholarship, program development, quality improvement, committee service, and contributions to professional organizations require substantial time and effort. Service contributions have been described as invisible labor that is systematically undervalued relative to research metrics such as citation indices.[4] Despite progress in recognizing clinician-educator contributions, inconsistencies remain in how academic work is valued and rewarded.[5] Scholarship often comes at the expense of personal time, as academic structures continue to reward work performed outside standard working hours.[5]

The familiar image of a jar filled with rocks, pebbles, and sand remains useful, but perhaps it no longer fully captures modern academic medicine. The jar itself has become larger and heavier. New expectations, expanding clinical demands, administrative responsibilities, and electronic work have enlarged the jar while leaving unchanged the finite hours available to fill it.

Clarity remains necessary. But clarity alone cannot solve problems created by misaligned incentives, insufficient protected time, and growing clinical and administrative demands. Perhaps the next question for academic medicine is why so many talented physicians struggle to devote time to what matters most…and whether we have designed the jar wisely in the first place.

— Jayshil J. Patel, MD; Michael J. Malinowski, MD; Manpreet S. Mundi, MD

REFERENCES

1. Aziz F, Jarjour N. When everything matters: choosing what truly counts in academic medicine. *WMJ*. 2026;125(2):235-236.

2. Bradley EA, Winchester D, Alfonso CE, et al. Physician wellness in academic cardiovascular medicine: a scientific statement from the American Heart Association. *Circulation*. 2022;146(16):e229-e241. doi:10.1161/CIR.0000000000001093

3. Rao SK, Kimball AB, Lehrhoff SR, et al. The impact of administrative burden on academic physicians: results of a hospital-wide physician survey. *Acad Med.* 2017;92(2):237-243. doi:10.1097/ACM. 0000000000001461

4. Mannix R, Bell MJ. Elevating service in academic medicine: the S-index. *JAMA*. 2025;334;(19):1707-1708. doi:10.1001/jama.2025.17221

5. Chang A, Karani R, Dhaliwal G. Mission critical: reimagining promotion for clinician-educators. *J Gen Intern Med.* 2023;38(3):789-792. doi:10.1007/s11606-022-07969-5

• • •

Author affiliations: Division of Pulmonary, Critical Care, and Sleep Medicine, Medical College of Wisconsin (MCW) Milwaukee, Wisconsin (Patel); Division of Vascular Surgery, MCW, Milwaukee, Wisconsin (Malinowski); Division of Endocrinology, Mayo Clinic, Rochester, Minnesota (Mundi).

Corresponding author: Jayshil J. Patel, MD, Associate Professor of Medicine, Medical College of Wisconsin, 8701 W Watertown Plank Road, HUB, 8th Floor, Milwaukee, WI 53226; ORCID ID 0000-0003-0663-7670

Financial disclosures: None declared.

Funding/support: None declared.

Heat Stress and Chronic Kidney Disease Among Nepali Migrant Workers: A Global Health and Climate Change Perspective

To the Editor:

Climate change is increasingly shaping patterns of human disease, and chronic kidney disease of unknown etiology (CKDu) has emerged as a sentinel example of a climate-sensitive illness.[1] First recognized among agricultural workers in El Salvador in the 1990s as Mesoamerican nephropathy, CKDu now affects individuals across India, the Middle East, Africa, and the Americas. Unlike conventional kidney disease linked to diabetes or hypertension, CKDu predominantly affects younger workers exposed to extreme heat, dehydration, and intense physical labor. Recurrent heat stress leads to repeated subclinical kidney injury that progresses to chronic kidney failure.[2]

A similar crisis is affecting migrant workers from Nepal who return from the Middle East. Every year, over 1.5 million people leave Nepal to work in the extreme heat of the Gulf region, where temperatures often hit 45 °C to 50 °C (113 °F to 122 °F). While the money they send home makes up nearly a quarter of Nepal's entire economy, occupational protections remain limited. Data suggest that over 90% of returnee migrant workers presenting with renal failure have "unknown etiology," with many requiring dialysis before age 40.[3] Similar CKDu clusters have been documented among sugarcane workers in Central America, miners, and agricultural laborers across South Asia and Africa, underscoring that this is a global climate-linked occupational disease.[3-5]

Pathophysiology is increasingly understood for every 1°C rise in WetBulb Globe Temperature (WBGT); the risk of acute kidney injury increases by approximately 18%. Recurrent heat stress, dehydration, and nonsteroidal anti-inflammatory drug (NSAID) use contribute to subclinical tubular injury and medullary hypoxia, ultimately leading to irreversible renal failure.[4] Current safeguards are inadequate, as occupational protections are often clock-based rather than WBGT-based, and migration systems lack mandatory baseline renal screening.

We propose 3 priorities: (1) awareness – recog-

continued on page 335

What AI Cannot Do: Why Human Presence Will Always Matter in Medicine

Apurva Popat, MD; Fahad Aziz, MD

Every generation of physicians believes it is witnessing the greatest technological revolution in medicine. Two centuries ago, it was the stethoscope. Today, it is artificial intelligence (AI).

In 1816, a young French physician named René Laënnec was asked to evaluate a woman with symptoms of heart disease. At the time, physicians examined the chest by placing their ear directly against the patient's body. Finding this approach awkward and uncomfortable for both physician and patient, Laënnec rolled a sheet of paper into a tube and placed one end on the patient's chest while listening through the other. To his surprise, the heart sounds were clearer than they had ever been.[1]

That simple paper tube became the prototype of the stethoscope, one of the most transformative inventions in the history of medicine. For more than two centuries, the stethoscope has symbolized the physician's craft, representing scientific advancement, diagnostic precision, and clinical expertise.

Importantly, however, the stethoscope did not replace the bedside encounter. It enhanced it.

Today, medicine stands at another technological inflection point. AI may prove to be this generation's stethoscope, a powerful tool capable of transforming how physicians gather information, interpret data, and make clinical decisions. Yet as we embrace this new technology, we must ask a fundamental question: What remains uniquely human in medicine?

> AI will undoubtedly help us diagnose disease more accurately and deliver care more efficiently, but it cannot replace human presence.

For generations, physicians were valued largely for what they knew. Medical training emphasized mastery of facts, memorization of disease processes, and recall of increasingly complex diagnostic and therapeutic algorithms. Knowledge remains essential. However, the way knowledge is acquired, organized, and applied is changing rapidly.

AI can now summarize lengthy medical records in seconds, identify patterns across vast datasets, generate differential diagnoses, explain pathophysiologic mechanisms, and synthesize medical literature at a speed unimaginable just a few years ago. These capabilities will continue to improve. Physicians who learn to work alongside AI will likely provide more efficient, informed, and data-driven care.

Yet patients do not seek physicians solely because they need information.

Patients seek physicians because they are frightened. They seek guidance when facing uncertainty, reassurance when confronting vulnerability, and wisdom when navigating difficult decisions. They seek human connection during some of the most challenging moments of their lives.

AI can process information, but it cannot sit quietly with a family receiving devastating news. It cannot recognize the subtle fear behind a patient's smile or offer comfort through presence alone. These responsibilities remain uniquely human.

Gray and colleagues remind us that one of the most powerful interventions in medicine requires neither advanced technology nor additional time – it simply requires sitting down.[2] Their work demonstrates that patients perceive physicians who sit at the bedside as spending more time with them, even when the length of the encounter is unchanged. The act is deceptively simple: pull up a chair, sit at eye level, remove physical barriers, and focus on the patient rather than the computer screen. The diagnosis, treatment plan, and duration of the visit may remain exactly the same, yet the experience is transformed.[3] Patients rarely remember their serum creatinine, troponin level, imaging findings, or medication adjustments. They remember whether they felt heard, respected, and understood. This is why etiquette-based medicine deserves

Author affiliations: Dr Popat is a *WMJ* Editorial Fellow and Cardiovascular Disease Fellow, Sanford Health, Marshfield Clinic, Marshfield, Wisconsin; Dr Aziz is *WMJ* editor in chief; associate professor, Department of Medicine, and chief, Divsion of Nephrology, University of Wisconsin School of Medicine and Public Health (UWSMPH), Madison, Wisconsin.

renewed emphasis in medical education.[4] Communication is not an innate personality trait but a clinical skill that can be taught, practiced, and refined. Simple habits – knocking before entering, introducing oneself, sitting whenever possible, maintaining eye contact, minimizing distractions, and listening without interruption – can profoundly shape the patient's experience.

Equally important is recognizing that every patient is more than a diagnosis. Conversations about family, work, fears, and personal goals often reveal insights that no laboratory value or imaging study can capture. These moments build trust and remind patients that they are people, not problems to be solved. As AI becomes increasingly integrated into health care, physicians will still need to master medical science and responsibly harness technology, but knowledge alone will no longer define excellence. The physicians who will thrive are those who combine evidence-based medicine with AI-assisted medicine while preserving the human connection through etiquette-based medicine. AI will undoubtedly help us diagnose disease more accurately and deliver care more efficiently, but it cannot replace human presence. More than two centuries after Laënnec transformed medicine with the stethoscope, the lesson remains the same: the greatest technologies do not replace the bedside, they strengthen our ability to serve those who occupy it. In the age of AI, one of the most powerful tools in medicine may still be a physician who pulls up a chair, sits down, and listens.

REFERENCES

1. Sakula A. R T H Laënnec 1781-1826 his life and work: a bicentenary appreciation. *Thorax*. 1981;36(2):81–90. doi:10.1136/thx.36.2.81

2. Gray A, Hall AM, Feldman LS. Things we do for no reason: standing at the bedside. *J Hosp Med*. 2026;21(7):801-803. doi:10.1002/jhm.70293

3. Iyer R, Park D, Kim J, Newman C, Young A, Sumarsono A. Effect of chair placement on physicians' behavior and patients' satisfaction: randomized deception trial. *BMJ*. 2023; 383:e076309. doi:10.1136/bmj-2023-076309

4. Kahn MW. Etiquette-based medicine. *N Engl J Med*. 2008;358(19):1988–1989. doi:10.1056/NEJMp0801863

"The Weight Inside the Heart"

About the Artist

Mubashra Waseem, MBBS, a recent graduate of Karachi Medical and Dental College (Karachi Metropolitan University), is a self-taught traditional artist. She enjoys blending medicine with art, using creative expression to explore and communicate complex medical concepts in a visual and engaging way.

Heat Stress and Chronic Kidney Disease Among Nepali Migrant Workers

continued from page 333

nizing CKDu as a climate-sensitive occupational disease and strengthening surveillance; (2) advocacy – integrating kidney health into climate and labor policy; and (3) accountability: enforcing WBGT-based stop-work laws and evidence-based water–rest–shade protocols. Although these patterns have been described primarily abroad, rising temperatures and frequent heat waves in the United States – including the Midwest – underscore the need for greater clinical awareness of heat-related illness and occupational health risks, especially for our agricultural and construction sectors. Health care providers and educators can contribute by raising awareness, integrating climate considerations into clinical practice and curricula, promoting research, and advocating for policies that protect vulnerable populations. Protecting manual laborers from heat-related kidney disease is both a clinical priority and an issue of climate justice. As climate change alters occupational disease patterns worldwide, the medical community must support evidence-based policies to protect vulnerable migrant workers.

—Roshan Thapa, MD; Pinky Jha, MD

REFERENCES

1. Bell ML, Gasparrini A, Benjamin GC. Climate change, extreme heat, and health. *N Engl J Med*. 2024;390(19):1793–1801. doi:10.1056/NEJMra2210769

2. Sorensen C, Garcia-Trabanino R. A new era of climate medicine: addressing heat-triggered renal disease. *N Engl J Med*. 2019;381:693–696. doi:10.1056/NEJMp1907859

3. Aryal N, Regmi PR, Sedhain A, et al. Chronic kidney risk among Nepalese migrant workers in the countries of Gulf and Malaysia: a population-based cross-sectional survey in Nepal. *MedRxiv*. Preprint posted online May 22, 2025. doi:10.1101/2025.05.15.25327703

4. Elinder CG. Heat-induced kidney disease: understanding the impact. *J Intern Med*. 2025;297(1):101–112. doi:10.1111/joim.20037

5. García-Trabanino R, Jarquín E, Wesseling C, et al. Heat stress, dehydration, and kidney function in sugarcane cutters in El Salvador-- A cross-shift study of workers at risk of Mesoamerican nephropathy. *Environ Res*. 2015;142l765-746. doi:10.1016/j.envres.2015.07.007

• • •

Author affiliations: Department of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin (Jha, Thapa).

Corresponding author: Roshan Thapa, MD, MS, 8701 Watertown Plank Rd, Milwaukee, WI 53226; email rosthapa@mcw.edu; ORCID ID 0009-0002-8162-4204

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgments: This work was presented at the Healthy Wisconsin Climate Conference on November 15, 2025, in De Pere, Wisconsin.

Trees as Health Care Partners in Wisconsin

Kirsten M. M. Beyer, PhD; Jason Dampier, PhD; Olivia Witthun, BS

Wisconsin's natural beauty abounds, and the state has long recognized the interconnectedness of nature and human well-being – a legacy carried forward by Aldo Leopold. Leopold, author of *A Sand County Almanac* and professor of wildlife ecology at the University of Wisconsin, is regarded as a pioneer of modern conservation. He developed the "land ethic," a philosophy that extends the idea of community beyond people to include "soils, waters, plants, and animals – the land."[1] Since Leopold's time, we have learned much about nature and human interconnectedness. Harvard Biologist E.O. Wilson coined the term "biophilia" to capture this interconnectedness: simply put, biophilia is the love of life or love of other living organisms.[2] We are drawn to nature, to majestic landscapes, bucolic scenery, and its components – the animals, the plants, the trees. But can this lead to better human health outcomes?

With "land ethic" and "biophilia" as frameworks, scientists have examined how nature (and trees specifically) affect human health. Wolf et al conducted a comprehensive scoping review of more than 200 studies investigating the effects of urban trees on human health;[3] grouping these benefits in 3 domains. *Reducing Harm* describes how vegetation can lessen harmful environmental conditions, including exposure to air pollution, extreme heat, and crime. *Restoring Capacities* describes how time spent in natural environments supports psychological and physiological well-being through benefits such as improved cognitive function, stress reduction, and clinical outcomes. *Building Capacities* describes how experiences in nature support individual and community wellness through active living and social connections. Across these domains, the review clearly indicates that exposure to urban forests is associated with positive health outcomes. Similar findings have been reported in Wisconsin, where studies have demonstrated potential benefits for mental health, sleep, active transportation, and cardiovascular health.[4-7] In another recent review, Rosa et al specifically investigated the treatment of depression using forests therapeutically and found that "compared to antidepressants, similar activities in a hospital or a non-forested urban setting, or even diet and forest-based exercise, *forest therapy appears to be more likely to produce outcomes like remission and response to treatment, with adequate acceptability or adherence"* (emphasis added).[8]

How might health care organizations harness this knowledge for improved health outcomes? Based on the available evidence, investing in trees and natural features on Wisconsin's health care campuses could have a wide range of benefits for patients, staff, and communities.[3,8,9] A new benchmark offers a clear target for action. The 3-30-300 benchmark challenges organizations to ensure that there are 3 established trees visible from every building, 30% tree canopy cover in every neighborhood, and that no one is more than a 300 meter walk to a park or other green space.[10] In addition, the Arbor Day Foundation's Tree Campus Healthcare program guides health care organizations to invest in their campuses' trees and recognizes them for their accomplishments. According to an email on May 12, 2025 from Dayna Berry, program manager for Tree Campus, the program recognized 59 health care campuses across 18 states, with Wisconsin leading the nation with 20 campuses. Despite this leadership, opportunities for participation remain, given that approximately 150 hospi-

...investing in trees and natural features on Wisconsin's health care campuses could have a wide range of benefits for patients, staff, and communities.

Author affiliations: Institute for Health and Humanity, Medical College of Wisconsin, Milwaukee, Wisconsin (Beyer); Division of Forestry, Wisconsin Department of Natural Resources, Wautoma, Wisconsin (Dampier); Division of Forestry, Wisconsin Department of Natural Resources, Oshkosh, Wisconsin (Witthun).

Corresponding author: Kirsten Beyer, PhD, 8701 Watertown Plank Rd, Milwaukee, WI 53226; email kbeyer@mcw.edu; ORCID ID 0000-0002-7513-852

tals and health systems operate in Wisconsin.[11] Participating campuses commit to improving community wellness through tree education, investment, and community engagement. Achieving Tree Campus Healthcare recognition demonstrates a health care organization's commitment to promoting health beyond the clinic walls by investing in a healthier environment that supports the well-being of patients, staff, visitors, and communities.

To further understand the program, information was obtained through personal communication on August 20, 2025, with Jimmy Parilek, senior program manager for system facilities management and sustainability at Aspirus Health. Aspirus has demonstrated leadership in Wisconsin and nationally, with 13 designated campuses in Wisconsin, 2 in Minnesota, and 3 in Michigan. Parilek emphasized that the program aligns with broader organizational values, including doing the right thing for Wisconsin's communities and creating inviting campuses for patients, visitors, and staff to enjoy, seek respite, and remember fondly. He stated, "Our mission of healing people, promoting health, and strengthening communities really ties into this … continuing our path forward and evolving our sustainability program, as well as helping those around us" (Zoom, August 20, 2025). According to Parilek, this mission directly supports the continued evolution of the organization's sustainability initiatives. He emphasized the importance of giving patients something beautiful to look at while they go through the healing process. In addition, he described benefits for staff, ranging from the pride facilities teams take in beautifying the grounds, to excitement for events, including tree giveaways where all available saplings were distributed within an hour.

Given the operational demands of health care settings, questions were raised regarding whether maintaining such a program poses challenges. Parilek acknowledged that keeping things up and running can create challenges, but there was no question about moving forward: "We're going to continue those things moving forward … everybody here at the organization was excited that all 18 hospitals were able to receive that Tree Campus designation … it was really awesome to see everybody come together to want to achieve that. From the executive level all the way down, we're all looking for ways that we can help the environment" (Zoom, August 20, 2025). He noted strong organizational support across multiple levels. For health care organizations considering the program or related efforts on greening and sustainability, Parilek emphasized the widespread availability of resources, including the Arbor Day Foundation and Practice Green Health, as well as potential financial and technical assistance through state-level programs such as the Wisconsin Department of Natural Resources (DNR) Urban Forestry Grant Program. The DNR offers a range of forestry grants, including both regular ($25,000) and startup ($5000) grants.[12]

The 3-30-300 benchmark and Tree Campus program offer tangible goals and support for achieving them. Implementation can begin with feasible actions such as improving visible tree cover, improving access to nearby green spaces, and integrating trees into planned site improvements and redevelopment projects. Partnerships with municipal forestry programs, nonprofit organizations, and grant-supported initiatives may help reduce technical and financial barriers. Based on the available evidence, health care campuses may realize improved health outcomes by reaching these goals. Which campus in Wisconsin will be the next to find out?

Acknowledgments: Thanks to Jimmy Parilek at Aspirus Health for sharing his perspective, Dayna Berry at the Arbor Day Foundation for confirming data on Tree Campus Healthcare participation numbers by state, and to members of Wisconsin's Urban Forestry Council for their ongoing support.

Funding/support: None declared.

Financial disclosures: None declared.

REFERENCES

1. The Land Ethic®. The Aldo Leopold Foundation. Updated 2025. Accessed August 20, 2025. https://www.aldoleopold.org/about/the-land-ethic

2. Wilson EO. Biophilia. Harvard University Press; 1986.

3. Wolf KL, Lam ST, McKeen JK, Richardson GRA, van den Bosch M, Bardekjian AC. Urban trees and human health: a scoping review. *Int J Environ Res Public Health.* 2020;17(12):4371. doi:10.3390/ijerph17124371

4. Beyer KM, Kaltenbach A, Szabo A, Bogar S, Nieto FJ, Malecki KM. Exposure to neighborhood green space and mental health: evidence from the survey of the health of Wisconsin. *Int J Environ Res Public Health.* 2014;11(3):3453-3472. doi:10.3390/ijerph110303453

5. Tsai WL, Yngve L, Zhou Y, et al. Street-level neighborhood greenery linked to active transportation: a case study in Milwaukee and Green Bay, WI, USA. *Landsc Urban Plan.* 2019;191:103619. doi:10.1016/j.landurbplan.2019.103619

6. Johnson BS, Malecki KM, Peppard PE, Beyer KMM. Exposure to neighborhood green space and sleep: evidence from the Survey of the Health of Wisconsin. *Sleep Health*. 2018;4(5):413-419. doi:10.1016/j.sleh.2018.08.001

7. Cheruvalath H, Homa J, Singh M, Vilar P, Kassam A, Rovin RA. Associations between residential greenspace, socioeconomic status, and stroke: a matched case-control study. *J Patient Cent Res Rev*. 2022;9(2):89-97. doi:10.17294/2330-0698.1886

8. Rosa CD, Larson LR, Collado S, Profice CC. Forest therapy can prevent and treat depression: evidence from meta-analyses. *Urban For Urban Green.* 2021;57:126943. doi:10.1016/j.ufug.2020.126943

9. Bikomeye JC, Namin S, Anyanwu C, et al. Resilience and equity in a time of crises: investing in public urban greenspace is now more essential than ever in the US and beyond. *Int J Environ Res Public Health.* 2021;18(16):8420. doi:10.3390/ijerph18168420

10. Konijnendijk CC. Evidence-based guidelines for greener, healthier, more resilient neighbourhoods: introducing the 3-30-300 rule. *J For Res (Harbin).* 2023;34(3):821-830. doi:10.1007/s11676-022-01523-z

11. Hospital member directory. Wisconsin Hospital Association. Updated 2026. Accessed January 10, 2026. https://www.wha.org/about-wha/wisconsin-hospital-finder/hospital-member-directory

12. Wisconsin Department of Natural Resources. Urban Forestry Grants. Accessed January 10, 2026. https://dnr.wisconsin.gov/topic/urbanforests/grants

The Health and Environmental Costs of Artificial Intelligence

Caidon Iwuagwu, BS; Abby Novinska-Lois, MPH; Joanne Bernstein, MD, MSE

Generative artificial intelligence (AI) has rapidly integrated into everyday life, offering immediate assistance with tasks ranging from composing emails to generating personalized recommendations. Its utility is undeniable, streamlining communication, increasing efficiency, and supporting decision-making across disciplines, including medicine. However, this convenience is not without consequence. Each AI-generated query, document, or image carries an often-overlooked environmental and public health cost that warrants critical attention from the health care and scientific communities.

For the first time in decades, national energy demand is increasing. This is largely driven by data centers used for AI computing. By 2028, AI-related energy use is projected to equal the amount needed to power 22% of US households annually, despite technology efficiency gains.[1] Closer to home, in Mount Pleasant, Wisconsin, Microsoft's new data center could require the same energy needed to power 300000 homes, surpassing the number of homes in the cities of Milwaukee or Madison.

• • •

Author affiliations: Medical College of Wisconsin, Milwaukee, Wisconsin (Bernstein, Iwuagwu); Healthy Climate Wisconsin, Madison, Wisconsin (Novinska-Lois); Zablocki VA Medical Center, Milwaukee, Wisconsin (Bernstein).

Corresponding author: Caidon Iwuagwu; email ciwuagwu@mcw.edu; ORCID ID 0009-0008-2250-9891

To meet this demand, utilities – including We Energies, Wisconsin's largest electric utility – are proposing new fossil fuel power plants. Air pollution from fossil fuels is well-documented to exacerbate asthma, cardiovascular disease, and premature mortality, all while driving climate change. One proposed plant in Oak Creek, Wisconsin, alone is estimated to impose up to $144.8 million annually in health-related costs, in addition to higher electricity bills to cover the cost of the facility.[2] This coincides with increasingly severe climate-related events in Wisconsin. For example, smoke from the 2023 Canadian wildfires resulted some of the poorest air quality measurements in the world. Smoke returned to Wisconsin in July 2025, when Milwaukee, Beloit, Rhinelander, Madison, Waukesha, and Green Bay accounted for 6 of the 10 US cities with the most hazardous air quality. Shortly thereafter, historic floods in Milwaukee destroyed 51 homes and caused an estimated $76 million in damages. It is clear that Wisconsin residents are already experiencing the health effects of climate change, and soon, the rapid growth of AI-related energy demand may further exacerbate these effects.

> Each AI-generated query, document, or image carries an often-overlooked environmental and public health cost that warrants critical attention from the health care and scientific communities.

Beyond air pollution, AI's infrastructure consumes vast quantities of water for cooling servers. To generate just eight short emails, a large language model like ChatGPT-4 requires 4.15 L (approximately 1 gallon) of potable water. Multiplied across more than 1 billion daily queries, the collective toll is staggering. In 2021, Google data centers in The Dalles, Oregon, consumed more than 355 million gallons of water, representing more than one-quarter of the city's annual water consumption. Additionally, an estimated 20% of data centers rely on watersheds that are already moderately to highly stressed.[3] Because current cooling technologies rely mostly on potable water, it's no surprise that the Great Lakes region is becoming a target for data center expansion. With the Great Lakes water levels lowering in recent years, partly because of climate-related factors, Wisconsin residents will need to carefully consider how much to risk this valuable resource.

Data center development also raises questions of equity in resource allocation and environmental justice. Proposed facilities are often where land may be less expensive and regulatory oversight weaker. These areas

can be both rural, such as Caledonia where a proposed data center would have required approximately 244 acres currently used for agriculture, or urban, such as Port Washington, which will house the nation's largest data center and require power consumption equivalent to that of Los Angeles, the nation's second-largest city. However, in Caledonia, Microsoft withdrew its proposal there in late 2025 after sustained local opposition, demonstrating that people coming together can still change the course of these projects.

Although water stress depends on where a data center sits, the fossil-fuel emissions required to power these centers originate at power plants scattered across Wisconsin. In addition to the global climate effects of carbon dioxide, these plants release mercury, fly ash, and other particulates and carcinogens that have localized health effects, worsening asthma, cardiovascular disease, and cancer risk.[4] These exposures exacerbate existing health disparities and place both rural and urban residents at risk, even when the data center itself is miles away. The growing footprint of these facilities, along with their consumption of shared natural resources, forces a deeper reckoning with who benefits from AI infrastructure and who bears its costs.

Nonprofit and for-profit initiatives signal recognition of the problem, but their impact is limited. The National Academies convened experts across fields to form the Roundtable on Artificial Intelligence and Climate Change to foster collaboration; however, whether or not this think tank will result in tangible outcomes, such as policy or technological innovation, is unclear.[5] As communities push back against proposed projects, companies are increasingly trying to distance themselves through greenwashing – a tactic to appear environmentally responsible to deter public outrage and regulation, but with limited implementation plans or failure to address the full scope of the problem. For example, Google now discloses site-level water use and promises to replenish 120% of its consumption by 2030. However, its data is self-reported, and data centers often use village and municipal water supplies to avoid more trackable and transparent water permits. Additionally, the Green Software Foundation, a collaboration that includes Microsoft, promotes "carbon-aware" computing allowing AI tasks to be timed or moved to places where cleaner energy – such as solar or wind – is more available. However, overall, these approaches are distant, rely on questionable offsets, and do little to decarbonize the electrical grid as a whole.

As stewards of public health, health care professionals must engage in paving the path forward. We can help educate the public and advocate for accountability among developers and policymakers. We can also advocate for renewable energy and solutions that optimize resource use justly, closing health disparities rather than widening them. One starting point is engaging collectively through state organizations already working on this issue, such as Healthy Climate Wisconsin. Additionally, those of us using AI can adopt more intentional usage patterns by limiting nonessential queries and recognizing the hidden costs associated with convenience. As AI continues to expand, it's clear that the path to a sustainable, health future must include widespread regulation of the technology sector to protect communities from rising energy bills, adverse health effects, and environmental harms. The growing climate crisis also requires that we also collectively ask ourselves tough and uncomfortable questions, including whether convenience is truly worth the consequences.

Funding/support: None declared.

Financial disclosures: None declared.

Acknowledgements: The opinions reflect those of the authors and should not, in any way, be construed to reflect those of the Department of Veterans Affairs or the US government.

REFERENCES

1. O'Donnell J, Crownhart C. We did the math on AI's energy footprint. Here's the story you haven't heard. *MIT Technology Review.* Published May 20, 2025. Accessed June 12, 2025. https://www.technologyreview.com/2025/05/20/1116327/ai-energy-usage-climate-footprint-big-tech/

2. Healthy Climate Wisconsin. New analysis details the public health impacts of proposed gas plants in Wisconsin. Published January 16, 2025. Updated January 27, 2025. Accessed June 12, 2025. https://www.healthyclimatewi.org/post/new-analysis-details-the-public-health-impacts-of-proposed-gas-plants-in-wisconsin

3. Ahmad R. Engineers often need a lot of water to keep data centers cool. American Society of Civil Engineers. Published March 4, 2024. Accessed June 12, 2025. https://www.asce.org/publications-and-news/civil-engineering-source/civil-engineering-magazine/issues/magazine-issue/article/2024/03/engineers-often-need-a-lot-of-water-to-keep-data-centers-cool

4. United States Environmental Protection Agency. Human health and environmental impacts of the electric power sector. Updated December 12, 2025. Accessed June 12, 2025. https://www.epa.gov/power-sector/human-health-environmental-impacts-electric-power-sector

5. National Academies of Sciences, Engineering, and Medicine. *Implications of Artificial Intelligence–Related Data Center Electricity Use and Emissions: Proceedings of a Workshop.* National Academies Press; 2025. doi:10.17226/29101

Prox1: A Novel Barrier to Retinal Regeneration and a Potential Target for Vision Restoration

Manahil Mubeen, MBBS; Syeda Neha Ahmed, MBBS; Hania Rizwan, MBBS; Karan Bansari, MBBS; Hassan Saleem, MBBS

Irreversible vision loss resulting from retinal ganglion cell degeneration, such as that occurring in glaucoma, optic neuropathies, and retinitis pigmentosa, continues to present profound clinical challenges. Globally, more than 80 million individuals are affected by glaucoma alone,[1] with projections rising to 111.8 million by 2040,[2] making retinal nerve damage one of the leading causes of irreversible blindness. Similarly, macular degeneration affects approximately 8.7% of the global population, with the number of affected individuals expected to increase from approximately 196 million in 2020 to 288 million by 2040.[3] This growing burden underscores the need for regenerative strategies for retinal neurodegenerative diseases.

Current therapies, such as intraocular pressure-lowering treatments and neuroprotective agents, can slow disease progression but cannot regenerate lost retinal ganglion cells or reverse established neural damage. Mammalian retinas lack significant endogenous regenerative capacity because Müller glia (MG), the retina's intrinsic support cells with latent progenitor potential, fail to reenter the cell cycle and differentiate into neurons after injury because of epigenetic and signaling constraints.[4] In contrast, zebrafish and amphibians mount robust MG-mediated regenerative responses through neurogenic pathways such as Wnt/β-catenin and Ascl1a/Dkk signaling.[5-7]

Globally, more than 80 million individuals are affected by glaucoma alone...Similarly, macular degeneration affects approximately 8.7% of the global population...This growing burden underscores the need for regenerative strategies for retinal neurodegenerative diseases.

Recent advances identify Prospero-related homeobox 1 (Prox1), a homeodomain transcription factor critical for neural development and lymphatic endothelial differentiation, as a novel extracellular barrier to retinal regeneration in mammals.[4] In mammalian retinal injury models, Prox1 protein accumulates in MG through intercellular transfer from neighboring retinal interneurons (bipolar and amacrine cells) and suppresses MG proliferation and reprogramming into retinal progenitor cells, thereby arresting the regenerative response.[1,4,8] Recent studies have restored MG proliferative capacity and differentiation into retinal neurons, including photoreceptors and retinal ganglion cell-like cells, by blocking Prox1 transfer using an anti-Prox1 nanobody delivered via an adeno-associated virus (AAV) vector. This intervention delayed vision loss in murine retinitis pigmentosa models, highlighting Prox1 as a promising therapeutic target for overcoming intrinsic regenerative barriers in the mammalian retina.[1] Below, we examine Prox1 as a potential therapeutic target for retinal regeneration and advocate for increased translational research focused on this novel regenerative strategy.

Müller Glia and Retinal Regeneration

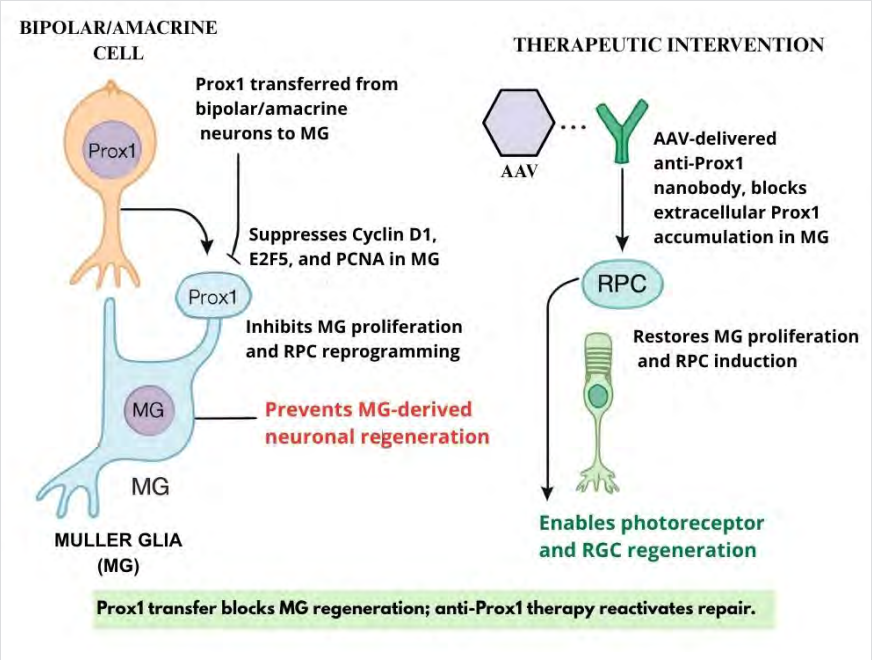
MG are radial glial cells that span the entire thickness of the vertebrate retina and provide structural support, neurotransmitter recycling, osmotic balance, and metabolic support to retinal neurons. Retinal regeneration requires MG activation, dedifferentiation, proliferation, and generation of progeny capable of neuronal differentiation and integration into circuits to restore vision.[6] Uniquely, MG in cold-blooded vertebrates dedifferentiate in response to injury, downregulate glial markers, upregulate

Author affiliations: Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan (Mubeen); Karachi Medical and Dental College, Karachi, Pakistan (Ahmed); Jinnah Sindh Medical University, Karachi, Pakistan (Rizwan); Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan (Bansari); Rashid Latif Medical College, Pakistan (Saleem).

Corresponding author: Manahil Mubeen, Baba-E-Urdu Road, Karachi 74200, Pakistan; email manahilmubeen4751@gmail.com; ORCID ID 0009-0002-6211-9114

progenitor genes such as *Pax6* and *Ascl1a*, reenter the cell cycle, and generate MG-derived progenitor cells that proliferate and differentiate into lost neuronal subtypes.[8] In zebrafish, injury activates Wnt, Notch, Shh, Fgf, HB-EGF, and Yap/Taz pathways to drive progenitor cell proliferation and complete retinal regeneration.[7] Avian MG can partially reprogram after excitotoxic damage and persist as undifferentiated progenitors for weeks, unless they are supplemented with exogenous factors.[5] By contrast, mammalian MG are unable to spontaneously reprogram after retinal injury without transgenic manipulation or growth factor stimulation. For example, MG in the mouse retina can migrate to sites of injury and upregulate the retinal progenitor cell marker Pax6, but they do not fully reenter the cell cycle or undergo neurogenesis, suggesting incomplete activation of regenerative gene expression programs and the presence of intrinsic inhibitory mechanisms that limit endogenous regeneration.[5,8]

Figure. Prox1-Mediated Suppression and Reversal of Müller Glia Neurogenesis



Abbreviation: Prox1, Prospero-related homeobox 1.

Prox1 as a Barrier to Regeneration

Prox1 is a homeodomain transcription factor with well-documented roles in neuronal differentiation and cell fate determination in the central nervous system and retina.[4,9-11] In vertebrates, it is essential for lymphatic endothelial identity and the development of specific neuronal lineages, including horizontal interneurons, and plays important regulatory roles in MG differentiation. However, its accumulation in MG after retinal injury acts as a regenerative blockade.[9] Notably, Prox 1 undergoes intercellular transfer from neighboring neurons into MG rather than being produced through endogenous transcription, creating a barrier to glia-to-progenitor conversion and representing a rare example of a transcription factor functioning in a non-cell-autonomous manner.[4] Within MG, Prox1 suppresses Cyclin D1, E2F5, and PCNA, enforcing G1-phase cell-cycle arrest. Moreover, it blocks activation of proneural factors and represses progenitor markers, including *Hbegf* and *Gadd45a*, thereby maintaining MG in a quiescent, gliotic state.[4,11]

Given this role, genetic disruption or experimental blockade of Prox 1 transfer using AAV-mediated delivery of a secreted anti-Prox1 single-chain antibody reduces MG Prox1 levels, restores MG proliferation, induces expression of retinal progenitor markers (*Hes1*, *Notch1, Gadd45a*, *Hbegf*), and generates nascent photoreceptors and bipolar cells, as demonstrated by EdU incorporation and single-cell RNA sequencing (scRNA-seq).[4] In murine models of N-methyl-N-nitrosourea-induced retinal injury and genetic retinitis pigmentosa (eg, rd10 models), anti-Prox1 therapy increased outer nuclear layer thickness, reduced Prox1 protein levels by 60% within 2 weeks, increased MG progenitor cell proliferation and generation of rhodopsin-positive photoreceptors by 45% compared with controls, enhanced scotopic electroretinogram amplitudes by 30 µV, and improved visual acuity by 20% during early disease stages.[4,11] Although AAV vector silencing reduced long-term therapeutic efficacy, this approach leverages the resident MG population and may reduce immunogenicity and cellular integration challenges associated with exogenous stem cell therapies while allowing cell type-specific modulation through minimally invasive delivery.[12] The Figure illustrates the inhibitory effects of Prox1 transfer on MG regeneration and the restoration of regenerative activity following anti-Prox1 therapy.

Translational Opportunities and Challenges

Despite strong proof-of-concept data in murine models, translational research remains in its infancy. No human retinal tissue or retinal organoid studies have yet validated Prox1-mediated regeneration. Translating these findings into clinical reality will require careful evaluation of species-specific differences in retinal architecture and biology. Key challenges include validating Prox1-dependent mechanisms in human retinal explants or organoid systems, as sex-based differences, divergent gene expression profiles, and distinct signaling pathways may influence the role of Prox1 in human retinal tissue.

Safety concerns for clinical translation include uncontrolled MG proliferation resulting from overactivation or impaired regulation of MG progenitor cells, potentially leading to disorganized tissue growth, retinal gliosis, ectopic tissue formation, or tumorigenesis.[3,5] These risks may be mitigated through tightly controlled, transient gene expression systems[11] that limit proliferation once differentiation is achieved. In addition, viral vector delivery can elicit retinal immune responses and inflammation, particularly at high AAV viral loads.[10] This

challenge may be addressed through the alternative AAV serotypes and engineered capsids designed to enhance tropism and transduction efficiency at lower, safer doses.

Another major concern is aberrant differentiation or off-target effects, in which MG-derived progenitor cells generate inappropriate neuronal subtypes or integrate abnormally into retinal circuits.[9] Long-term functional and structural assessments, including electroretinography and optical coherence tomography, can confirm the stability, specificity, and synaptic integration of newly generated neurons. Complementary histological and molecular analyses could further verify neuronal lineage fidelity and circuit connectivity.

Long-term vector expression and specificity also remain unresolved challenges. AAV vector silencing has been shown to reduce the durability of transgene expression, potentially through host-mediated DNA methylation or histone modification, resulting in epigenetic silencing of vector genomes.[13] Several alternative delivery strategies may help overcome these limitations. Lentiviral vectors, for example, offer sustained expression through stable genomic integration and have demonstrated prolonged retinal gene expression, although insertional mutagenesis remains a concern.[14] Nonviral platforms, including lipid nanoparticles, offer potentially safer and repeatable delivery options and are already being evaluated for retinal applications.[15] In addition, next-generation engineered AAV capsids, such as AAV2.7m8 and AAV9-PHP.B, demonstrate improved retinal tropism, reduced interaction with neutralizing antibodies, and enhanced transgene persistence.[16] Incorporation of regulatory DNA elements, including ubiquitous chromatin-opening elements and CpG-depleted promoters, may further mitigate epigenetic silencing and prolong vector activity.[17] Collectively, improving vector durability, safety, and specificity will be critical to advancing clinical translation. Human retinal organoid models, improved AAV capsid designs, alternative delivery routes such as suprachoroidal administration, and combinatorial regenerative approaches are essential to advance clinical relevance.[4]

Conclusions

The growing global burden of irreversible retinal neurodegeneration highlights the urgent need for novel regenerative strategies. The identification of Prox1 as a key inhibitor of MG-driven retinal regeneration provides a promising target for promoting intrinsic retinal repair. Preclinical studies in murine models demonstrate that blockade of extracellular Prox1 can restore MG regenerative capacity, promote neuronal replacement, and preserve visual function. To translate these findings into clinical practice, further research is needed to validate underlying mechanisms in human systems, refine gene delivery platforms, and establish long-term safety. Continued collaborative investigation of Prox1-targeted therapies may ultimately expand treatment options for glaucoma, inherited retinal dystrophies, and retinitis pigmentosa, conditions historically associated with irreversible vision loss – offering hope to millions affected by retinal nerve degeneration.

Funding/support: None declared.

Financial disclosures: None declared.

REFERENCES

1. Shan S, Wu J, Cao J, et al. Global incidence and risk factors for glaucoma: a systematic review and meta-analysis of prospective studies. *J Glob Health*. 2024;14:04252. doi:10.7189/jogh.14.04252

2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121(11):2081-2090. doi:10.1016/j.ophtha.2014.05.013

3. Wong WL, Su X, Li X, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *Lancet Glob Health*. 2014;2(2):e106-e116. doi:10.1016/S2214-109X(13)70145-1

4. Lee EJ, Kim M, Park S, et al. Restoration of retinal regenerative potential of Müller glia by disrupting intercellular Prox1 transfer. *Nat Commun*. 2025;16(1):2928. doi:10.1038/s41467-025-58290-8

5. Todd L, Reh TA. Comparative biology of vertebrate retinal regeneration: restoration of vision through cellular reprogramming. *Cold Spring Harb Perspect Biol*. 2022;14(6):a040816. doi:10.1101/cshperspect.a040816

6. Taylor OB, El-Hodiri HM, Palazzo I, Todd L, Fischer AJ. Regulating the formation of Müller glia-derived progenitor cells in the retina. *Glia*. 2025;73(1):4-24. doi:10.1002/glia.24635

7. Lenkowski JR, Raymond PA. Müller glia: Stem cells for generation and regeneration of retinal neurons in teleost fish. *Prog Retin Eye Res*. 2014;40:94-123. doi:10.1016/j.preteyeres.2013.12.007

8. Ramachandran R, Zhao XF, Goldman D. Ascl1a/Dkk/beta-catenin signaling pathway is necessary and glycogen synthase kinase-3beta inhibition is sufficient for zebrafish retina regeneration. *Proc Natl Acad Sci U S A*. 2011;108(38):15858-15863. doi:10.1073/pnas.1107220108

9. Grigoryan EN. Cell Sources for retinal regeneration: implication for data translation in biomedicine of the eye. *Cells*. 2022;11(23):3755. doi:10.3390/cells11233755

10. Hoang T, Wang J, Boyd P, et al. Gene regulatory networks controlling vertebrate retinal regeneration. *Science*. 2020;370(6519):eabb8598. doi:10.1126/science.abb8598

11. Dyer MA, Livesey FJ, Cepko CL, Oliver G. Prox1 function controls progenitor cell proliferation and horizontal cell genesis in the mammalian retina. *Nat Genet*. 2003;34(1):53-58. doi:10.1038/ng1144

12. Pavlou M, Probst M, Kaplan L, et al. AAV-mediated expression of proneural factors stimulates neurogenesis from adult Müller glia in vivo. *EMBO Mol Med*. 2025;17(4):722-746. doi:10.1038/s44321-025-00209-3

13. Das A, Vijayan M, Walton EM, Stafford VG, Fiflis DN, Asokan A. Epigenetic silencing of recombinant adeno-associated virus genomes by NP220 and the HUSH complex. *J Virol*. 2022;96(4):e0203921. doi:10.1128/JVI.02039-21

14. Arsenijevic Y, Berger A, Udry F, Kostic C. Lentiviral vectors for ocular gene therapy. *Pharmaceutics*. 2022;14(8):1605. doi:10.3390/pharmaceutics14081605

15. Chambers CZ, Soo GL, Engel AL, et al. Lipid nanoparticle-mediated delivery of mRNA into the mouse and human retina and other ocular tissues. *Transl Vis Sci Technol*. 2024;13(7):7. doi:10.1167/tvst.13.7.7

16. Dalkara D, Byrne LC, Klimczak RR, et al. In vivo-directed evolution of a new adeno-associated virus for therapeutic outer retinal gene delivery from the vitreous. *Sci Transl Med*. 2013;5(189):189ra76. doi:10.1126/scitranslmed.3005708

17. Zhang F, Frost AR, Blundell MP, Bales O, Antoniou MN, Thrasher AJ. A ubiquitous chromatin opening element (UCOE) confers resistance to DNA methylation-mediated silencing of lentiviral vectors. *Mol Ther*. 2010;18(9):1640-1649. doi:10.1038/mt.2010.132

Addressing Burnout Among Emergency Services Professionals Through Patient Follow-up: An Exploratory Study

Jacqueline Christianson, PhD, FNP-C; Tiffany Warthon, BA; Tala Fuad Hatem Abu Zahra, PhD, RN; Robyn Cicero, BSN, RN; Stuart Matthias, BS

ABSTRACT

Introduction: Emergency services professionals (eg, emergency medical technicians, paramedics, and emergency department registered nurses) work in high-stress, low-resource environments and are consequently vulnerable to burnout. Additionally, many lack opportunities to learn patient outcomes, which may contribute to dissatisfaction or uncertainty regarding their role in the patient care.

Objectives: This study evaluated the feasibility, acceptability, appropriateness and estimated the effect size of a patient follow-up program implemented in a rural Wisconsin service area among both prehospital and emergency department-based emergency services professionals on burnout, compassion satisfaction, secondary traumatic stress, and job satisfaction.

Methods: Participants were provided follow-up summaries for patients they cared for over a 12-week period. Feasibility, acceptability, and appropriateness were measured using a validated instrument and free-text responses analyzed via content analysis after the intervention. Burnout, compassion satisfaction, and secondary traumatic stress were measured using the Professional Quality of Life Scale, and job satisfaction was measured using 2 items from the Satisfaction of Employees in Health Care survey, administered before and after the intervention.

Results: Forty-one participants enrolled in the study. They rated feasibility, acceptability, and appropriateness highly. The majority reported that patient follow-up summaries were valuable and provided clinically useful information that supported their practice.

Conclusions: Patient follow-up summaries are valued by emergency services professionals and provide opportunities to learn from patient outcomes.

• • •

Author affiliations: Marquette University College of Nursing, Milwaukee, Wisconsin (Christianson, Warthon); CoxHealth Medical Center, Springfield, Missouri (Abu Zahra); Tamarack Health, Ashland, Wisconsin (Cicero); Ashland Fire Department, Ashland, Wisconsin (Matthias).

Corresponding author: Jacqueline Christianson, PhD, Marquette University College of Nursing, PO Box 1881, Milwaukee WI, 53201; email jacqueline.christianson@marquette.edu; ORCID ID 0000-0001-7149-4587

INTRODUCTION

Emergency services professionals (eg, emergency medical technicians [EMTs], paramedics, and emergency department [ED] registered nurses) work in high-stress, low-resource environments and are frequently exposed to unsafe situations. The Wisconsin workforce shortage, particularly among prehospital professionals and in rural areas, is critical: over the past decade, more than two-thirds of the emergency medical services (EMS) workforce has left, and more than 40% of Wisconsin EMS agencies report periods during which they could not respond to calls.[1] Patients in rural areas are often chronically underserved due to a paucity of health care resources, including subspecialty care and adequate staffing.[2,3] Longer patient wait times are associated with increased risk of morbidity and mortality.[4,5] Additionally, health care workers in rural or underresourced emergency settings may be more likely to perceive discontinuity in patient care or feel that their roles are futile.[3,6,7]

Excessive turnover due to burnout—a syndrome characterized by exhaustion and cynicism relating to one's work—is particularly impactful for rural health care systems and EMS agencies, where recruiting qualified replacements is challenging.[7-10] Poor compassion satisfaction (ie, the pleasure derived from helping others), burnout, and high turnover are interrelated and associated with poorer patient outcomes.[11-13] The combined effects of these phenomena may contribute to a cyclic pattern that undermines well-being and retention, particularly in rural emergency

settings. Emergency services professionals may witness poorly mitigated suffering—often among individuals they know personally in small communities—and may struggle to contextualize their role in patient outcomes or derive compassion satisfaction from their work.[8,14] Lower compassion satisfaction has been associated with increased burnout and intent to leave the profession.[4,15,16] Preventable turnover further strains the remaining workforce, increasing the likelihood of preventable patient suffering due to limited health care resources.[9]

Both burnout and secondary traumatic stress—a source of occupational stress resulting from exposure to others' suffering—may be partially mitigated by compassion satisfaction, which provides a sense of meaning for health care professionals.[15,17-20] Compassion satisfaction is associated with lower burnout, improved job satisfaction, and greater intention to remain in health care professions.[15,21] Many emergency services professionals report that making a positive impact on patients serves as both a coping mechanism and motivator.[19,20,22] However, most provide care for only minutes to hours before patients leave their care. This limited interaction, together with lack of reliable follow-up information, often leaves these professionals without knowledge of patient outcomes.[23] Lack of follow-up or closure may contribute to poor compassion satisfaction, lower job satisfaction, and increased burnout.

Compounding the issue, emergency services professionals often report feeling neglected and isolated from other medical professionals despite a desire to learn from subsequent patient care by these professionals.[24,25] Providing access to follow-up information may help improve compassion satisfaction by supporting meaning-making and reinforcing the value of one's role in patient care, thereby reducing perceived futility, job dissatisfaction, and burnout.[15]

Therefore, this pilot study evaluated a program providing emegency services professionals in a rural Wisconsin service area with patient follow-up summaries. Specifically, we aimed to: (1) assess the feasibility, acceptability, and appropriateness of follow-up summary provision and (2) estimate the effect size of the intervention on burnout, compassion satisfaction, secondary traumatic stress, and job satisfaction.

Conceptual Framework

The Professional Quality of Life (ProQOL) framework is widely used to conceptualize relationships among compassion satisfaction, compassion fatigue, work-related trauma, and burnout in health care professionals.[15,26-30] According to this framework, work characteristics, clients (patient populations), and the fit between the individual goals and the work environment influence compassion satisfaction and contribute to compassion fatigue (a syndrome related to caregiving), burnout, and work-related trauma for health care professionals.[15] Compassion satisfaction, compassion fatigue, and work-related trauma are each associated with burnout. Although intention to leave is not explicitly included in the ProQOL framework, burnout has been correlated with intent to leave in studies utilizing this framework.[26]

Within the ProQOL framework, compassion satisfaction supports meaning-making for individuals who witness others' suffering.[15,18] Meaning making—the ability to attribute causality to and contextualize adverse events—is believed to facilitate compassion satisfaction.[30-32] Although reflection and contextualization may occur individually, they also may be facilitated by external sources.[33] Reflection on one's impact on patient care may enhance meaning-making but may be limited by ambiguity or uncertainty regarding outcomes.[34,35]

METHODS

Intervention

The study intervention consisted of providing each enrolled participant with follow-up summaries for every patient they transported to Tamarack Health Ashland or one of its affiliates (for prehospital EMTs and paramedics) or for patients admitted from the ED to the hospital or one of its affiliates (for ED nurses). Follow-up summaries included the patient's diagnosis associated with the encounter, treatment course, ED dispostion (eg, discharged home, deceased, admitted, transferred to another facility), and, if applicable, a summary of the patient's hospitalization course and hospital discharge disposition.

Participants received follow-up summaries for all eligible patients—all transported patients for prehospital EMTs and paramedics and all admitted patients for ED nurses—except those treated at hospitals that did not participate in data sharing with the critical access hospital described. Follow-up summaries were provided weekly in paper form via interdepartmental mail.

Follow-up information was limited to the episode of care in which the participant was involved, in accordance with the Health Information Portability and Accountability Act (HIPAA).[36] Participants were instructed to treat the follow-up information provided as protected health information and to dispose of materials using document-shredding bins after revivew. Additional information describing the intervention process in provided in Appendix A.

This intervention was developed collaboratively with the Ashland Fire Department, Washburn Emergency Medical Services, and Tamarack Health Ashland emergency department to address a need identified by participating agencies: access to formal patient follow-up information was inconsistent and typically limited to patients with severe trauma or critical illness. This intervention also addressed a need identified by the receiving institution by providing follow-up information without burdening participants with additional paperwork. Furthermore, this approach reduced concerns regarding unauthorized access to patient information.

Design

This study utilized a preintervention-postintervention design. Feasibility, acceptability, and appropriateness were measured using a postintervention survey adapted from Weiner et al[37] and through content analysis of open-ended questions.

All study data were collected via online surveys; no patient-level data were retained or analyzed. Burnout, compassion satisfaction, secondary traumatic stress, and job satisfaction were evaluated using repeated-measures analysis, in which the same variables are assessed before the intervention and after completion of the 12-week intervention period. Each survey instrument and associated scoring are described in Appendix B.

Feasibility, Acceptability, Appropriateness

Feasibility, acceptability, and appropriateness were measured using a public-domain instrument developed by Weiner et al.[37] These constructs are established indicators of implementation success.[38] The instrument demonstrates acceptable internal consistency (Cronbach α, 0.85-0.91), structural validity (confirmatory factor loadings, 0.7-0.89), and test-retest validity (coefficients, 0.73-0.88).[37] The instrument is adaptable to a range of implementation contexts. Higher scores indicate greater feasibility, acceptability, and appropriateness.

Feasibility, acceptability, and appropriateness were also evaluated using the following free-text questions on the postintervention survey:

- "What did you like or dislike about receiving patient follow-up information?"
- "What types of patients would you like to receive follow-up information about in the future?"
- "How did you feel about receiving patient follow-up information from patients who did not have positive outcomes?"
- "If given the choice, would you prefer to receive follow-up communications about patients on a scheduled basis or would you prefer to have access to a privacy-compliant system where you could look up follow-up information yourself?"
- "Is there anything else you would like to share about your thoughts or experiences on receiving patient follow-up information?"

Burnout, Compassion Satisfaction, Secondary Traumatic Stress

The Professional Quality of Life 5 Scale (ProQOL-5), a validated and widely used 30-item public domain instrument, was used to measure burnout, compassion satisfaction, and secondary traumatic stress.[15] All 3 constructs demonstrate acceptable internal consistency, reliability, inter-item correlation, and validity and have been used in studies of health care workers, including EMTs, paramedics, and nurses.[4,14,39]

Job Satisfaction

Job satisfaction was assessed using the Global Job Satisfaction subscale of the Satisfaction of Employees in Health Care (SEHC) survey.[40,41] The subscale, which consists of 2 items, was developed and validated as an independent measure of overall job satisfaction.[40]

Demographics

Demographics were assessed at baseline (pre-intervention survey). Variables included gender, highest degree, role (eg, EMT-basic, paramedic, registered nurse), age, race, ethnicity, years in the current position, and total years in emergency medical services.

Age, years in the current position, and years in emergency services were collected as categorical variables to preserve participant anonymity. Race and ethnicity were measured using multiple-choice questions. Weekly scheduled hours were self-reported using a slider (range, 0-80 hours). The number of patient follow-up summaries provided to each participant was tracked throughout the study and reported as a mean.

Sample and Inclusion/Exclusion Criteria

The sample comprised EMTs and paramedics employed at Ashland Fire Department and Washburn Emergency Medical Services, the primary EMS providers for the cities of Ashland and Washburn, Wisconsin, and registered nurses providing direct care in the ED at Tamarack Health in Ashland, Wisconsin. All participants met the following inclusion criteria: (1) age >18 years; (2) employment of ≥0.5 full-time equivalent; (3) ability to speak and understand English; and (4) access to an internet-enabled electronic device. All EMTs and paramedics worked in a prehospital setting, and all nurses worked in ED settings.

Human Subjects Protection

This study was reviewed and approved by the Marquette University institutional review board and Tamarack Health Ashland for compliance with patient privacy regulations. Participants were necessarily identified to the researchers during the intervention period to ensure accurate delivery of follow-up summaries; however, survey responses were anonymized using Qualtrics,[42] a secure digital survey platform.

Participants received a $25 gift card for completing the preintervention and postintervention surveys and were informed that participation was voluntary and that they could withdraw at any time. Written informed consent was obtained from all participants.

Analysis

Descriptive statistics were used to examine feasibility, acceptability, and appropriateness scores. Qualitative responses to the free-text questions were analyzed using content analysis, a qualitative method in which data are coded and categorized to identify themes.[43,44]

No a priori framework was applied to preserve participants' intended meaning. Three researchers—JC, TW, and TZ—independently reviewed responses, coded data, and identified themes. Discrepancies were resolved through consensus. Exemplar quotes

were selected and agreed upon by all 3 researchers to illustrate identified themes.

Cohen d was calculated to estimate effect sizes for burnout, compassion satisfaction, secondary traumatic stress, and job satisfaction by subtracting postintervention means from preintervention means and dividing by pooled standard deviation.[45]

RESULTS

Demographics

Participants received an average of 2.46 patient follow-up summaries per week; hospital-based participants (registered nurses) received an average of 2 summaries per week, and prehospital participants (EMTs, paramedics) received an average of 2.71 summaries per week. Approximately 20 follow-up summaries were unavailable due to patient transport to institutions that did not participate in data sharing with the critical access hospital.

Aim 1: Feasibility, Acceptability, and Appropriateness

Enrollment included 96% of eligible EMTs and paramedics (n = 26) and 75% of eligible nurses (n = 15). No participants withdrew from the study. The maximum possible score per subscale was 20. The mean feasibility score was 18.28 (SD, 1.7), acceptability score was 17.9 (SD, 2.3), and appropriateness score was 17.4 (SD, 2.1).

The following themes were identified during content analysis of free-text responses (reported by 21 participants).

Desire for Patient Follow-Up

The majority of participants (n = 16) reported a strong desire for follow-up information and high satisfaction with receiving follow-up summaries. Participant 16 wrote:

> "For 12 weeks, [receiving patient follow-up summaries] eliminated my biggest complaint about EMS [emergency medical services]: that once we leave the room in the ED, we often don't know what happens to our patients."

Participant 1 wrote, "Nice to see the outcomes in a profession where it is rare to hear about outcomes. It is good to know if our care made a difference for the better." Some participants also reported that they appreciated having closure regarding patients outcomes. Participant 2 noted, "We always wondered how a patient fared after leaving our care. Having that closure significantly improved my work satisfaction."

Twenty participants reported that they preferred to receive follow-up information regardless of whether the outcome was positive or negative. Participant 3 preferred that "all results be communicated," and Participant 15 wrote: "I did have several patients who had negative outcomes in this program and in a few cases it was expected by those of us on the call, but it is still a little sad."

Seventeen participants reported the greatest interest in receiving follow-up summaries from patients with higher acuity or complex medical conditions, including "trauma, stroke, MI [myocardial infarction], and high-acuity" (Participant 7) and "critical care, cardiac, trauma, and pediatrics" (Participant 20). Participant 1 stated a desire for expanded follow-up across receiving hospitals. Two participants indicated preferences for follow-up on diagnostically uncertain cases or personally meaningful patients, and 2 participants preferred follow-up for all patients.

Seventeen participants reported that they would prefer access to a privacy-compliant system to look up patient information themselves, rather than receiving all follow-up information on a scheduled basis. Participant 16 noted, "I'd prefer to have control over who and when I looked them up. A number of the follow-ups I got were [known patients] who rarely have changes in condition."

One participant expressed concerns regarding patient privacy, particularly in a small community:

> "I feel my job satisfaction increased by receiving the follow-ups. However, patient privacy does concern me. We live in a small community, and I know I would feel humiliated if colleagues received the same information about me. During the study, this was a real worry of mine—that I might have an auto accident and require transport, and my colleagues would be able to read my personal info" (Participant 9).

Additional Learning

Eight participants reported that follow-up summaries provided valuable opportunites for ongoing learning. Participant 16 wrote, "What surprised me about receiving patients' follow-ups was many of the diagnoses the ED presented to me that were different from my impression on the scene. It was highly educational." Participant 13 agreed, "I think it [patient follow-up summaries] is beneficial for those who want to further development." Participant 2 added, "I learned a great deal about the patient's general health and treatment that will assist me in becoming a better EMT."

Affirmation of Competence

Participants also reported satisfaction reflecting on the care they provided. Five indicated that reading follow-up summaries validated their clinical competence. Participant 15 said, "It was nice to see the times my differential diagnosis was validated." Participant 7 said, "It affirmed my skills and knowledge as a prehospital provider," and Participant 13 noted that follow-up summaries "reaffirmed my initial suspicions of a likely negative outcome."

Aim 2: Intervention Effect Sizes

Burnout, compassion satisfaction, and global job satisfaction mean scores increased slightly between preintervention and postintervention surveys, with Cohen d values of 0.25, 0.02, and 0.05, respectively. Secondary traumatic stress scores decreased, with a Cohen d of 0.29.

DISCUSSION

This pilot study highlights the effects of a patient follow-up communication program implemented among emergency services professionals in a rural US setting. Participant feedback supported the feasibility, acceptability, and appropriateness of

the program and demonstrated a strong desire for follow-up information.

Barriers to Patient Follow-up Summary Program Uptake

Prior research indicates that programs communicating patient outcomes are desired by emergency services professionals.[24] However, many existing programs are limited by barriers such as data-sharing restrictions, institutional governance challenges, and requirements to request informtion on specific patients.[24,46]

In contrast, this study's protocol was designed to reduce these barriers. For example, participants were not required to request follow-up information, reducing effort and improving accessibility. Additionally, the structured format of the program was designed to ease concerns regarding unauthorized access to patient data. Despite these features, some participants expressed concerns regarding privacy, particularly within small communities.

Burnout, Compassion Satisfaction, Secondary Traumatic Stress, and Job Satisfaction

Despite positive qualitative findings, burnout scores increased and compassion satisfaction decreased following the intervention. One possible explanation is that, although participants expressed a desire for follow-up information and reported improvements in both secondary traumatic stress and job satisfaction, exposure to patient outcomes may not reduce burnout.

Another explanation is the lack of selectivity in follow-up content; participants received summaries for all patients. Previous research suggests that improved mental health or job satisfaction is more likely when clinicians receive feedback on the patients they are most interested in.[46]

Nonemergent patients and frequent users of emergency services are estimated to account for over 12% of emergency ambulance transports and over 40% of ED visits in the United States.[47,48] Such encounters are often associated with frustration due to perceived overutilization of limited emergency services resources.[49,50] This study's follow-up protocol did not discriminate based on patient complexity or services received, which may have inadvertently reinforced perceptions of resource strain, contributing to increased burnout and reduced compassion satisfaction.

Additionally, personal familiarity with patients in rural communities may influence these outcomes. Emergency services professionals in rural settings are more likely to know the patients they care for. One participant described discomfort with receiving follow-up information given the community's small size, suggesting that community connectedness may contribute to increased emotional burden.

Limitations and Recommendations for Further Research

The small sample size and self-selection from a single rural service area limit generalizability. Additional studies with larger and more diverse samples are needed. Approximately 20 patient follow-up summaries were unavailable, all involving patients transferred to tertiary care centers, highlighting limited data-sharing as a barrier to implementation.[51]

This study did not have sufficient statistical power to control for other confounding factors associated with burnout, such as number of hours worked per week. Further research should examine additional outcomes, including perceived competence.

The ProQOL-5 burnout measure does not include subscales assessing specific dimensions such as emotional exhaustion and depersonalization, which may limit the generalizability of our findings. Future studies should consider instruments with subscales to better assess how follow-up interventions affect different aspects of burnout.

Finally, future interventions should consider prioritizing follow-up summaries for patients with greater clinical complexity or personal relevance to maximize benefit.

CONCLUSIONS

Patient follow-up summaries were acceptable to study participants, who qualitatively reported high satisfaction with receiving follow-up information. Following intervention, secondary traumatic stress decreased with a small effect size, and job satisfaction increased with a very small effect size. Although burnout increased following intervention, modifications to the program may improve this outcome, such as limiting follow-up summaries to higher-acuity patients.

Agencies providing EMS should consider the potential benefits of partnering with local hospitals to develop mechanisms for requesting patient follow-up information in a manner that is compliant and acceptable to both EMS agencies and hospitals.

Financial disclosures: None declared.

Funding/support: This study was funded in part by an internal grant from the Marquette University College of Nursing.

Appendices: Available at www.wmjonline.org

REFERENCES

1. Bahl A. Wisconsin EMS providers are 'in crisis.' lawmakers have ideas. *The Cap Times.* April 25, 2025.

2. Loccoh EC, Joynt Maddox KE, Wang Y, Kazi DS, Yeh RW, Wadhera RK. Rural-urban disparities in outcomes of myocardial infarction, heart failure, and stroke in the United States. *J Am Coll Cardiol*. 2022;79(3):267-279. doi:10.1016/j.jacc.2021.10.045

3. Bethea A, Samanta D, Kali M, Lucente FC, Richmond BK. The impact of burnout syndrome on practitioners working within rural healthcare systems. *Am J Emerg Med*. 2020;38(3):582-588. doi:10.1016/j.ajem.2019.07.009

4. Kaplan GR, Frith T, Hubble MW. Quantifying the prevalence and predictors of burnout in emergency medical services personnel. *Ir J Med Sci*. 2024;193(3):1545-1556. doi:10.1007/s11845-023-03580-7

5. Eubanks J. *The EMS Deficit: A Study on the Excessive Staffing Shortages of Paramedics and its Impact on EMS Performance in the States of South Carolina and North Carolina and Interventions for Organizational Improvements*. Dissertation. Liberty University; 2022.

6. Hansen N, Jensen K, MacNiven I, Pollock N, D'Hont T, Chatwood S. Exploring the impact of rural health system factors on physician burnout: a mixed-methods study in Northern Canada. *BMC Health Serv Res*. 2021;21(1):869. doi:10.1186/s12913-021-06899-y

7. Sporer C. Burnout in emergency medical technicians and paramedics in the USA. *Int J Emerg Serv.* 2021;10(3):366-389. doi:10.1108/IJES-03-2020-0012

8. Dekeseredy P, Landy CMK, Sedney CL. An exploration of work related stressors experienced by rural emergency nurses. *Online J Rural Nurs Health Care*. 2019;19(2):2-24. doi:10.14574/ojrnhc.v19i2.550

9. Taylor K. *Improving Critical Access Hospital Nurse Turnover, Retention, and Satisfaction Through Mentorship.* Doctoral Thesis. McKendree University; 2021.

10. Russell D, Mathew S, Fitts M, et al. Interventions for health workforce retention in rural and remote areas: a systematic review. *Hum Resour Health*. 2021;19(1):103. doi:10.1186/s12960-021-00643-7

11. Caulfield R, Wiseman T, Gullick J, Ogilvie R. Factors preceding occupational distress in emergency nurses: an integrative review. *J Clin Nurs*. 2023;32(13-14):3341-3360. doi:10.1111/jocn.16461

12. Baier N, Roth K, Felgner S, Henschke C. Burnout and safety outcomes - a cross-sectional nationwide survey of EMS-workers in Germany. *BMC Emerg Med.* 2018;18(1):24. doi:10.1186/s12873-018-0177-2

13. Dasan S, Gohil P, Cornelius V, Taylor C. Prevalence, causes and consequences of compassion satisfaction and compassion fatigue in emergency care: a mixed-methods study of UK NHS consultants. *Emerg Med J*. 2015;32(8):588-594. doi:10.1136/emermed-2014-203671

14. Hăisan A, Hogaș S, Măirean C, et al. Compassion fatigue and compassion satisfaction among Romanian emergency medicine personnel. *Front Med (Lausanne)*. 2023;10:1189294. doi:10.3389/fmed.2023.1189294

15. Stamm B. *The Concise ProQOL Manual.* 2nd ed. ProQOL.org; 2010.

16. Dehghannezhad J, zamanzadeh V, Gilani N, Rahmani A, Dadashzadeh A. Compassion satisfaction and compassion fatigue among emergency medical technicians in Iran. *Australas J Paramed*. 2020;17:1-7. doi:10.33151/ajp.17.642

17. Ames M, Salmond E, Holly C, Kamienski M. Strategies that reduce compassion fatigue and increase compassion satisfaction in nurses: a systematic review protocol. *JBI Database System Rev Implement Rep*. 2017;15(7):1800-1804. doi:10.11124/JBISRIR-2016-003142

18. Hinderer KA, VonRueden KT, Friedmann E, et al. Burnout, compassion fatigue, compassion satisfaction, and secondary traumatic stress in trauma nurses. *J Trauma Nurs*. 2014;21(4):160-169. doi:10.1097/JTN.0000000000000055

19. Kaplan Serin E, Özdemir A, Işik K. The effect of nurses' compassion on burnout: a cross-sectional study. *Perspect Psychiatr Care*. 2021;57(1):371-379. doi:10.1111/ppc.12607

20. Belotto M. *Emergency Medical Service Career Longevity: Impact of Alignment Between Preemployment Expectations and Postemployment Perceptions*. Dissertation. Walden University; 2017.

21. Crowe RP, Bower JK, Cash RE, Panchal AR, Rodriguez SA, Olivo-Marston SE. Association of burnout with workforce-reducing factors among EMS professionals. *Prehosp Emerg Care.* 2018;22(2):229-236. doi:10.1080/10903127.2017.1356411

22. Babaei S, Haratian M. Compassion satisfaction and fatigue in cardiovascular nurses: a cross-sectional descriptive study. *Iran J Nurs Midwifery Res*. 2020;25(3):212-216. doi:10.4103/ijnmr.IJNMR_112_19

23. Cash RE, Crowe RP, Rodriguez SA, Panchal AR. Disparities in feedback provision to emergency medical services professionals. *Prehosp Emerg Care*. 2017;21(6):773-781. doi :10.1080/10903127.2017.1328547

24. Morrison L, Cassidy L, Welsford M, Chan TM. Clinical performance feedback to paramedics: what they receive and what they need. *AEM Educ Train*. 2017;1(2):87-97. doi:10.1002/aet2.10028

25. Iserson KV. Empowering clinician education with patient-outcome feedback. *AEM Educ Train.* 2020;4(4):395-402. doi:10.1002/aet2.10489

26. Yu H, Gui L. Compassion fatigue, burnout and compassion satisfaction among emergency nurses: a path analysis. *J Adv Nurs.* 2022;78(5):1294-1304. doi:10.1111/jan.15034

27. Copeland D, Henry M. The relationship between workplace violence, perceptions of safety, and Professional Quality of Life among emergency department staff members in a Level 1 Trauma Centre. *Int Emerg Nurs*. 2018;39:26-32. doi:10.1016/j.ienj.2018.01.006

28. Ericsson CR, Nordquist H, Lindström V, Rudman A. Finnish paramedics' professional quality of life and associations with assignment experiences and defusing use - a cross-sectional study. *BMC Public Health*. 2021;21(1):1789. doi:10.1186/s12889-021-11851-0

29. Renkiewicz GK, Hubble MW. Secondary traumatic stress in emergency services systems (stress) project: quantifying and predicting compassion fatigue in emergency medical services personnel. *Prehosp Emerg Care*. 2022;26(5):652-663. doi:10.1080/10903127.2021.1943578

30. Kopacz MS, Lockman J, Lusk J, et al. How meaningful is meaning-making? *New Ideas Psychol.* 2019;54:76-81. doi:10.1016/j.newideapsych.2019.02.001

31. Hruska B, Barduhn MS. Dynamic psychosocial risk and protective factors associated with mental health in emergency medical service (EMS) personnel. *J Affect Disord*. 2021;282:9-17. doi:10.1016/j.jad.2020.12.130

32. Gonzalez-Mendez R, Díaz M, Aguilera L, Correderas J, Jerez Y. Protective factors in resilient volunteers facing compassion fatigue. *Int J Environ Res Public Health.* 2020;17(5):1769. doi:10.3390/ijerph17051769

33. Sattler D, Smith A. Facilitating posttraumatic growth in the wake of natural disasters: considerations for crisis response. In: Schulenberg S, ed. *Positive Psychological Approaches to Disaster: Meaning, Resilience, and Posttraumatic Growth.* Springer Nature; 2020:169-186.

34. Walsh F. Loss and resilience in the time of COVID-19: meaning making, hope, and transcendence. *Fam Process*. 2020;59(3):898-911. doi:10.1111/famp.12588

35. Sitvast J. *How Nurses Can Facilitate Meaning-Making and Dialogue: Reflections on Narrative and Photo Stories.* Cambridge Scholars Publishing; 2021.

36. *HIPAA Administrative Simplification: Regulation Text*. U.S. Department of Health and Human Services; 2013. 45 CFR Parts 160, 162, and 164.

37. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. *Implement Sci*. 2017;12(1):108. doi:10.1186/s13012-017-0635-3

38. Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Adm Policy Ment Health.* 2011;38(2):65-76. doi:10.1007/s10488-010-0319-7

39. Hemsworth D, Baregheh A, Aoun S, Kazanjian A. A critical enquiry into the psychometric properties of the professional quality of life scale (ProQol-5) instrument. *Appl Nurs Res*. 2018;39:81-88. doi:10.1016/j.apnr.2017.09.006

40. Alpern R, Canavan ME, Thompson JT, et al. Development of a brief instrument for assessing healthcare employee satisfaction in a low-income setting. *PLoS One*. 2013;8(11):e79053. doi:10.1371/journal.pone.0079053

41. Chang E, Cohen J, Koethe B, Smith K, Bir A. Measuring job satisfaction among healthcare staff in the United States: a confirmatory factor analysis of the Satisfaction of Employees in Health Care (SEHC) survey. *Int J Qual Health Care.* 2017;29(2):262-268. doi:10.1093/intqhc/mzx012

42. *Qualtrics XM – experience management software*. Qualtrics; 2024. Accessed Dec 20, 2024. http://www.qualtrics.com

43. Erlingsson C, Brysiewicz P. A hands-on guide to doing content analysis. *Afr J Emerg Med.* 2017;7(3):93-99. doi:10.1016/j.afjem.2017.08.001

44. Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs.* 2008;62(1):107-115. doi:10.1111/j.1365-2648.2007.04569.x

45. Durlak JA. How to select, calculate, and interpret effect sizes. *J Pediatr Psychol.* 2009;34(9):917-928. doi:10.1093/jpepsy/jsp004

46. Wilson C, Janes G, Lawton R, Benn J. Feedback for emergency ambulance staff: a national review of current practice informed by realist evaluation methodology. *Healthcare (Basel).* 2023;11(16):2229. doi:10.3390/healthcare11162229

47. Sommers-Olson B, Christianson J, Neumann T, et al. Reducing nonemergent visits to the emergency department in a Veterans Affairs multistate system. *J Emerg Nurs.* 2023;49(4):539-545. doi:10.1016/j.jen.2023.02.010

48. Birmingham LE, Arens A, Longinaker N, Kummet C. Trends in ambulance transports and costs among Medicare beneficiaries, 2007-2018. *Am J Emerg Med*. 2021;47:205-212. doi:10.1016/j.ajem.2021.04.039

49. McGarry E, O'Connor L. Assessing burnout rates and contributing factors in emergency medical services clinicians. *J Workplace Behav Health*. 2023;39(3):288-301. doi:10.1080/15555240.2023.2292119

50. Bodenmann P, Kasztura M, Graells M, et al. Healthcare providers' perceptions of challenges with frequent users of emergency department care in Switzerland: a qualitative study. *Inquiry*. 2021;58:469580211028173. doi:10.1177/00469580211028173

51. Anumula N, Sanelli PC. Meaningful use. *AJNR Am J Neuroradiol*. 2012;33(8):1455-1457. doi:10.3174/ajnr.A3247

Assessing Human Papillomavirus Knowledge and Vaccination Intentions Following a Virtual Educational Intervention for Parents and Guardians

Lalee Lo, PharmD; Cristin Marchese, PharmD; Julia Prajdic, PharmD; Timika Robertson, PharmD; Angela Saber, PharmD, MPH; Destiny Self, PharmD; Lisa Dinkins, PharmD

ABSTRACT

Introduction: Human papillomavirus (HPV) is the most common sexually transmitted infection globally, with high-risk strains contributing to cancers of the cervix, penis, anus, vulva, vagina, and oropharynx. Despite the availability of an effective vaccine (Gardasil-9) and broad support from public health organizations, vaccination rates remain suboptimal due to parental hesitancy and misinformation. This study assessed the impact of an educational intervention on HPV knowledge and vaccination intent among parents and guardians of children aged 8 to 17 years.

Methods: Pharmacy students conducted virtual educational sessions via Zoom for parents of children aged 8 to 17 years. Sessions covered HPV transmission, associated risks, and benefits of Gardasil-9. Participants completed presession and postsession surveys assessing knowledge and willingness to vaccinate.

Results: A total of 50 participants attended the sessions; 48 completed the presurvey and 39 completed the postsurvey. Knowledge improved significantly following the intervention (53% vs 90% correct; P<.001). Willingness to vaccinate daughters increased from 68% to 89% reporting "very willing," while willingness to vaccinate sons increased from 70% to 91%. Parents were 1.2 times more likely to report being "very willing" to vaccinate their children against HPV after the intervention.

Conclusions: A virtual educational intervention significantly improved parental knowledge and positively influenced their intent to vaccinate against HPV. Addressing vaccine hesitancy through structured, accessible educational programs may help increase HPV vaccination rates and reduce the burden of HPV-related cancers.

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection among individuals in their late teens and early 20s worldwide.[1] HPV is a group of more than 200 related viruses that infect cells on the skin surface and moist inner linings of body cavities. Low-risk HPV types may affect the skin, throat, and genital area, leading to abnormal tissue growth, including cutaneous and genital warts. If left untreated, high-risk HPV can lead to 6 types of cancer. HPV accounts for approximately 90% of cervical and anal cancers, 70% of vaginal and vulvar cancers, 60% of penile cancers, and 70% of oropharyngeal cancers. It is transmitted through intimate skin-to-skin contact including vaginal, anal, and oral sex. Importantly, asymptomatic individuals can unknowingly transmit HPV.[2]

The prevalence of HPV in the United States is substantial, with more than 42 million Americans currently infected and approximately 13 million new cases annually.[3] In 2022, HPV accounted for approximately 660 000 new cases of cervical cancer and 350 000 cancer-related deaths worldwide. It is the fourth-leading cause of cervical cancer and cancer-related deaths among women worldwide.[4] Approximately 36 000 new cases of HPV-related cancers are diagnosed annually among men and women in the United States, with an estimated 4000 cervical cancer-related deaths among women each year.[3,5] The highest incidence and mortality rates from cervical cancer occur in low- and middle-income countries. During 2004-2007, the estimated annual medical cost in the United States amounted to $9.36 billion for cervical cancer screening and follow-up, treatment of HPV-related cancers and anogenital warts, and recurrent respiratory papillomatosis.[6] This burden underscores the need for improved awareness of and access to the HPV vaccine.

Protection against HPV is achieved by completing a 2- or

Author affiliations: Wingate University School of Pharmacy, Wingate, North Carolina (Dinkins, Lo, Marchese, Pradjic, Robertson, Saber, Self).

Corresponding author: Destiny Self, email de.self400@wingate.edu; ORCID ID 0009-0007-1770-082X

3-dose series of Gardasil-9 prior to exposure. Gardasil-9 is a noninfectious, recombinant vaccine.[7] More than 15 years of research confirm that the vaccine is well tolerated and effective in preventing HPV-related cancers.[8] The most common adverse effects include injection-site reactions (pain, swelling, redness) and headache, each with a reported incidence greater than 10%.[9] Rare but more serious side effects include autoimmune conditions (approximately 2%) and oropharyngeal pain (1%-3%).[9] The Centers for Disease Control and Prevention (CDC) recommends initiation of the Gardasil-9 series at ages 11 to 12 years; however, vaccination can be initiated as early as age 9 years.[10] "Within 12 years of vaccine introduction, Gardasil-9 reduced infections by 88% in females aged 14 to 19 years," according to the CDC.[11] Additionally, the percentage of cervical lesions caused by HPV decreased by 40% among vaccinated women since the vaccine's introduction,[11] and one study found that vaccination reduced the prevalence of genital lesions by 60.2% in males aged 16 to 26 years.[12] These findings support early vaccination to maximize protection against HPV.

The American Academy of Pediatrics recommends HPV vaccination as early as 9 years of age.[13] Initiating vaccination at age 9 enables timely completion of the series within 6 to 12 months before potential exposure.[13] Additionally, children mount a stronger immune response when vaccinated at younger ages.[14] A previous trial found that clinical staff were more willing to recommend vaccination at the earliest eligible age compared with ages 11to 12 years. Parents were more likely to vaccinate their children when vaccination was recommended at age 9 versus 11 to 12 years.[15] Early vaccination reduces the risk of HPV-related cancers and diseases later in life and represents an important step in safeguarding long-term health.

Vaccine hesitancy is a global challenge driven primarily by concerns about safety. However, studies have identified and refuted common misconceptions associated with HPV vaccination. A 2023 study found that 65% of parents were hesitant to initiate HPV vaccination due to perceptions that it was unnecessary, concerns about safety or adverse effects, lack of knowledge, belief that their child was not sexually active, or lack of a health care provider recommendation. Between 2013–2014 and 2019–2020, hesitancy related to reasons such as "not needed or necessary," "not recommended," "lack of knowledge," and "not sexually active" declined among parents of unvaccinated adolescents.[16] This change may reflect increased public health efforts, greater awareness of HPV and vaccine benefits, and provider recommendations. It is important to recognize public uncertainty and provide education to distinguish opinions from evidence-based findings.

In a 2024 study, a lack of knowledge about the HPV vaccine was the most cited reason minority patients reported little interest in vaccinating themselves or their children. Among unvaccinated adults unwilling to receive the vaccine, common factors included low perceived risk of HPV infection, limited awareness of the vaccine, and doubts about its benefit. Providing education about HPV and its consequences to minority populations may help address a major barrier to vaccination. Efforts to improve access, convenience, and health literacy may increase uptake among underserved populations.[17]

Although support for the HPV vaccine is high among numerous health organizations including the CDC and the American Cancer Society, a 2023 study found that limited knowledge of HPV and Gardasil-9 significantly influences parental decision-making.[2] To address this knowledge gap, we designed a study to assess changes in parents' knowledge and willingness to vaccinate their children against HPV before and after an educational intervention. We hypothesized that the intervention would increase both parents' knowledge of HPV and willingness to vaccinate.

METHODS

Study Design

The study involved parents or guardians of children ages 8 to 17 years old. Parents of children outside this age group and children who had already received the HPV vaccine were excluded. Participants were recruited through flyers distributed at a local community health fair and social media. As an incentive, 1 participant was randomly selected to receive a $50 Visa gift card. Third-year pharmacy students conducted 28 Zoom sessions covering HPV, complications of untreated infection, and vaccine benefits. Each session consisted of a presurvey, a 10-minute educational presentation, and a postsurvey. Participants accessed the presurvey via a QR code and were encouraged to complete it within 10 minutes of joining the session. Surveys assessed parents' knowledge of HPV and willingness to vaccinate before and after the presentation. The study was approved by the Wingate University Institutional Review Board, and all participants provided written informed consent.

Educational Intervention

A 10-minute virtual slideshow was delivered via Zoom. The presentation included an overview of HPV, modes of transmission, and symptoms associated with low- and high-risk strains, as well as a comparison of these strains. Education on Gardasil-9 included dosing schedule, benefits, potential adverse effects, and common myths and facts. Participants were informed that the vaccine protects against 9 HPV types, including those most strongly associated with cancer.

Presurvey and Postsurvey

Participants completed online surveys via Qualtrics (Qualtrics, LLC) before and after the presentation. The presurvey contained 4 demographic questions, 5 knowledge-based questions, and 2 questions assessing willingness to vaccinate sons and/or daughters. Demographic questions included parents' gender, race, and children's ages. The postsurvey repeated the knowledge and willingness questions. Each knowledge question had only 1 correct

Table 1. Parent Demographics (N = 48)

Characteristics	n (%)
Gender	
Male	17 (35)
Female	28 (58)
Prefer not to answer	3 (6)
Race/ethnicity	
African American	23 (48)
White	19 (40)
Hispanic/Latino	4 (8)
Asian	1 (2)
Native American	1 (2)

Table 2. Performance on HPV Knowledge Questions

Question	Presurvey Correct n (%)	Postsurvey Correct n (%)
What is human papillomavirus (HPV)?	21 (44)	35 (90)
How is HPV transmitted?	25 (52)	34 (87)
What are the benefits of the HPV vaccine?	32 (67)	36 (92)
What are the adverse effects of the HPV vaccine?	24 (50)	32 (82)
Untreated HPV can cause which of the following?	26 (54)	38 (97)

$P < .001$

response, and the percentage of correct answers per participant was calculated. Willingness was measured on a 4-point Likert scale (1 = not willing; 4 = very willing). Participants could optionally enter a drawing for the $50 Visa gift card.

Data Analysis

Data collected via Qualtrics were exported to Microsoft Excel (Microsoft Corp). Survey responses were deidentified. Descriptive statistics were used for demographic data, and a *t* test assessed changes in knowledge and willingness between presurveys and postsurveys.

RESULTS

A total of 50 participants attended Zoom-based educational sessions. Of these, 48 completed the presurvey and 39 completed the postsurvey. Forty-eight percent were African American and 58% were female (Table 1). Two presurveys and 11 postsurveys were excluded due to duplication or incomplete responses, as their inclusion would have introduced potential outliers and reduced the overall statistical integrity of the results.

Knowledge scores improved significantly from presurvey to postsurvey (53% vs 90% correct; $P < .001$) (Table 2). The proportion of participants reporting they were "very willing" to vaccinate their daughters increased from 68% at baseline to 89% postintervention (Figure 1). For sons, this increased from 70% to 91% (Figure 2). Overall, participants were 1.2 times more likely to report being "very willing" to vaccinate their children against HPV after the intervention.

Figure 1. Parental Willingness to Vaccinate Daughters

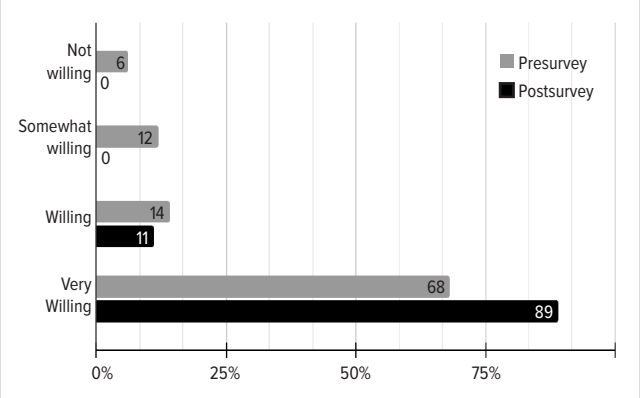
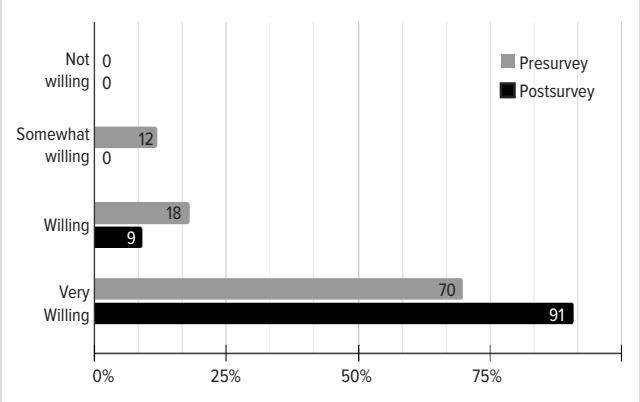


Figure 2. Parental Willingness to Vaccinate Sons



DISCUSSION

Parental vaccine hesitancy is associated with lower childhood vaccination rates.[18] Hesitancy often stems from misconceptions about HPV and the Gardasil-9 vaccine. This study sought to address potential barriers to early HPV vaccination, including limited access to education and stigma surrounding vaccination. Addressing these barriers may improve health literacy and reduce vaccine hesitancy.

Survey data demonstrated that knowledge improved significantly (53% vs 90%, $P < .001$), reinforcing the impact of education on parental attitudes. Additionally, willingness to vaccinate both daughters and sons increased following the intervention, underscoring the role of health literacy in parents' vaccination decisions.

A 2012 study found that mothers were less willing to vaccinate sons than daughters, largely due to lower perceived risk of HPV among males.[19] In contrast, our study found similar willingness to vaccinate both sons and daughters. This may be due to the intervention's educational emphasis on HPV risk in males: that they have a threefold higher prevalence of HPV than females and greater than 5 times the rate of oropharyngeal cancer.[20]

Many participants demonstrated baseline willingness to vacci-

nate their children against HPV, possibly reflecting increased public awareness, expanded vaccine recommendations, increased research on vaccine safety and effectiveness, and a growing acknowledgment of HPV as a public health issue. Following the intervention, parents were 1.2 times more willing to vaccinate their children and no participants remained unwilling to vaccinate. Many participants also had high presurvey knowledge scores, which may reflect the use of external resources, such as online search engines, during online survey completion.

Our findings are consistent with prior research demonstrating that earlier recommendation (eg, age 9 years) by clinicians improves vaccination uptake and series completion.[14] In this study, "very willing" responses increased by 21% for daughters and 9% for sons.

Research indicates that HPV vaccination rates are lower in minority populations due to lack of awareness and knowledge.[16] This study included a diverse patient population, with substantial minority representation (48% African American, 8% Hispanic/Latino, 2% Asian, and 2% Native American). As awareness among minority communities increases, more individuals may choose to get vaccinated, ultimately contributing to community-wide immunity by reducing the overall risk of infection.

Additionally, the use of Zoom as an educational platform eliminated transportation and in-person attendance requirements, enhancing accessibility and scheduling flexibility, as various dates and times were offered. The intervention required minimal time and no specialized equipment or infrastructure. Costs for materials and personnel were modest relative to the long-term costs if HPV-related disease. Despite its low cost, the intervention significantly improved knowledge and vaccination intent, demonstrating strong potential public health value.

Study Limitations

Several limitations were identified. Recruitment challenges and lack of reminder emails or text messages may have reduced participation. Eligibility criteria limited participation to parents and guardians of children aged 8 to 17 years. Survey responses were analyzed at the group level, potentially reducing generalizability. Technological barriers, including lack of technological proficiency (eg, scanning QR codes, joining Zoom sessions, navigating computer systems) and limited internet access, also may have restricted participation. Additionally, parents may have chosen not to participate due to a bias toward pharmacy students, preferring to receive information from licensed health professionals.

Future research should examine differences between maternal and paternal attitudes, address racial and ethnic disparities, and evaluate optimal timing and messenger (eg, clinicians vs students) for education. This study lacked long-term follow-up, limiting assessment of actual vaccination uptake. Future studies should include objective behavioral outcomes to evaluate sustained impact.

CONCLUSIONS

The Gardasil-9 vaccine provides well-tolerated, effective protection against cancers linked to HPV infection. Addressing barriers, misconceptions, and variability in vaccination across genders and age groups is critical to addressing this public health issue. This intervention employed virtual education sessions delivered via Zoom as a strategy to overcome persistent barriers to HPV vaccination. This format improved accessibility and convenience while maintaining educational quality.

As global vaccination efforts expand, the potential to save lives, lower health care costs, and decrease the burden on health systems increases. The impact of HPV vaccination on reducing cervical cancer incidence and mortality is greatest among women with limited access to regular screening or comprehensive health care services. Although the vaccine benefits all populations, its overall public health impact may be lessened among women who already receive high-quality preventive care, such as routine Papanicolaou (Pap) testing and HPV screening, which reduce baseline risk through early detection. Continued advocacy, education, and equitable access to vaccination are essential to maximize its benefits and improve population health outcomes worldwide.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Teen newsletter: January 2021 – HPV. Centers for Disease Control and Prevention. Last Reviewed January 11, 2021. Accessed September 26, 2024. https://www.cdc.gov/museum/education/newsletter/2021/jan/index.html

2. HPV and cancer. National Cancer Institute. Updated October 18, 2023. Accessed September 26, 2024. https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-and-cancer

3. About HPV. Centers for Disease Control and Prevention. July 3, 2024. Accessed October 24, 2024. https://www.cdc.gov/hpv/about/index.html

4. Human papillomavirus and cancer. World Health Organization. March 5, 2024. Accessed September 19, 2024. https://www.who.int/news-room/fact-sheets/detail/human-papilloma-virus-and-cancer

5. Cancers caused by HPV. Centers for Disease Control and Prevention. March 3, 2025. Accessed September 22, 2024. https://www.cdc.gov/hpv/about/cancers-caused-by-hpv.html

6. Clay PA, Thompson TD, Markowitz LE, Ekwueme DU, Saraiya M, Chesson HW. Updated estimate of the annual direct medical cost of screening and treatment for human papillomavirus associated disease in the United States. *Vaccine*. 2023;41(14):2376-2381. doi:10.1016/j.vaccine.2023.02.049

7. Human papillomavirus (HPV) vaccination: information for health care providers. Centers for Disease Control and Prevention. November 16, 2021. Accessed September 26, 2024. https://www.cdc.gov/vaccines/vpd/hpv/hcp/vaccines.html

8. HPV vaccine safety and effectiveness data. Centers for Disease Control and Prevention. July 9, 2024. Accessed September 26, 2024. https://www.cdc.gov/hpv/hcp/vaccination-considerations/safety-and-effectiveness-data.html

9. Human papillomavirus vaccine (9-Valent). In: *Lexi-Drugs*. UpToDate Inc. Accessed August 18, 2025.

10. HPV vaccine recommendations. Centers for Disease Control and Prevention. July 24, 2024. Accessed September 26, 2024. https://www.cdc.gov/hpv/hcp/vaccination-considerations/index.html

11. HPV vaccine safety and effectiveness data. Centers for Disease Control and Prevention. July 9, 2024. Accessed September 27, 2024. https://www.cdc.gov/hpv/hcp/vaccination-considerations/safety-and-effectiveness-data.html

12. Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males. *N Engl J Med.* 2011;364(5):401-411. doi:10.1056/NEJMoa0909537

13. O'Leary ST. Why the American Academy of Pediatrics recommends initiating HPV vaccine at age 9. *Hum Vaccin Immunother.* 2022;18(6):2146434. doi:10.1080/21645515.2022.2146434

14. Brewer NT, Kahn BZ, Kritikos KI, Heisler-MacKinnon JA, Young JD, Gilkey MB. How to make effective HPV vaccine recommendations starting at age 9. *Hum Vaccin Immunother.* 2023;19(2):2216117. doi:10.1080/21645515.2023.2216117

15. Kahn BZ, Reiter PL, Kritikos KI, Gilkey MB, Queen TL, Brewer NT. Framing of national HPV vaccine recommendations and willingness to recommend at ages 9-10. *Hum Vaccin Immunother.* 2023;19(1):2172276. doi:10.1080/21645515.2023.2172276

16. White JL, Grabowski MK, Rositch AF, et al. Trends in adolescent human papillomavirus vaccination and parental hesitancy in the United States. *J Infect Dis.* 2023;228(5):615-626. doi:10.1093/infdis/jiad055

17. Lin ME, Ayo-Ajibola O, Davis R, et al. Knowledge of HPV vaccination and associated HNC and treatment decision-making among minority populations. *Am J Otolaryngol.* 2024;45(6):104458. doi:10.1016/j.amjoto.2024.104458

18. Taumberger N, Joura EA, Arbyn M, Kyrgiou M, Sehouli J, Gultekin M. Myths and fake messages about human papillomavirus (HPV) vaccination: answers from the ESGO Prevention Committee. *Int J Gynecol Cancer.* 2022;32(10):1316-1320. doi:10.1136/ijgc-2022-003685

19. Nguyen KH, Santibanez TA, Stokley S, et al. Parental vaccine hesitancy and its association with adolescent HPV vaccination. *Vaccine*. 2021;39(17):2416-2423. doi:10.1016/j.vaccine.2021.03.048

20. Berenson AB, Rahman M. Gender differences among low income women in their intent to vaccinate their sons and daughters against human papillomavirus infection. J *Pediatr Adolesc Gynecol.* 2012;25(3):218-220. doi:10.1016/j.jpag.2012.01.003

21. Villalona S, Stroup AM, Villalona S, Ferrante JM. Racial/ethnic disparities in HPV-related oropharyngeal cancer outcomes among males in the United States: a national cohort study. *Ann Cancer Epidemiol.* 2022;6:4. doi:10.21037/ace-22-1

Assessing the Health Needs of Northcentral Wisconsin's Transgender Population

Liane Kee, MD; Corina Norrbom, MD

ABSTRACT

Introduction: The body of literature surrounding transgender health care primarily focuses on metropolitan populations and resource-rich areas. This qualitative study examines the perspectives of transgender patients in northcentral Wisconsin to identify recommendations for more comprehensive, inclusive health care practices.

Methods: A series of semistructured interviews was conducted with recipients of gender-affirming care residing in northcentral Wisconsin. A mixed deductive-inductive approach was used for qualitative thematic analysis.

Results: A total of 10 interviews were completed. Qualitative analysis revealed 3 key themes contributing to positive and negative experiences with health care providers: education, cultural competency, and access.

Discussion: Patients reported feeling supported by health care providers but not always that providers were well equipped to address their specific health needs. The attitudes of all members of the health care team contributed to participants' feelings of acceptance and comfort in the health care environment. Participants living in rural areas cited transportation challenges and provider scarcity as barriers to gender-affirming care.

Conclusions: Health care providers play an important role in mitigating health disparities among transgender patients. Experience providing gender-affirming care, nonjudgmental attitudes, and visible displays of allyship are associated with positive clinician-patient relationships.

INTRODUCTION

Despite increasing representation and acceptance of transgender people, defined by the World Professional Association for Transgender Health as those whose gender identities or expressions differ from those attributed to their sex assigned at birth,[1,2] transgender individuals in the United States continue to report unequal treatment or harassment in health care settings.[3] With increasing politicization of transgender identities and efforts to curtail or restrict access to gender-affirming care (GAC),[4] transgender patients experience social, institutional, and financial obstacles to obtaining necessary health care—particularly in rural settings. In Wisconsin, a 2019 study found that transgender patients were 2.76 times more likely to receive poor-quality health care compared with their heterosexual cisgender counterparts and 2.78 times more likely to report lifetime experiences of unfair treatment in health care.[5] Nationally, transgender individuals are more than twice as likely as cisgender individuals to delay health care due to cost, particularly in rural areas.[6] For some transgender patients, health care may be associated with negative emotions such as anxiety and depression.[7] Mental illness, illicit substance use, and risky sexual behaviors—which are more prevalent among transgender than cisgender persons, even in rural areas—pose additional burdens to patients seeking care.[8]

Recent advancements, including the establishment of GAC in areas such as northcentral Wisconsin—loosely defined as the region north of Adams and Marquette counties and extending from Iron to Florence counties—have made health care more accessible for transgender patients. However, whether these changes have led to measurable improvements in perceived health outcomes and experiences remains unclear. This study sought to assess current health needs among transgender individuals in northcentral Wisconsin, including needs for GAC and attitudes toward GAC providers.

While numerous health care facilities serve northcentral Wisconsin, there are few clinicians trained specifically to meet the

• • •

Author affiliations: Medical College of Wisconsin-Central Wisconsin, Wausau, Wisconsin (Kee, Norrbom).

Corresponding author: Liane Kee, MD, email liane.kee@gmail.com; ORCID ID 0009-0006-3255-0834

needs of transgender patients. The Aspirus Wausau Family Medicine Residency program in Wausau, Wisconsin, founded in 2019, includes GAC in its curriculum, including management of hormone therapy (HT) based on an informed consent model. This makes it one of the few institutions in northcentral Wisconsin that does not require referral from a mental health professional attesting to gender identity/dysphoria.[9] As with most rural programs, the residency program's reach extends beyond Wausau, and it relies heavily on larger health systems for specialized services such as gender-affirming surgery (GAS). However, its patient population—which includes residents of both urban and rural areas—provides an opportunity to examine the intersection of rurality and transgender identity. Previous qualitative studies have explored rural-urban differences in transgender health care,[6,7,10] but northcentral Wisconsin is unique because of its connection to sparsely populated northern counties and reliance on large academic health care institutions in the southern half of the state. This study offers an opportunity to evaluate the health needs of transgender patients who are within reach of rural outreach efforts but are overlooked in favor of urban populations.

Box. Semistructured Interview Script

1. How would you describe your gender identity? Sexual orientation?
2. How would you describe your educational background?
3. How would you describe your current socioeconomic status?
   a. How does this affect your health care decisions?
4. What are the most important parts of your identity (race, gender, sexuality, etc.)?
5. What is your gender transition timeline? How would you describe your story/process of transition?
6. Who/what is your primary resource for health concerns (PCP, Internet, friends)?
7. Have you previously disclosed your gender/sexual identity to your health care provider(s)?
   a. If so, what prompted it?
   b. If not, why?
8. Have you ever felt uncomfortable disclosing your gender/sexual identity to a health care provider?
9. Have you ever felt disrespected in a health care setting because of your gender/sexual identity?
10. Have you ever felt supported/respected in a health care setting after disclosing your gender/sexual identity?
11. What made you feel comfortable or uncomfortable about the setting?
12. Do you receive gender-affirming care through your PCP?
    a. If not, from whom do you currently or plan to receive gender-affirming care?
13. Do you receive sexual/reproductive health information or care from your PCP?
14. Do you feel that your PCP is adequately equipped to answer questions about your specific health needs?
15. Do you receive mental health care? If so, from whom? Does your relationship with this provider differ from that with your PCP?
    a. Do you disclose your sexuality to your mental health provider?
16. What are the qualities you most value in a health care provider?
17. Do you think that your gender transition process was supported by your health care provider?
18. Have you ever felt included or excluded by the physical health care environment? What does a "welcoming" space look like?
19. What are some gaps in health care or education in the community that you have personally identified? What could be improved?
20. Is there anything else you'd like to mention?

Abbreviation: PCP, primary care provider.

METHODS

A series of semistructured interviews was conducted among transgender patients at the Aspirus Wausau Family Medicine Residency Clinic to (1) identify recommendations for more inclusive transgender health care in northcentral Wisconsin, (2) identify shared characteristics contributing to positive and negative health care experiences, and (3) identify gaps in health care provision for this community. This project was reviewed and approved by the Aspirus Institutional Review Board (IRB # 23-02-649).

Participant Recruitment

Participants were recruited from a convenience sample of clinic patients who were (1) aged 18 years and older, (2) identified as transgender (eg, diagnosis of gender dysphoria or similar), (3) had an established primary care provider (PCP), and (4) had seen their PCP between January 2022 and December 2024 (N = 115). Snowball sampling was also used. Participants were contacted via documented phone numbers and email addresses (N = 16, response rate = 13.9%) to voluntarily opt-in. No incentives were provided.

Data Collection

A 20-question interview guide (Box) was developed based on a preliminary review of literature on transgender health disparities[10,11] identifying gaps such as sexual and reproductive health, mental health care, and clinician knowledge of transgender health care.[11] The investigators drew on Fredriksen-Goldsen et al's Health Equity Promotion Model—which examined the intersectionality of transgender identity with education, socioeconomic status, and race—and Meyer's Minority Stress Model—which proposed that negative mental health outcomes in minorities are prompted by internal and external stressors.[12,13] Questions addressing these factors were included to contextualize participants' lived experiences and investigate their effect on health care encounters. Most questions were open-ended, per Consensual Qualitative Research recommendations,[14] to allow follow-up probes and elicit personal experiences.

Interviews ranged from 15 to 60 minutes and were conducted by study team member LK between October 2023 and March 2025 via telephone, video conference, and in person. Participants consented to audio recording for transcription. All identifiers were removed from the transcripts before analysis; only gender and age were available to coders.

Table. Qualitative Themes on Transgender Health Care Experiences

Key Theme/Subtheme	Mentions n (%)	No. of Mentions	Representative Quote
Education			
Provider expertise	10 (100)	41	"[My doctor] has even asked me things that I didn't even think about; for example, if I wanted to freeze my sperm and if I had any plans for kids in the future."
Rural representation	9 (90)	28	"I just feel like right now gender-affirming care, even these days, is severely lacking in rural communities and that's where most care needs to be focused and updated."
Continuing medical education	5 (50)	12	"She was supportive, but she didn't feel comfortable with the actual medicine side of it. She acknowledged a gap in knowledge on her part, and she just felt really intimidated by that."
Cultural Competence			
Community stigma	9 (90)	51	"I often feel pretty uncomfortable just living in Wausau and in Wisconsin. It's not like some places I've been, for sure, but I've been harassed. I've had people threaten me. I definitely think twice about a lot of stuff."
Provider stigma	8 (80)	23	"I was asked the question 'Are you sexually active…What was your partner's gender?' I said, 'I'm a lesbian.' And she said, 'Well when's the last time you had straight sex?'"
Symbols of allyship	8 (80)	14	"As far as what stuff that I might look for [in the physical health care environment]…even those little pride stickers that say, 'this is a safe space'…goes a long way."
Use of correct pronouns	6 (60)	8	"You can tell when people are having trouble doing it. You can tell when people are comfortable with it, and they use my name and pronouns without hesitation."
Documentation of name	5 (50)	13	"I had a psych admission due to a suicide attempt…They took me into the hospital, and they put a band on my wrist that said my deadname – or my birth name – and that just made me feel worse."
Misgendering	4 (40)	5	"I am aware that to most people I look 'trans'…because people who are trying to be supportive still misgender you. It's not like they're trying to hurt me; it's just somewhere in the back of their head they think 'boy.."
Access			
Cost	9 (90)	27	"I had all this hope that I was going to get top surgery relatively soon, but now I learned I can't, and I have to pay out of pocket for it."
Autonomy	9 (90)	41	"I don't think anybody wants to be told 'I'm the doctor, I know everything, you can't have an opinion.' That doesn't feel great."
Informed consent model	4 (40)	5	"I know some people have had to see somebody for mental health first before being given a diagnosis of gender dysphoria so they could get treatment."
Transportation	3 (30)	11	"I notice that there's still a lack of HRT [hormone replacement therapy] doctors, because I still have to go to Wausau to see one, and that's 45 minutes away from me."

Data Analysis

Transcripts were analyzed by 4 independent coders and 1 auditor (undergraduate and medical students). Coders met prior to analysis to discuss potential biases. Preliminary themes were identified inductively and iteratively refined through reduction and merging until consensus was reached. This process generated a pooled preliminary codebook (domains), which was further refined to create a revised version containing themes (core ideas) and subthemes. An independent auditor reviewed the codebook and discussed reconciliation and refinement of themes with coders. Themes were then applied across all interviews for cross-analysis.[14] A mixed deductive-inductive approach was used to categorize core ideas: inductive identification of themes followed by categorization within the study framework.

RESULTS

Of 16 interested participants, 11 interviews were scheduled, and 10 were completed. Participants were aged 19 to 75 years. Five identified as transgender women, 3 as transgender men, 1 as transmasculine nonbinary, and 1 as transfeminine nonbinary. Eight participants were current residents of northcentral Wisconsin and 2 were former residents. Nine identified as lesbian, gay, bisexual, or queer in addition to transgender. No participants identified race as central to their identity. Education ranged from high school diploma to some undergraduate education, and 8 described their socioeconomic status as "low."

Qualitative analysis identified 3 major themes: education, cultural competence, and access (Table).

Education

Most participants cited gaps in provider and community education as barriers to GAC, particularly in rural areas. One participant, a 75-year-old transgender woman, stated that her transition was suppressed for most of her life due to a lack of transgender visibility in her community.

> *"I didn't plan on coming out. I really didn't understand what transitioning was. I didn't even know the word. I hadn't even met a trans person until I was 72 years old. I didn't know anybody. I didn't read anything about it. All I knew is that I wanted to be a girl and it just wouldn't go away."*

Participants who received GAC at the clinic endorsed satisfaction with provider knowledge of hormone therapy and other GAC procedures and specifically sought clinicians advertising themselves as LGBTQ+ friendly. However, several noted generational differences in training:

> *"When there are providers that see fewer trans people…they don't*

really encounter them that often, so they have a lot of misconceptions and they don't keep themselves updated, things like that."

Due to this knowledge gap, participants often felt compelled to research their own health conditions and educate their clinicians about their health needs.

Cultural Competence

Nearly all participants reported antitrans stigma from community members or health care providers. Community stigma often involved overt harassment, according to a transgender woman:

"Twice, people have yelled things at me. One person shouted at me across a whole restaurant and [my dad] chased him out to the parking lot. And someone else mumbled something under their breath and ran out [right after]...people occasionally shout something out of their car."

Meanwhile, provider-related stigma was often subtle and nonverbal.

"As a trans person, you learn how to read people's body language; because it's a professional setting, they're not going to say anything. But to know how they really feel, you just read their body language. Whether they wince away from you or seem kind of grossed out by you, not wanting to look at you, or on the flipside staring at you, acting strange."

Supportive behaviors included correct use of names and pronouns and visible signs of allyship, such as pride flags and badges. Clinicians perceived as "supportive" also demonstrated open, nonjudgmental body language.

Access

Patients faced multiple barriers to GAC, including financial difficulties and/or insurance coverage, particularly for GAS and sterilization procedures.

"My health insurance has something specifically written in their policy about how they won't cover anything gender-affirming. I was looking at getting top surgery...I found out my insurance covers the surgery, but with the diagnosis code of gender dysphoria, they won't cover it."

However, the most frequent complaint was limited patient autonomy, with clinicians perceived as exerting a disproportionate amount of power, gatekeeping care that participants felt was necessary to their health and well-being.

"You're all alone in this sterile little room with this person that—based on what kind of impression you, this vulnerable patient, [make] on them—can decide whether or not to treat you...You're at the whim of this one person who has a lot of power over you."

Conversely, patients praised the informed consent model, which improved access to medically assisted transition by removing requirements for a gender dysphoria diagnosis from a mental health care provider.

DISCUSSION

Although participants praised GAC providers' efforts at the Aspirus Wausau Family Medicine Residency, limited clinician knowledge remains a barrier to accessing local care. Because GAC is not universal in residency or continuing medical education, these knowledge gaps are likely to persist without intervention or curricula revision. However, pilot programs have demonstrated improvements in clinician empathy and awareness toward transgender patients.[15]

GAC management is an emerging skillset, and health care for LGBTQ+ patients extends well beyond the physical. Cultural competency is essential as clinician attitudes towards gender identity significantly influence the patient-provider relationship. Documentation of gender, sex assigned at birth, and sexuality in electronic medical records may provide quantitative insight into health disparities within this population,[16] while displays of allyship—such as using a patient's correct name and pronouns and minimizing gendered language—can foster an atmosphere of acceptance and support, as can recognition of microaggressions (ie, acts of unconscious discrimination that may convey hostile or derogatory attitudes).[17] Importantly, this commitment must be upheld by all members of the care team, as interactions across the care team shape the overall experience.[18] While this study focused primarily on the attitudes of health care providers, valuable insight can be gained by examining the behaviors of nurses, medical assistants, social workers, and other professions involved in patient care.

Access to care for transgender patients in rural areas is particularly challenging due to financial strain and provider scarcity. GAC is more accessible to patients with high health literacy who understand the informed consent model and can independently identify GAC providers, underscoring the need for proactive communication by clinicians with GAC experience.[19] However, as transgender identity becomes increasingly politicized, there are potential social and financial costs of openly advertising such information, highlighting the importance of system-level support. Although Wisconsin has relatively supportive policies,[4] challenges with insurers and clinician availability often prevent patients from obtaining care in a timely manner.

Our findings with prior research showed that systemic factors—such as insurance exclusions and rural health care access—shaped transgender patients' health care experiences just as much as patient-provider interactions.[18,20] While many of these factors are beyond individual control, clinicians play a key role in facilitating access and affirming patients' identities.

Limitations

This study was limited by a small sample size (N = 10), representing a fraction of patients who receive GAC from Aspirus Health. While this study captured perspectives of transgender patients of lower socioeconomic status, it did not explore the impact of other

marginalized identities such as race. Self-selection bias may have influenced participation due to concerns of prejudice or confidentiality and may reflect more polarized attitudes toward health care systems. Participants varied in transition stage and experience with GAC, potentially affecting their perspectives. Further research is needed to assess the degree of comfort with individual members of the health care team and which professions within the clinic are most or least likely to provide support.

CONCLUSIONS

Semistructured interviews (N = 10) conducted with transgender patients in northcentral Wisconsin identified 3 primary themes: education, cultural competence, and access. Provider knowledge gaps remain a major barrier to obtaining local care. Positive experiences were associated with culturally competent practices, including correct use of names and pronouns and displaying symbols of allyship in the clinic. External factors – including transportation, financial burden, and insurance coverage – limit GAC access despite informed consent models removing the need for mental health referral.

Expansion of GAC services in rural settings is encouraging but remains limited. Improving health outcomes for transgender patients will require enhanced provider education and integration of transgender health into broader health care systems. Clinicians can support transgender patients by incorporating continuing medical education into their practice and upholding cultural competence across all members of the care team.

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgments: The authors thank Kevin O'Connell, MD, Chanteal Findling, DO, and Jacob Prunuske, MD, Aspirus Family Medicine Residency Clinic, for their support and guidance on their project as well as their commitment to transgender health care in northcentral Wisconsin; Samantha Smazal, Aspirus Family Medicine Residency Clinic, for her support during the data collection process; Clayton Piergrossi, Area Health Education Communities, and Autumn Capper, Carolyn Storch, and Marin Stowe, Medical College of Wisconsin-Central Wisconsin, for their coding assistance.

REFERENCES

1. James SE, Herman JL, Rankin S, Keisling M, Mottet L, Anafi M. *Executive Summary of the Report of the 2015 U.S. Transgender Survey.* National Center for Transgender Equality; 2016.

2. Coleman E, Radix AE, Bouman WP, et al. Standards of care for the health of transgender and gender diverse people, version 8. *Int J Transgend Health.* 2022;23(Suppl 1):S1-S259. doi:10.1080/26895269.2022.2100644

3. Lerner JE, Robles G. Perceived barriers and facilitators to health care utilization in the United States for transgender people: a review of recent literature. *J Health Care Poor Underserved*. 2017;28(1):127-152. doi:10.1353/hpu.2017.0014

4. Kline NS, Webb NJ, Johnson KC, Yording HD, Griner SB, Brunell DJ. Mapping transgender policies in the US 2017-2021: the role of geography and implications for health equity. *Health Place*. 2023;80:102985. doi:10.1016/j.healthplace.2023.102985

5. Jennings L, Barcelos C, McWilliams C, Malecki K. Inequalities in lesbian, gay, bisexual, and transgender (LGBT) health and health care access and utilization in Wisconsin. *Prev Med Rep*. 2019;14:100864. doi:10.1016/j.pmedr.2019.100864

6. MacDougall H, Henning-Smith C, Gonzales G, Ott A. Access to health care for transgender and gender-diverse adults in urban and rural areas in the United States. *Med Care Res Rev.* 2024;81(1):68-77. doi:10.1177/10775587231191649

7. Knutson D, Koch JM, Arthur T, Mitchell TA, Martyr MA. "Trans broken arm": health care stories from transgender people in rural areas. *J Res Women Gend*. 2016;7:30-46.

8. Horvath KJ, Iantaffi A, Swinburne-Romine R, Bockting W. A comparison of mental health, substance use, and sexual risk behaviors between rural and non-rural transgender persons. *J Homosex.* 2014;61(8):1117-1130. doi:10.1080/00918369.2014.872502

9. Ashley F, St Amand CM, Rider GN. The continuum of informed consent models in transgender health. *Fam Pract.* 2021;38(4):543-544. doi:10.1093/fampra/cmab047

10. Knutson D, Martyr MA, Mitchell TA, Arthur T, Koch JM. Recommendations from transgender healthcare consumers in rural areas. *Transgend Health*. 2018;3(1):109-117. doi:10.1089/trgh.2017.0052

11. Wanta JW, Unger CA. Review of the transgender literature: where do we go from here? *Transgend Health*. 2017;2(1):119-128. doi:10.1089/trgh.2017.0004

12. Fredriksen-Goldsen KI, Simoni JM, Kim HJ, et al. The health equity promotion model: reconceptualization of lesbian, gay, bisexual, and transgender (LGBT) health disparities. *Am J Orthopsychiatry*. 2014;84(6):653-663. doi:10.1037/ort0000030

13. Meyer IH. Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: conceptual issues and research evidence. *Psychol Bull*. 2003;129(5):674-697. doi:10.1037/0033-2909.129.5.674

14. Hill CE, Knox S. *Essentials of Consensual Qualitative Research*. American Psychological Association; 2021.

15. Lelutiu-Weinberger C, Pollard-Thomas P, Pagano W, et al. Implementation and evaluation of a pilot training to improve transgender competency among medical staff in an urban clinic. *Transgend Health*. 2016;1(1):45-53. doi:10.1089/trgh.2015.0009

16. Cahill S, Makadon H. Sexual orientation and gender identity data collection in clinical settings and in electronic health records: a key to ending LGBT health disparities. *LGBT Health*. 2014;1(1):34-41. doi:10.1089/lgbt.2013.0001

17. Nadal KL, Whitman CN, Davis LS, Erazo T, Davidoff KC. Microaggressions toward lesbian, gay, bisexual, transgender, queer, and genderqueer people: a review of the literature. *J Sex Res.* 2016;53(4-5):488-508. doi:10.1080/00224499.2016.1142495

18. Hostetter CR, Call J, Gerke DR, Holloway BT, Walls NE, Greenfield JC. "We are doing the absolute most that we can, and no one is listening": barriers and facilitators to health literacy within transgender and nonbinary communities. *Int J Environ Res Public Health*. 2022;19(3):1229. doi:10.3390/ijerph19031229

19. Holloway BT, Gerke DR, Call J, et al. "The doctors have more questions for us": geographic differences in healthcare access and health literacy among transgender and nonbinary communities. *Qual Soc Work.* 2022;22(6):1073-1091. doi:10.1177/14733250221128000

20. Tillewein H, Becker J, Kruse-Diehr A. Institutional barriers to healthcare services among transgender individuals in the rural Midwest. *J Homosex.* 2024;71(9):2099-2115. doi:10.1080/00918369.2023.2222204

Perspectives of Clinical Genetics in Wisconsin: A Qualitative Analysis to Enhance Awareness About the Specialty and Guide Improvement

Isabella A. Sorci, BS; Nathan J. Siewert, BS; Elizabeth M. Petty, MD

ABSTRACT

Introduction: Genomic advances have launched medicine into a new frontier of preventive and personalized care, driving increased demand for services amid a recognized provider shortage. We aimed to highlight perspectives of clinical geneticists to support growth and sustain genetics care for patients in Wisconsin in the face of rising demand.

Methods: A literature review informed the development of interview questions for appreciative inquiry-guided interviews. University of Wisconsin-affiliated geneticists were interviewed in the summer of 2024 about their experiences and insights. Transcripts were analyzed using an open inductive process, and hierarchical qualitative analyses were conducted to identify themes and opportunities to increase interest in genetics as a career.

Results: Regarding their profession, 92% of respondents identified "problem-solving" as a favorite aspect, highlighted the benefits of interprofessional collaboration, and identified diagnostic improvements as the most notable change over their careers. Regarding the future of genetics, 75% expressed excitement about improving treatments, anticipated a shift in their roles from diagnostics to management, and encouraged trainees across health professions to engage in genomic medicine learning opportunities.

Conclusions: Clinical geneticists expressed strong enthusiasm for their careers, noting problem-solving, continuity of care, and patient diversity as key highlights. Their roles provide opportunities to lead interdisciplinary teams, collaborate across specialties, and engage in lifelong learning. Their experiences offer insight into future diagnostic and treatment advances, which will require innovative care delivery approaches, including greater delegation and expanded training for the broader health care workforce. These perspectives may help foster interest in clinical genetics among health care trainees.

• • •

Author affiliations: University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Petty, Siewert, Sorci).

Corresponding author: Isabella A. Sorci, email Sorci@wisc.edu; ORCID ID 0009-0008-8218-1621

INTRODUCTION

Over the last decade, significant advances in the field of genetics have had a positive impact on patient care. With personalized approaches to preventive medicine, providers are making more accurate diagnoses, providing more effective treatments, and identifying risk factors to help mitigate health complications.[1] These advances range from pharmacogenetics—using genomic data to predict therapeutic responses and avoid adverse reactions[2]—to advances in prenatal care that can significantly influence health outcomes for future generations.[3]

As genomic testing becomes increasingly accessible, demand for these services has increased, although payer-related barriers remain.[4] Genetic testing has rapidly evolved from sequencing single genes to genome- and exome-wide sequencing, placing increasing burdens on the already limited pool of qualified clinical geneticists.[5] These test results yield large volumes of data that require substantial time and effort to interpret. Often, there are many variants of uncertain significance, necessitating additional testing, thoughtful follow-up, and investigation in the literature and the Clinical Genome Resource, a standardized international organization with expert panels that delineate genetic variants.[6]

The multisystem involvement and complexity of many genetic conditions—including incomplete penetrance, variable expressivity, etiologic heterogeneity, and diverse inheritance patterns—require that providers understand a broad spectrum of

symptoms presenting in patients and their families. Exome-wide sequencing is becoming a standard of practice to help diagnose some conditions, while genome-wide sequencing is becoming more readily available, resulting in increased demand for clinical genetics services.[7]

With this growing need, there is concern regarding multiple factors, including the limited number of trainees entering the field, with residency and fellowship positions going unfilled, and a workforce in which many clinical geneticists are approaching retirement.[8] Despite newer delivery models such as telehealth to improve access, limitations persist due to the overall shortage of providers.[9]

To address the demand for genetic services, we aimed to gain a deeper understanding of the field in Wisconsin by gathering insights directly from clinicians affiliated with the University of Wisconsin School of Medicine and Public Health (UWSMPH). Our goal was to identify strengths and successes that could inform quality improvement interventions to expand and sustain clinical genetics care for patients in Wisconsin and beyond.

METHODS

Project Design

A literature review spanning 6 years (2019-2025) was performed to outline the current state of clinical genetics in the United States. The following search terms were used: ("medical genetics workforce"[tiab] OR "genetics, medical"[tiab] OR "medical genetics"[tiab] OR "medical geneticist"[tiab] OR "clinical geneticist"[tiab] OR "clinical genetics"[tiab] OR "genetics, clinical"[tiab] OR "genetic services"[tiab]) AND (workforce[tiab] OR workforces[tiab] OR "work force"[tiab] OR staffing[tiab]).

Insights from the review guided development of 6 interview questions and probes to explore the perspectives of clinical geneticists currently or recently affiliated with UWSMPH, including changes they have observed in their practice over time, and perceptions of the field's future. The interview questionnaire was developed by research team members (IAS and EMP) using an appreciative inquiry approach[10] based on the "Discover and Dream" structure. This strengths-based approach emphasizes interviewees' positive experiences to identify opportunities for sustainable and transformative change.[11]

A preamble was used before each interview to outline study goals and obtain consent for recording and transcription. The University of Wisconsin-Madison Institutional Review Board (IRB) Quality Improvement/Program Evaluation Self-Certification Tool (irb.wisc.edu/is-it-research) was used to determine that this project met criteria for quality improvement, met the federal definition of research pursuant to 45 CFR 46, and did not require IRB review.

Participant Recruitment

To recruit interviewees, 16 emails were sent to all current physicians practicing genomic medicine, 2 former faculty members, and 1 former trainee affiliated with UWSMPH. Of the 15 who responded, 1 declined participation and 2 were unavailable within the 4-week study period. All 12 physicians who were available and willing were chosen as participants.

Table 1. Respondent Demographics

	Percent (n)
Primary certification	
Pediatrics	83% (10)
Secondary genetics certification	
Biochemical	33% (4)
Clinical	92% (11)
Molecular/Cytogenetics	8% (1)
Years of experience practicing genomic medicine	
0–9 years	25% (3)
10–19 years	33% (4)
20–29 years	8% (1)
30+ years	33% (4)
University of Wisconsin School of Medicine and Public Health Affiliation	
Current faculty member	75% (9)
Training (medical school, residency, or fellowship)	75% (9)
Former faculty member	17% (2)
Respondent race	
American Indian or Alaska Native	0%
Asian	17% (2)
Black or African American	0%
Hispanic or Latino	0%
Native Hawaiian or Other Pacific Islander	0%
White	83% (10)
Respondent gender	
Female	50% (6)
Male	50% (6)
Nonbinary/other	0%

Following each interview, demographic data were collected, including institutional affiliation, board certification, years of experience, and self-reported race and gender identity.

Data Analysis

Transcripts were generated from interview recordings and evaluated and corrected as needed to ensure accuracy. Using an open inductive process,[12] a codebook was developed from concepts identified in the transcripts. An independent coder (NJS) was recruited, and the codebook was used as a guide for the 2 coders (IAS and NJS) to independently code transcripts.

Initial intercoder reliability was approximately 90% (211/235 agreements). Following independent coding, the coders met to reach consensus on 24 discrepancies among the 235 codes. Using the finalized data, hierarchical qualitative analyses were performed to identify key themes and potential areas for intervention to address the clinical geneticist shortage.

RESULTS

Physician Interviews

Of the 12 current and former UW faculty members and trainees who participated, 6 identified as female and 6 as male; most identi-

Table 2. Discover Medical Genetics: Themes Identified Highlighting the Field

Themes,	% of Respondents (n)	Quote
Highlights of being a clinical geneticist		
Problem-solving	92% (11)	I like the problem-solving aspect; you're presented with unusual signs, symptoms, examination, features, laboratory results, trying to put that all together. It's like putting a puzzle together or being a detective, I imagine.
Continuity of care	67% (8)	We see them throughout their lifespan – for several of these disorders, we can have a child that would otherwise have significant developmental delay or may have passed away from that disorder – they can be happy toddlers coming into your office and then normal sullen teens and now… we get to help care for them as they have their own families too.
Patient diversity	50% (6)	In genetics, you deal with all populations, so I have patients from basically the newborn period through geriatric age patients… there's also diversity in terms of the kinds of issues they're dealing with, from intellectual and cognitive issues to physical issues… and there's a lot of long-term chronic issues but there's also acute issues… I really like that diversity.
Lifelong learning	33% (4)	We learn new things and get to apply new kinds of cutting-edge technology to patient questions that maybe could not have been answered a year or 2 years ago, that now we can answer… I find that sort of constant learning and interpretation of literature to real world, practical patient care very exciting and stimulating.
Good community	33% (4)	I think the people who are in genetics are awesome.
Public health/ advocacy	25% (3)	Newborn screening is a great public health program, and as clinical geneticists we are an important component to that public health program that really can provide great preventive care and help with morbidity and mortality for rare metabolic disorders.
Practice variety	8% (1)	It's also been rewarding in terms of related nonclinical issues like being able to participate in research and teaching and mentoring.
Roles of a clinical geneticist		
Multidisciplinary teamwork within clinic	92% (11)	In our clinic, I work with genetic counselors, nurses, medical assistants, a genetic counseling assistant, and also dietitians.
Multidisciplinary teamwork across specialties	83% (10)	Most of the multidisciplinary clinics or teams that we're involved with as geneticists deal with relatively rare conditions. When they involve other specialists, I mean the clinics that I think about are involving surgeons, sometimes neurosurgeons, sometimes other surgical specialists, dermatology is a very common accompanying service, neurology…
Leadership role	50% (6)	I had more of a leadership role in genetics, really making sure we had really strong interdisciplinary teams and conferences.
Multidisciplinary teamwork across institutions	33% (4)	I find that when you reach out for help, people are really willing to give you advice on what their experience has been and also let you know either who are the right people to ask for if there's clinical trials going or not, but there's ways to get in contact with them… there's a lot of collaboration within the community and I shouldn't just say in the US because it is abroad as well.
Educator role	25% (3)	One of the other things I love about [being a clinical geneticist] is that there's learners from different backgrounds and fields.
Learner role	17% (2)	If you have a patient where you really haven't seen this before, there's always someone who is happy to have you run it by them and you can learn from their experience to help better care for the patients.
Changes in the field of clinical genetics		
Diagnostic improvement	92% (11)	We're able to diagnose so much more now that we have higher yield in the testing… that has limited the diagnostic Odyssey. For years…we'd do all kinds of blood work and MRIs and muscle biopsies… A lot of the things we find now we never would have anticipated… that has just revolutionized the field, and it's just made it more productive.
Increased need for lifelong learning	33% (4)	My role is really lifelong learning and trying to keep up to date. Every patient I see in clinic – literally there are hours of preparation in the sense of reading like what's all the current research, what's new because things change so rapidly. I guess I really like… the intellectual curiosity.
Expanding diversity of patients/conditions	25% (3)	With the increase in testing, we can help people with other conditions that we might not have seen as much before.
Increased utilization of genetics services	25% (3)	Thinking about utilization management around genetic testing, especially if a genetic specialist is not shepherding every single genetic test through the process. How do we put up guardrails to help people successfully order testing, order the right test at the right time?
Increasing negative financial pressure	17% (2)	Trying to make a financial case for our services, even a simple financial case for our services is very challenging.
Newborn screening improvement	8% (1)	Now, in the NICU when we suspect something, within days, we have… [a] diagnosis back. So, it's very reassuring that we can do diagnoses very fast, and it can change management."

Abbreviations: MRI, magnetic resonance imaging; NICU, neonatal intensive care unit.

fied as White (10/12), with the remaining respondents identifying as Asian (2/12). Most respondents held a primary board certification in pediatrics (10/12) and a secondary certification in clinical genetics and genomics (11/12). Although their primary certification was in pediatrics, these clinicians treat patients of all ages, including those with adult-onset genetic conditions. Additionally, one-third of the respondents had been practicing for 30 years or more, and 9 were current UWSMPH faculty members (Table 1).

Discover Themes: Responses to Questions About the Profession

Highlights of Being a Clinical Geneticist: Participants most frequently cited problem-solving (11/12) when asked to identify highlights of being a clinical geneticist. Continuity of care was

Table 3. Future of Medical Genetics: Themes Identified in Discussing the Future

Themes	% of Respondents (n)	Quote
Future benefits of clinical genetics		
Treatment improvement	75% (9)	I'm much more optimistic in my counseling of families than I was earlier in my career, because I honestly believe that many of these disorders, most of them are going to have treatments in the near future.
Diagnostic improvement	58% (7)	The more we learn about the human genome and the more tests we do on our patients the better we'll be able to make diagnoses.
Greater understanding of variants and polygenic disease	33% (4)	The collation and understanding of variants – which variants are pathogenic. I think we will get there, because ultimately there is a finite number of variants. But, maybe that's through the use of AI (artificial intelligence) where we start to determine which variants we need to worry about.
Prognostic improvement	33% (4)	The broader, more accessible genomic testing means in general people are getting diagnosed earlier and that gives us a longer runway to kind of understand their trajectories and to lean on research to optimize their care.
Improvement of genomic medicine delivery	25% (3)	Working with genetic counselors to figure out what is the most effective way to utilize clinical geneticists that are broadly trained in genetics versus in specific specialty areas. I don't think the old model where we saw every patient with genetic conditions is a viable model in the future and so we [need to] harness our expertise as well as share that expertise.
Public health and access improvement	17% (2)	We're on the cusp of sort of a new generation of clinical genomic testing that we'll have access to that insurance will pay for.
Newborn screening improvement	8% (1)	We've increased the number of disorders we can screen for so we can start our treatments really early, and I think we're going to see genomic newborn screening.
Future of the clinical geneticist role		
Increased delegation/ oversight role	75% (9)	There's a mismatch between demand and my ability to have a personal touch on every case… I think there might have to be an evolution where certainly we have to teach people to better understand the nuances of genetic testing and… interpretation. I wonder if there needs to be a sort of more supervisory role of geneticists or expansion of other people with expertise.
Increase access to genomic medicine training for other providers	67% (8)	I think we need to do more with collaborating with other boards… internal medicine or family practice. There should be opportunities to get certifications in genetics to show that these individuals have taken courses, passed knowledge tests, and are capable of doing more advanced genetic practice than others who haven't had that training. They can be sort of the ones in their specialties focused on genetic aspects that their colleagues can go to for help if there's not a geneticist immediately available.
Diagnostician to management	25% (3)	I'm hoping that we will be able to be not only diagnosticians but have an increased role in management and treatment than what we've previously had.
More involved in common disorders	25% (3)	I hope that we have testing for multifactorial common disorders. I hope that we are involved in that in some way and that can be kind of rolled out to the general medical field, so things like polygenic risk scores. Even better than that, to be able to predict how multiple small effects result in common disorders.
Increased advocacy for health equity	17% (2)	Especially thinking about health equality – we need to make sure that this type of care is available regardless of what your insurance is and regardless of where you live… we need to be very mindful of how we go about training people to make sure that everybody has the opportunity to take advantage of genomic medicine and have their care improved from [it].
More specialized	17% (2)	I think we're going to be more specialized, where a geneticist might focus in a particular area, somebody who is trained in cancer genetics or neurogenetics or some other discipline and they focus on patients in that with that population and/or general geneticists that really focus on the multisystemic conditions that are more complex and that are rare enough or unique enough.
Advice for current trainees in health care		
Embrace lifelong learning	75% (9)	[I hope] that everybody in every specialty would be interested in the genomic basis to the kinds of conditions they're seeing in their own clinical practices and that they would have opportunities for additional lifelong learning and training to gain that expertise so that they're comfortable and understand the utility [and validity] of genomic tests [and know] how to provide information.
Increase collaboration with genetics	50% (6)	People in genetics are happy to talk with other subspecialties about how it could be integrated into their field… so that the right patients are getting to us and the right type of genomic medicine is being used within their practice. Those are conversations we're going to need to have to make sure everybody can benefit from this expansion of testing and knowledge.
Know your own limitations	25% (3)	If you think you're able to provide genetics care, even limited in your specialty, you need to do all the aspects that that care provision requires, including the counseling, navigating the insurance parts, and all of that.
Understand the limitations of genomic	17% (2)	Sometimes we get consults for very nonspecific sorts of things because they don't know what's going on. Well, that's not a use for genomic technology in most cases. You need to have objective clinical findings that are suggestive of a testing Mendelian disorder if you want to use single gene or genomic testing to try to solve that problem.
Advocate for health equity	8% (1)	I want to make sure that if we have new technology, be it new gene therapies or new genetic tests, that those are widely available by the insurance we have, that we apply those opportunities equally, and everybody has the opportunity to benefit. I think working towards those equity issues is really important.

the second most common theme identified (8/12), followed by patient diversity (6/12).

Role of a Clinical Geneticist: When asked to "tell me about your role as a clinical geneticist on a multidisciplinary team," 11 respondents emphasized the diversity of their teams within genetics clinics, including medical assistants, nurses, advanced practitioners, and genetic counselors, while 10 respondents discussed the specialists and subspecialists whom they work alongside. Leadership within and across clinics was the third most commonly highlighted role (6/12).

Changes in the Field of Clinical Genetics: Nearly all respondents (11/12) commented on significant improvements in diagnostic testing, with the increased need for lifelong learning mentioned next most often (4/12). "Expanding diversity of patients and conditions" and '"increased utilization of genetic services" were each mentioned by 3 respondents (Table 2).

Dream Themes: Responses to Questions About the Future of Clinical Genetics

Future Benefits of Clinical Genetics: When asked about some of the most promising ways medical genetics may benefit patients in the coming years, respondents most frequently identified improved treatments for genomic disorders (9/12), followed by diagnostic improvements (7/12) and greater understanding of variants and polygenic diseases, as well as improved prognostication (4/12 each).

Future of the Clinical Geneticist Role: The majority of participants anticipated that the role of the clinical geneticist will shift toward greater oversight, with increased delegation of responsibilities to genetic counselors, advanced practitioners, or other physicians (9/12). Similarly, 8 respondents noted increased access to genomic medicine training materials for nongenetics physicians and other providers, and 3 predicted a shift from predominantly diagnostic roles to greater involvement in patient and condition management (3/12).

Advice for Current Health Care Trainees: In response to, "What are your hopes or advice for trainees in various health care roles as genomic medicine becomes more clinically applicable, accessible, and in demand?" participants most commonly encouraged embracing lifelong learning—particularly regarding genetic disorders and treatments (9/12—and recommended that nongenetics providers increase collaboration with clinical geneticists (6/12). Additionally, 3 respondents emphasized awareness of providers' own limitations when delivering genomic medicine (Table 3).

DISCUSSION

Discover Themes

A "Discover and Dream" approach was used in the interviews to identify highlights that could help guide future recruitment efforts, given workforce shortages. Overall, participants expressed strong enthusiasm for their careers. The majority reported enjoying the problem-solving aspects of their roles, citing the ability to spend substantial time with patients, answer questions, and achieve a deeper understanding of conditions.

Participants also valued continuity of care, noting they care for entire families, see patients grow up, and support them building families of their own. Half of the interviewees cited patient diversity as a major contributor to their job satisfaction, noting that patients span all ages, backgrounds, and abilities across both acute and chronic conditions.

Regarding their roles, participants cited examples of multidisciplinary teamwork within their clinics and across specialties, institutions, and even internationally. Some attributed this to the field's collaborative and close-knit nature, particularly in the context of diagnosing and managing rare disorders. Participants also valued their roles as leaders, educators, and lifelong learners, as many work with students and find opportunities to learn through teaching and collaborating with patients and colleagues.

When asked about changes in the field, participants identified rapid advances in diagnostic techniques and treatment options. One respondent stated, "Gene therapy, gene editing, and gene modification are technologies that are already in place today. There are FDA-approved products now—gene therapies, gene modifications - that are essentially curing our patients. That was inconceivable when I started."

Given this rapidly evolving landscape, respondents also emphasized the need for lifelong learning, including the effort required to interpret emerging research and stay current with developments in the field (Table 2).

Dream Themes

Overall, respondents expressed excitement regarding the future of clinical genetics. Most anticipated that the treatment of genetic disorders will evolve, with more gene therapy and precision medicine options on the horizon. Some also noted anticipated advances in prognostic disease monitoring, enhanced newborn screening, and improved access to genomic services.

Many participants mentioned the value of expanding diagnostic capabilities and improving understanding of variants and polygenic disease in the future to optimize patient care. It was through this lens that some discussed the role of the clinical geneticist expanding into care teams of more common, chronic diseases that have genetic components, such as hypertension and diabetes.

In response to these changes and increasing demands, most respondents anticipated that they will delegate more to advanced practice providers and genetic counselors to help address the shortage of clinical geneticists. Many also emphasized the need for access to comprehensive genomic medicine training for providers and trainees at all levels as precision medicine continues to grow in applicability and relevance.

Some participants noted challenges affecting the field's desirability, including limited positive exposure to clinical genetics during training, increasing training costs relative to lower compensation compared with other specialties, and complexity of insurance coverage and reimbursement for emerging genetic tests and technology. These factors, combined with rising patient demand, were viewed as further compounding the provider shortage.

Most participants recommended that current health care trainees embrace lifelong learning and maintain curiosity about the field. Specifically, they encouraged trainees to understand the genetic and genomic basis of conditions affecting their patient populations to provide the most accurate and effective diagnoses, management, and treatments. Some also conveyed the importance of recognizing the limitations of genomic testing, as well as one's own expertise.

Participants expressed hope that more providers reach out to genetics colleagues when questions arise regarding testing and treatment for patients with genetic conditions. Finally, one respondent emphasized the importance of advocating for health equity, especially as new diagnostic and therapeutic options—many of which are not yet covered by insurance and can be costly—become available. They highlighted the need to engage historically marginalized and underrepresented communities in policy decisions and to work together to best serve all populations, particularly in the field of genetics (Table 3).

Study Limitations

Qualitative research has inherent limitations, including subjectivity of data and potential researcher influence during interviews. The generalizability of this quality improvement study is limited by the small sample size and focus on a single institution. Additionally, the appreciative inquiry "Discover and Dream" approach may have biased findings toward positive aspects of the field. The study did not comprehensively address in-depth the challenges or threats to the profession.

Future Directions

To more completely investigate the perspectives of clinical geneticists in Wisconsin, future studies should include all practicing clinical geneticists in the state and expand to other professionals providing genetic services, such as advanced practice providers, genetic counselors, and dietitians.

Research examining care models that fully integrate genetic counselors and advanced practice providers into genetics specialty clinics may identify ways to expand access and improve equity, particularly in underserved rural and urban populations. Exploring training opportunities for advanced practice providers and subspecialists to obtain certifications in genomic medicine may also ensure there are enough clinicians adequately trained to provide genomic services within their respective fields.

Similarly, genetics service workflows should be analyzed and optimized to meet increasing patient demand. These areas warrant further investigation, including more comprehensive literature review and potential meta-analysis to better define current trends and inform recruitment and genomic medicine delivery efforts.

Finally, further exploration of health care trainees' perspectives may help identify opportunities to enhance education and address the plateau in interest in advanced genetics training. Future studies should examine factors that may discourage learners from pursuing careers in genetics—including compensation insurance-related challenges—while identifying strategies to attract and retain physicians in this field.

CONCLUSIONS

Clinical geneticists in this study expressed strong enthusiasm for their profession, noting problem-solving, continuity of care, and patient diversity as key highlights. Their roles afforded opportunities to lead and participate in interdisciplinary teams, collaborate with a variety of specialists, and engage in lifelong learning. Their experiences provided insight into the future of the field, highlighting diagnostic and treatment innovations that will require new care delivery approaches, including greater delegation to other providers.

Participants also recognized the importance of ensuring adequate training for all providers to better address the genetic and genomic contributions to health, morbidity, and mortality. Overall, their reflections illustrate both the current rewards of the profession and its future promise, which may help encourage health care trainees to consider clinical genetics when exploring careers.

Financial disclosures: Elizabeth Petty, MD, reports honorariums received from the Kern National Network for Flourishing in Academic Medicine for lectures on topics related to education and well-being generally, not specific or directly related to this manuscript.

Funding/support: Isabella Sorci was supported by a summer research award from the Herman and Gwendolyn Shapiro Foundation.

Acknowledgments: The authors thank the physicians and genetic counselors who took the time to engage with this project.

REFERENCES

1. Flannery DB. Challenges and opportunities for effective delivery of clinical genetic services in the U.S. healthcare system. *Curr Opin Pediatr.* 2018;30(6):740-745. doi:10.1097/MOP.0000000000000693

2. Mosch R, van der Lee M, Guchelaar HJ, Swen JJ. Pharmacogenetic panel testing: a review of current practice and potential for clinical implementation. *Annu Rev Pharmacol Toxicol.* 2025;65(1):91-109. doi:10.1146/annurev-pharmtox-061724-080935

3. Hayeems RZ, Luca S, Xiao B, et al. The clinician-reported Genetic Testing Utility Index (C-Guide) for prenatal care: initial evidence of content and construct validity. *Genet Med.* 2025;27(1):101306. doi:10.1016/j.gim.2024.101306

4. Wiedower J, Smith HS, Farrell CL, Parker V, Rebek L, Davis SC. Payer perspectives on genomic testing in the United States: a systematic literature review. *Genet Med.* 2025;27(2):101329. doi:10.1016/j.gim.2024.101329

5. Raspa M, Moultrie R, Toth D, Haque SN. Barriers and facilitators to genetic service delivery models: scoping review. I*nteract J Med Res*. 2021;10(1):e23523. doi:10.2196/23523

6. ClinGen Consortium. The Clinical Genome Resource (ClinGen): advancing genomic knowledge through global curation. *Genet Med*. 2025;27(1):101228. doi:10.1016/j.gim.2024.101228

7. Dragojlovic N, Borle K, Kopac N, et al. The composition and capacity of the clinical genetics workforce in high-income countries: a scoping review. *Genet Med*. 2020;22(9):1437-1449. doi:10.1038/s41436-020-0825-2

8. Jenkins BD, Fischer CG, Polito CA, et al. The 2019 US medical genetics workforce: a focus on clinical genetics. *Genet Med*. 2021;23(8):1458-1464. doi:10.1038/s41436-021-01162-5

9. Maiese DR, Keehn A, Lyon M, Flannery D, Watson M; Working Groups of the National Coordinating Center for Seven Regional Genetics Service Collaboratives. Current conditions in medical genetics practice. *Genet Med*. 2019;21(8):1874-1877. doi:10.1038/s41436-018-0417-6

10. Arundell F, Sheehan A, Peters K. Developing and conducting appreciative inquiry interviews. *Nurse Res*. 2021;29(4):36-43. doi:10.7748/nr.2021.e1811

11. Carter CA, Ruhe MC, Weyer S, Litaker D, Fry RE, Stange KC. An appreciative inquiry approach to practice improvement and transformative change in health care settings. *Qual Manag Health Care*. 2007;16(3):194-204. doi:10.1097/01.QMH.0000281055.15177.79

12. Guest G, Namey E, Chen M. A simple method to assess and report thematic saturation in qualitative research. *PLoS One*. 2020;15(5):e0232076. doi:10.1371/journal.pone.0232076

An Online, Patient-Guided, Mental Health Tool Improves Anxiety Symptom Scores in Patients With Infertility

Micaela Stevenson Wyszewianski, MD; Paige Johnson, RN, BS; Ryan Hanson, MS; Amy Pan, PhD; Melodee Liegl, MS; Kate Schoyer, MD; Jayme Bosler, MD; Robert Rydze, MD; Jamie Neary, APNP; Stephanie Gunderson, MD

ABSTRACT

Introduction: Patients undergoing infertility evaluation and treatment frequently experience anxiety and depressive symptoms. Easily available and highly accessible online mental health tools have not previously been evaluated using validated screening measures in this population. The objective of this study was to assess whether SilverCloud, an online, self-guided mental health program, is associated with reductions in anxiety and depressive symptom scores among patients experiencing infertility.

Methods: A retrospective cohort study was conducted among female patients undergoing an initial infertility consultation at a single academic center. Patients completed Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) questionnaires and were offered enrollment in SilverCloud at their initial infertility consultation. Baseline PHQ-9 and GAD-7 scores from initial consultations were compared between patients who enrolled in SilverCloud and those who did not. For patients who engaged in SilverCloud, Wilcoxon signed-rank tests were used to compare PHQ-9 and GAD-7 scores before and after completion of SilverCloud modules.

Results: A total of 354 patients were included in the analysis. Fifty-two patients enrolled in SilverCloud, and 32 completed at least 1 module. Baseline data demonstrated that patients who enrolled in SilverCloud had significantly higher GAD-7 scores (0.5 vs 0; $P = .006$). Among patients who completed at least 1 SilverCloud module, PHQ-9 and GAD-7 scores decreased significantly decreased after engagement (PHQ-9: 8.0 vs 6.5; $P < .04$; GAD-7: 12.5 vs 9.5; $P = .02$).

Conclusions: Patients experiencing infertility who utilized SilverCloud experienced significant decreases in PHQ-9 and GAD-7 scores, suggesting improvement in anxiety and depression symptoms.

• • •

Author affiliations: Department of Obstetrics and Gynecology, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Bosler, Gunderson, Neary, Rydze, Schoyer, Stevenson Wyszewianski); School of Medicine, MCW, Milwaukee, Wisconsin (Johnson); Froedtert Hospital, Milwaukee, Wisconsin (Hanson); Department of Pediatrics, MCW, Milwaukee, Wisconsin (Pan); Department of Qualitative Health Sciences, MCW, Milwaukee, Wisconsin (Liegl).

Corresponding author: Micaela Stevenson Wyszewianski, MD, 9200 W Wisconsin Ave, Milwaukee, WI 53226; email micaelastevenson1@gmail.com

INTRODUCTION

Depression and anxiety rates have increased in the general population over the past decade, with women and adults aged 18 to 29 years having the highest prevalence of anxiety and depression (23.8% and 24.6%, respectively).[1] Among individuals experiencing infertility, rates of anxiety and depression are even higher.[2] The emotional toll of infertility has long been linked to anxiety and depression, with some studies estimating the prevalence of anxiety in women experiencing infertility at 36% and the prevalence of depression at as high as 52%.[2]

The increased prevalence of anxiety and depression in patients experiencing infertility is likely multifactorial[3] and due to a combination of psychological, social, treatment-related, and biological factors.[3] Patients experiencing infertility may experience cycles of intense hopefulness and disappointment with each round of fertility treatment, leading to complex feelings of uncertainty regarding their reproductive ability, limited control over their future, and distress.[3] Infertility also affects social well-being, with many patients reporting reduced social support and difficulty interacting with others in settings involving pregnancy, fertility, and children.[3] Additionally, commonly used fertility medications, including gonadotropins, leuprolide, and clomiphene, have been linked to symptoms of depression and anxiety.[4]

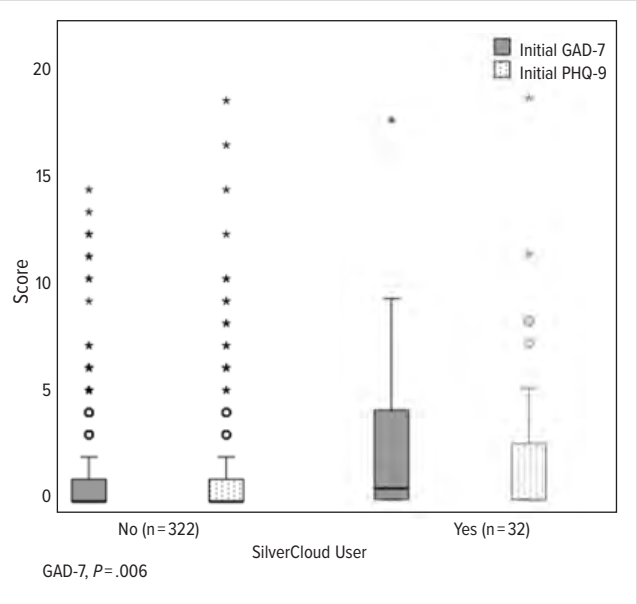
Depression and anxiety symptoms are commonly assessed using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) screening tools, respectively.[5] The

Table. Demographic Data

	SilverCloud User		*P* value
	No (n = 322)	Yes (n = 32)	
Median Age (years)	34	35	.738
White	72.4% (233)	78.1% (25)	
African American	12.4% (40)	15.6% (5)	
Asian	9.6% (31)	3.1% (1)	
Hispanic	4% (13)	3.1% (1)	
Other	1.6% (5)	0.0%	
Median no. of months of TTC	22	18	.267
History of prior live birth	24.8% (80)	28.1% (9)	.672
History of at least 1 prior fertility treatment cycle	33.2% (107)	12.5% (4)	.016
Prior mental health diagnosis	29.5% (95)	31.3% (10)	.840
Enrolled in mental health services	9.6% (31)	18.8% (6)	.125

Abbreviation: TTC, time to conception.

Figure 1. Fisher Exact *t* Test Demonstrating Mean PHQ-9 and GAD-7 Scores at Initial Appointment as Indicated by a Box and Whisker Plot ($P < .05$)



Abbreviations: GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

validity of these instruments for assessing anxiety and depression in the general population is well established.[5-8] Additionally, these screening tools have been validated in patients experiencing infertility.[5,9] Common interventions for the management of anxiety and depression include psychotherapy and medication management, which have been explored in patients experiencing infertility and shown to be effective in reducing anxiety and depressive symptoms.[10,11] However, both treatment options often involve long wait times for initial evaluation, are time-intensive, and can be expensive.[12,13]

Web-based and mobile applications have been explored to assist patients in coping with anxiety and depression symptoms while undergoing infertility treatment,[14] Including guided meditation, sleep support, and online group therapy.[14] However, these programs have not previously incorporated validated screening tools such as the PHQ-9 and GAD-7 to assess their effect on anxiety and depressive symptoms.[14]

SilverCloud is an online program based on cognitive behavioral therapy[15] that includes modules designed to help manage anxiety, depression, insomnia, stress, chronic pain, alcohol use, and diabetes. It can be ordered and prescribed by any licensed clinician or psychologist through a platform accessible on computers, tablets, and smartphones.[15] PHQ-9 and GAD-7 scores are collected upon enrollment in the program, every 2 weeks during participation, and upon completion of modules.[15] This program has previously been associated with decreases in GAD-7 and PHQ-9 scores in pilot populations and in university-based groups,[16,17] but it has not been studied in patients undergoing infertility evaluation and treatment.

The objective of this study was to determine whether patients experiencing infertility demonstrate changes in anxiety and depressive symptoms after engagement with SilverCloud, as determined by changes in PHQ-9 and GAD-7 scores. We hypothesized that patients would demonstrate significant decreases in anxiety and depressive symptoms, as evidenced by reductions in GAD-7 and PHQ-9 scores.

METHODS

The Institutional Review Board deemed this quality improvement study exempt. SilverCloud was first introduced within Froedtert Hospital in July 2017. In February 2022, clinicians at the Froedtert and Medical College of Wisconsin Reproductive Medicine Clinic began offering SilverCloud to all patients presenting for new infertility consultations.

A retrospective cohort study was performed. Patients were included if they presented for new infertility consultations between September 1, 2022, and September 1, 2023. Patients were excluded if they did not meet the American Society for Reproductive Medicine (ASRM) diagnostic criteria for infertility or if they were seeking fertility preservation. Baseline PHQ-9 and GAD-7 scores from the initial infertility consultation were recorded in the electronic medical record for all new patients. For patients who accepted a SilverCloud referral, PHQ-9 and GAD-7 scores were recorded at enrollment, every 2 weeks while enrolled in the program, and at completion of a module. Demographic data collected for all new patients included age, race, gravida, parity, infertility diagnosis, number of months of timed intercourse, history of mental health disorders, and previous and current treatment for mental health disorders (Table).

Fisher exact tests were used to compare baseline PHQ-9 and GAD-7 scores between new patients who enrolled in SilverCloud and those who did not. For patients who engaged in the

SilverCloud program, Wilcoxon signed-rank tests were used to compare PHQ-9 and GAD-7 scores immediately before engagement in SilverCloud and at the conclusion of a module. Level of engagement in SilverCloud was defined by the amount of time participants spent in the program (minutes). Mean time spent and standard deviations were calculated.

RESULTS

A total of 354 patients were included in this study. Fifty-two patients enrolled in the SilverCloud program, and 32 patients completed individualized modules. Patients were homogenous, with most being White, experiencing a similar duration of infertility, and having a similar history of prior live birth (Table). There was no significant difference in the history of a prior mental health diagnosis (29.4% vs 31.3%; $P = .847$) or utilization of mental health services (9.6% vs 18.8%; $P = .847$) between those who engaged in the program and those who did not (Table). However, patients who engaged in SilverCloud were less likely to have had prior fertility treatment (12.5% vs 33.3% $P = .016$) (Table).

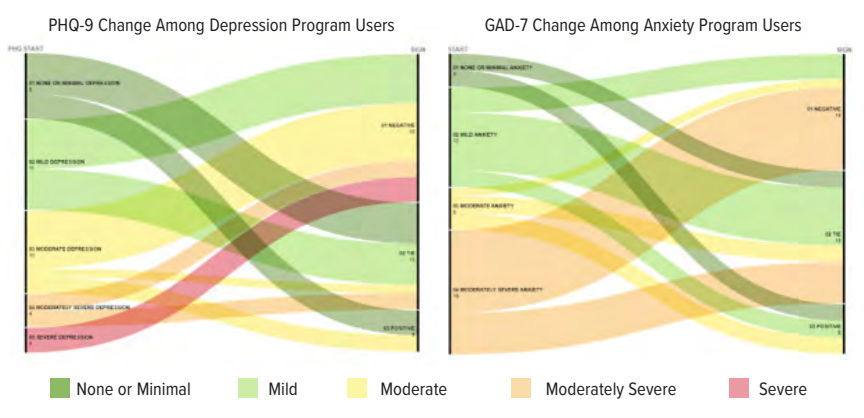
Initial consultation PHQ-9 scores did not differ significantly between patients who elected to engage in SilverCloud and those who did not (0 vs 0; $P = .21$) (Figure 1). However, initial consultation GAD-7 scores were significantly higher among patients who elected to engage in SilverCloud than among those who did not (0.5 vs 0; $P = .006$) (Figure 1).

The mean time between the new patient visit and initiation of a SilverCloud module was 11.8 days. During this time, patients underwent an initial infertility evaluation, began a diagnostic work-up, received prognostic information, and were provided information regarding treatments cost and financing options, consistent with standard clinic practice. Initial PHQ-9 and GAD-7 scores were assessed at enrollment in SilverCloud and again upon module completion.

Following utilization of SilverCloud, patients had significantly lower PHQ-9 scores (median initial score, 8.0, vs median final score, 6.5) (Z = -2.05, $P = .04$, $|r| = -0.34$) (Figures 2 and 3). Patients also demonstrated significant reductions in GAD-7 scores following utilization of SilverCloud (median initial score, 12.5, vs median final score, 9.5) (Z = -2.43, $P = .02$, $|r| = -0.41$) (Figures 2 and 3).

The mean amount of time patients spent in the SilverCloud was 39.4 minutes ± 93.8 minutes (range <1-576 minutes) (Figure 4). Time spent in SilverCloud was not associated with changes in PHQ-9 or GAD-7 scores.

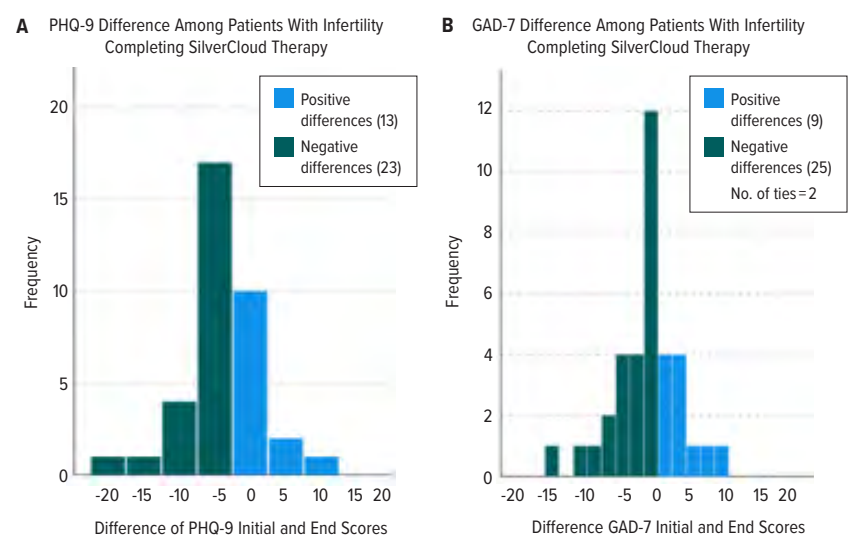
Figure 2. PHQ-9 and GAD-7 Score Changes Among Patients Using SilverCloud Between September 1, 2022, and September 1, 2023



Abbreviations: GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

Changes in both scores were calculated as the difference between the initial score at signup and the final at program completion. PHQ-9: median initial score, 8.0, vs median final score, 6.5 (Z = -2.05, $P = .04$, $|r| = -0.34$); GAD-7: median initial score, 12.5, vs median final score, 9.50 (Z = -2.43, $P = .02$, $|r| = -0.41$).

Figure 3. Wilcoxon Signed Rank Test (A) Showing Improvement (lowering) of Patient PHQ-9 Scores and Wilcoxon Signed Rank Test (B) Showing Improvement (lowering) of Patient GAD-7 Scores After SilverCloud Completion



$P = .04$ for PHQ-9 Scores and $P = .02$ for GAD-7 scores.

DISCUSSION

Infertility and its treatments are associated with significant anxiety and depression.[18,19] Fortunately, SilverCloud offers multiple self-guided modules to assist patients in managing these symptoms.[13]

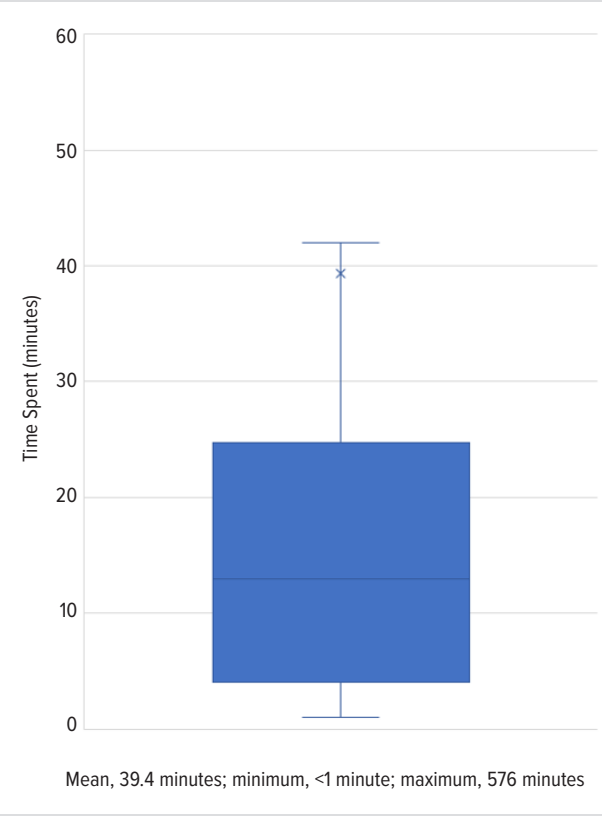
Our study showed that patients who engaged in SilverCloud demonstrated significant improvement in their GAD-7 and PHQ-9 scores, suggesting reduced depression and anxiety symptoms after program participation. Notably, there was no significant association between the amount of time spent using individual modules and improvement in PHQ-9 or GAD-7 scores. Thus, encouraging patients to engage with the program at any level may be reasonable for improving depression and anxiety symptoms.

Our study also demonstrated that PHQ-9 and GAD-7 scores obtained at the initial infertility consultation were lower than those recorded at enrollment in the SilverCloud program. During the mean 11.8 days between the initial consultation and SilverCloud enrollment, patients were likely presented with new information regarding their diagnosis, prognosis, management options, and the cost of treatment. The significant stressors associated with receiving this information, together with the smaller cohort of individuals who engaged in SilverCloud, likely contributed to the differences observed in PHQ-9 and GAD-7 scores. Patients who perceived infertility evaluation and treatment as more psychologically stressful may have self-selected to into the SilverCloud program compared with those who did not participate.

Our study demonstrated decreases in PHQ-9 and GAD-7 scores after completion of at least 1 SilverCloud module, with a median reduction in PHQ-9 scores of 1.5 points ($P = .04$) and a median reduction in GAD-7 scores of 3 points ($P = .02$). We recognize that, although PHQ-9 and GAD-7 scores changed significantly after engagement with SilverCloud, these changes may not necessarily correlate with clinical benefit. Because the PHQ-9 and GAD-7 scores are screening tools and rely on patient self-report, it may be difficult to fully characterize clinical benefit. However, previous studies have demonstrated that PHQ-9 and GAD-7 scores can assist in identifying clinically important changes in depression and anxiety symptoms,[18] and decreases in these scores have been associated with clinical improvement in anxiety and depressive symptoms, even when reductions are relatively small.[19]

These results are similar to findings from studies of other mobile app-based programs, which have demonstrated improvements in depressive and anxiety symptoms as reported by patients experiencing infertility.[14,20-24] Many internet-based programs offer nly brief interventions and do not use validated screening tools to assess changes in anxiety and depression symptoms associated with use.[14,20-24] In addition to currently available free, web-based interventions, SilverCloud offers a more longitudinal and analytical method for tracking changes in anxiety and depressive symptom in patients experiencing infertility. Although SilverCloud may not serve as an effective replacement for psychotherapy or psychopharmacotherapy, it may serve as an adjunct to traditional mental health treatment.

Figure 4. Participant Engagement in SilverCloud as Determined by Minutes Spent in the Program



Strengths

Strengths of this study include the use of validated screening tools to assess patient response to intervention, an approach not previously reported in similar studies. Additionally, all new patients were asked to complete PHQ-9 and GAD-7 to assess baseline anxiety and depression at the initial infertility consultation. The screening results were reviewed for each patient, and all patients were offered mental health services, highlighting the importance of access to mental health resources for patients experiencing infertility. Our data also demonstrated that individuals without prior infertility treatment were more likely to accept referral to and engage in SilverCloud. This finding may reflect the novelty of the infertility journey, with some individuals more readily acknowledging the mental toll of infertility, and therefore being more willing to utilize accessible resources.

Limitations

Limitations of this study include a racially homogenous patient population composed primarily of married individuals, which limits the generalizability of our findings to patients with more diverse demographic backgrounds. Therefore, we were unable to assess what impact of social and demographic factors on engagement with SilverCloud or responses to anxiety and depression screening measures. Additionally, we recognize that the number of patients who engaged in SilverCloud was limited. Patients were required to have access to a working email address and either a

smartphone or computer to access the modules, creating a potential barrier to participation and offering one explanation for the limited engagement observed in our study. Of the 52 individuals who accepted a SilverCloud referral, only 32 completed at least 1 module. Beyond access barriers, other explanations for limited uptake may include inadequate patient-centered descriptions of SilverCloud by clinicians or the well-documented stigma associated with mental health conditions and treatments.[25] Lastly, this study was performed at a single academic clinic; therefore, additional multi-institutional studies are needed to determine whether this program demonstrates efficacy on a larger scale in patients experiencing infertility.

Future studies should explore whether SilverCloud improves anxiety and depressive symptoms over the long term after program completion. Studies should also assess barriers to accessing and engaging with the program despite its self-paced format and lack of cost to users. Finally, additional research could assess whether engagement in mental health services such as SilverCloud affects progression to treatment.

CONCLUSIONS

SilverCloud is an online, self-guided mental health tool that may serve as a useful adjunct to standard mental health care for patients experiencing infertility who report anxiety and depressive symptoms.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Witters D. US depression rates reach new highs. Gallup. May 17, 2023. Accessed September 14, 2025. https://news.gallup.com/poll/505745/depression-rates-reach-new-highs.aspx

2. Kiani Z, Simbar M, Hajian S, et al. The prevalence of anxiety symptoms in infertile women: a systematic review and meta-analysis. *Fertil Res Pract*. 2020;6:7. doi:10.1186/s40738-020-00076-1

3. Swanson A, Braverman AM. Psychological components of infertility. *Fam Court Rev.* 2021;59(1)67-82. doi:10.1111/fcre.12552

4. Rooney KL, Domar AD. The relationship between stress and infertility. *Dialogues Clin Neurosci.* 2018;20(1):41-47. doi:10.31887/DCNS.2018.20.1/klrooney

5. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613. doi:10.1046/j.1525-1497.2001.016009606.x

6. Gilbody S, Richards D, Brealey S, Hewitt C. Screening for depression in medical settings with the Patient Health Questionnaire (PHQ): a diagnostic meta-analysis. *J Gen Intern Med.* 2007;22(11):1596-1602. doi:10.1007/s11606-007-0333-y

7. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. *Gen Hosp Psychiatry.* 2016;39:24-31. doi:10.1016/j.genhosppsych.2015.11.005

8. Parkerson HA, Thibodeau MA, Brandt CP, Zvolensky MJ, Asmundson GJ. Cultural-based biases of the GAD-7. *J Anxiety Disord.* 2015;31:38-42. doi:10.1016/j.janxdis.2015.01.005

9. Omani-Samani R, Maroufizadeh S, Ghaheri A, Navid B. Generalized Anxiety Disorder-7 (GAD-7) in people with infertility: a reliability and validity study. *Middle East Fertil Soc J*. 2018;23(4):446-449. doi:10.1016/j.mefs.2018.01.013

10. Abdolahi HM, Ghojazadeh M, Abdi S, Farhangi MA, Nikniaz Z, Nikniaz L. Effect of cognitive behavioral therapy on anxiety and depression of infertile women: a meta–analysis. *Asian Pac J Reprod*. 2019;8(6):251-259. doi:10.4103/2305-0500.270102

11. Faramarzi M, Alipor A, Esmaelzadeh S, Kheirkhah F, Poladi K, Pash H. Treatment of depression and anxiety in infertile women: cognitive behavioral therapy versus fluoxetine. *J Affect Disord.* 2008;108(1-2):159-164. doi:10.1016/j.jad.2007.09.002

12. Cuijpers P, Huibers M, Ebert DD, Koole SL, Andersson G. How much psychotherapy is needed to treat depression? A metaregression analysis. *J Affect Disord.* 2013;149(1-3):1-13. doi:10.1016/j.jad.2013.02.030

13. Quitkin FM, Rabkin JG, Ross D, McGrath PJ. Duration of antidepressant drug treatment. What is an adequate trial? *Arch Gen Psychiatry.* 1984;41(3):238-245. doi:10.1001/archpsyc.1984.01790140028003

14. Meyers AJ, Domar AD. Research-supported mobile applications and internet-based technologies to mediate the psychological effects of infertility: a review. *Reprod Biomed Online.* 2021;42(3):679-685. doi:10.1016/j.rbmo.2020.12.004

15. SilverCloud. Froedtert & Medical College of Wisconsin. Accessed May 1, 2024. https://www.froedtert.com/silvercloud

16. Palacios JE, Richards D, Palmer R, et al. Supported internet-delivered cognitive behavioral therapy programs for depression, anxiety, and stress in university students: open, non-randomised trial of acceptability, effectiveness, and satisfaction. *JMIR Ment Health.* 2018;5(4):e11467. doi:10.2196/11467

17. Doherty G, Coyle D, Sharry J. Engagement with online mental health interventions: an exploratory clinical study of a treatment for depression. In: CHI '12: *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*. Association for Computing Machinery; 2012:1421-1430.

18. Newman MW. Value added? A pragmatic analysis of the routine use of PHQ-9 and GAD-7 scales in primary care. *Gen Hosp Psychiatry.* 2022;79:15-18. doi:10.1016/j.genhosppsych.2022.09.005

19. Kroenke K, Wu J, Yu Z, et al. Patient health questionnaire anxiety and depression scale: initial validation in three clinical trials. *Psychosom Med*. 2016;78(6):716-727. doi:10.1097/PSY.0000000000000322

20. Clifton J, Parent J, Seehuus M, Worrall G, Forehand R, Domar A. An internet-based mind/body intervention to mitigate distress in women experiencing infertility: a randomized pilot trial. *PLoS One*. 2020;15(3):e0229379. doi:10.1371/journal.pone.0229379

21. Cousineau TM, Green TC, Corsini E, et al. Online psychoeducational support for infertile women: a randomized controlled trial. *Hum Reprod.* 2008;23(3):554-566. doi:10.1093/humrep/dem306

22. Domar, AD, Jasulaitis, L, Jasulaitis, S, Grill, EA, Uhler, ML. The impact of the FertiStrong app on anxiety and depression in men. *Fertil Steril.* 2019;112(3 Supp):e379. doi:10.1016/j. fertnstert.2019.07.1084

23. Grunberg PH, Dennis CL, Da Costa D, Gagné K, Idelson R, Zelkowitz P. Development and evaluation of an online infertility peer supporter training program. *Patient Educ Couns.* 2020;103(5):1005-1012. doi:10.1016/j.pec.2019.11.019

24. Boedt T, Dancet E, Lie Fong S, et al. Effectiveness of a mobile preconception lifestyle programme in couples undergoing in vitro fertilisation (IVF): the protocol for the PreLiFe randomised controlled trial (PreLiFe-RCT). *BMJ Open*. 2019;9(7):e029665. doi:10.1136/bmjopen-2019-029665

25. Economou M, Bechraki A, Charitsi M. The stigma of mental illness: a historical overview and conceptual approaches. *Psychiatriki.* 2020;31(1):36-46. doi:10.22365/jpsych.2020.311.36

The Development and Evolution of Group Medical Visits at UW Health

Sarah Walters, BS; Isabella Rodriguez Cardenas, BS; Karina Viloria Rodriguez, MD; Lisa Simpson, PA; Magnolia Larson, DO; Greta Kuphal, MD; Katherine Eby, RN; Melissa Stiles, MD; Lisa Grant, DO; Bruce Barrett, MD, PhD

ABSTRACT

Introduction: Chronic disease management presents substantial challenges for both patients and health care providers, often limited by time, resources, and operational complexities. Group medical visits (GMVs) at UW Health have evolved as a collaborative intervention, combining clinician-led care with peer support to address chronic conditions such as chronic pain, heart disease, anxiety, and more.

Methods: This program evaluation explores the development and characteristics of GMVs at UW Health through a qualitative approach, utilizing interviews, observations, and questionnaires to analyze GMV practices across multiple UW Health clinics.

Results: The findings highlight key themes, including a sense of community through group support, clinician satisfaction, the innovative structure of GMVs, wellness-based content, integrative facilitation of care, and areas for improvement.

Conclusions: As GMVs continue to evolve, enhancing support mechanisms, refining recruitment strategies, and expanding access will be crucial for optimizing their impact on chronic disease management. These insights offer valuable learnings for UW Health and other institutions seeking to refine and expand GMVs.

INTRODUCTION

Chronic disease management and preventive health services present substantial challenges for both patients and health care providers because of constraints that include limited time, resources, and the operational complexities associated with delivering timely, effective care. In response to these challenges, group medical visits (GMVs), also known as shared medical appointments,[1] have emerged as a collaborative approach to enhancing patient care. GMVs provide a supportive environment in which patients receive guidance from clinicians and other experts while benefiting from shared experiences and peer support. A multidisciplinary expert, such as a health coach, nutritionist, chef, or mindfulness instructor, typically co-leads GMVs alongside a clinician. GMVs address preventive care and a broad spectrum of conditions, from chronic pain, addiction, and heart disease to anxiety, insomnia, irritable bowel syndrome, and stress.[2,3] GMVs consist of multiple sessions held over an extended period, enabling patients to make informed decisions and improve health behaviors and lifestyles through hands-on, experiential learning in a trusted medical setting under clinician supervision.

Compared with standard care appointments of 15 to 30 minutes, GMVs offer visits lasting 90 to 120 minutes over multiple weeks. This extended session time allows clinicians and multidisciplinary experts to teach effectively and tailor guidance and recommendations to individual patient circumstances. By collaborating with experts such as dietitians, health coaches, behavioral therapists, exercise physiologists, and medical educators, care teams can foster a more effective and tailored approach to chronic disease and health behavior management. These experiences allow patients to adopt healthier behaviors alongside peers facing similar challenges. The combination of extended clinician-patient interaction and group support may contribute to the health benefits reported in the literature.[4-7] In addition to potential patient benefits, GMVs may positively affect clinician productivity and the quality of patient interactions,[8] potentially enhancing clinician job satisfaction.[9]

• • •

Author affiliations: Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison (UWSMPH), Wisconsin (Walters, Viloria Rodrigues, Simpson, Larson, Kuphal, Eby, Barrett); UWSMPH, Madison, Wisconsin (Rodriguez Cardenas, Grant).

Corresponding author: Bruce Barrett, MD, PhD, 610 N Whitney Way, Suite 200, Madison, WI 53705; email bruce.barrett@fammed.wisc.edu; ORCID ID 0000-0002-3953-4718

In a randomized controlled trial evaluating the effectiveness of GMVs for managing chronic pain and depression among a low-income, racially diverse population, participants in the intervention group experienced significant benefits compared with controls.[10] These included fewer emergency department (ED) visits during the active intervention phase and reduced pain medication use at the 21-week follow-up. These findings suggest that GMVs may improve health outcomes by integrating evidence-based education, hands-on practice, and community support within a clinician-led group setting, thereby improving access to care and empowering patients to manage their health more effectively. The GMV model also may support the financial viability of health care systems. For example, a study of patients with type 2 diabetes randomized to GMVs or standard care for 1 year found that participants in GMVs experienced fewer ED visits and lower total charges.[11]

Figure 1. Timeline of Group Medical Visits (GMVs) at UW Health

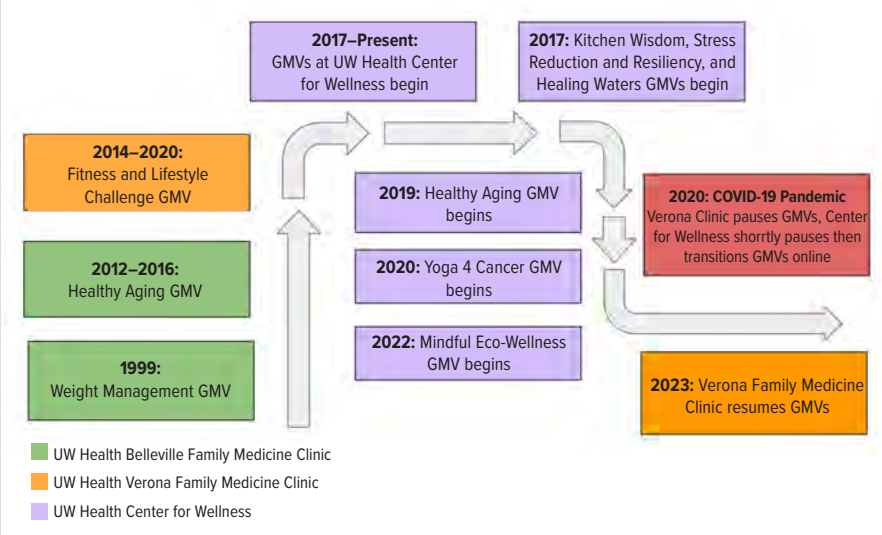


Figure highlights all GMVs held at the UW Health Belleville and Verona Family Medicine Clinics and a subset of GMVs held at the UW Center for Wellness. There was an extended gap between the initial GMV in Belleville and the resumption of the the GMV years later.

GMV Program at UW Health

GMVs have evolved substantially at UW Health during the past 25 years (Figure 1). The first GMV—a weight management program—was offered at the UW Health Belleville Family Medicine Clinic in Belleville, Wisconsin, in 1999. The UW Health Verona Family Medicine Clinic in Verona, Wisconsin, initiated GMVs in 2014 with sessions focusing on fitness and lifestyle. This program is designed to help adults with obesity improve their health through sessions featuring exercise, nutrition education, group discussions, and personalized goal setting, supported by community partnerships.[12] Beginning in 2017, UW Health expanded GMV programming, with much of the work coordinated by the UW Health Wellness Program and the Osher Center for Integrative Health, housed within the Department of Family Medicine and Community Health at the University of Wisconsin School of Medicine and Public Health. Over time, in addition to weight management, GMVs have addressed an array of health concerns, including chronic pain, stress management, nutrition, cancer survivorship, mindfulness, and cardiovascular health.

This paper explores the evolution and impact of GMVs at UW Health through a qualitative program evaluation that incorporates feedback from clinicians, administrators, multidisciplinary experts, and participants, along with an examination of GMV development and content over the past decade.

METHODS

This program evaluation employed a qualitative approach to examine the evolution and impact of GMVs at UW Health, the integrated academic health system affiliated with the University of Wisconsin-Madison. Methods included interviews with clinicians, administrators, multidisciplinary experts, and patients; direct observation of GMV sessions; and analysis of participant feedback questionnaires and clinician planning materials. Data were gathered from GMVs conducted across multiple sites, including the UW Health Belleville Family Medicine Clinic, UW Health Verona Family Medicine Clinic, and UW Health Center for Wellness. Interviews focused primarily on GMVs serving patients with chronic medical conditions, including diabetes, anxiety, and chronic pain. As a program evaluation and quality improvement initiative, the project was deemed exempt from institutional review board oversight.

Data collection involved semistructured interviews (Appendices A and B) with patients, clinicians, multidisciplinary experts, and administrators, including core developers and facilitators of the GMV experience. Direct observations of multiple GMV sessions were conducted to understand session dynamics and participant interactions. Additional evaluation included review of participant evaluation forms and questionnaires, as well as clinician planning documents.

The analysis involved independent reading and inductive thematic coding[13-15] of deidentified transcripts. Codes were refined through team discussions, resolution of discrepancies, and consensus-based identification and naming of themes. Each transcript was coded independently by 3 to 5 researchers, with the first and second authors reviewing all transcripts. This process aimed to identify the major characteristics of GMVs and key

themes related to patient experiences and health goals. Interviews with clinicians and administrative personnel were analyzed to identify themes related to job satisfaction and GMV design and implementation. Clinician planning documents and participant questionnaire responses were reviewed to characterize GMV structure, patient experiences, and outcomes. Observational notes from GMV sessions also underwent thematic coding.

RESULTS

Overview

Data were collected during 25 interviews with 10 patients and 15 UW Health personnel, including current GMV leaders and clinicians who conducted the first GMVs in Verona and Belleville. Thematic analysis of transcribed interview data was complemented by review of GMV planning materials, enrollment records, patient questionnaires, and direct participant observation of multiple GMVs.

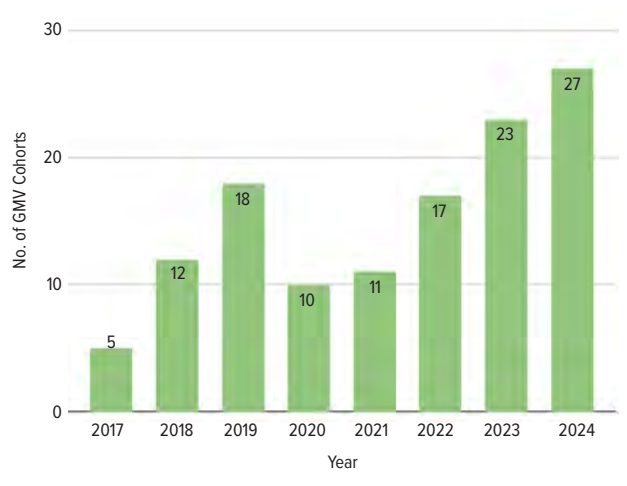
As of the end of 2024, the UW Health Wellness Program completed at least 123 GMV sessions serving approximately 1021 patients (Table 1, Figure 2). The GMVs at the UW Health Belleville Family Medicine Clinic served approximately 38 participants, and the GMVs at the UW Health Verona Family Medicine Clinic served approximately 161 participants. Thus, GMVs throughout the UW Health system have served at least 1220 patients over the past 25 years, underscoring the program's evolution and growing impact.

Table 1. Overview of Group Medical Visits Held at the UW Health Center for Wellness, 2017–2024

Group Medical Visit Title	Year(s)	Total No. of Sessions	Health Issues Addressed
Battlefield Acupuncture	2024	3	Chronic pain (back, neck, knee, etc)
Cooking for Heart Health	2018–2020	5	Nutrition, heart health
Culinary Connections to Health	2019, 2020	2	High blood pressure, high cholesterol, prediabetes, diabetes, heart disease
Goodbye Nicotine	2024	3	Nicotine use
Healing Chronic Pain	2024	3	Chronic neck and low back pain
Healing Waters	2017–2020	8	Chronic pain
Healthy Aging	2019, 2021–2023	9	Chronic diseases
Healthy Sleep	2019–2022	8	Insomnia and substandard sleep, anxiety, depression
Kitchen Wisdom	2017–2024	19	High blood pressure, high cholesterol, prediabetes, diabetes, heart disease
Knee and Hip Osteoarthritis	2017–2020	6	Knee and hip osteoarthritis
Living Well with Afib	2023, 2024	6	Atrial fibrillation
Mind and Body	2017	1	Chronic pain, fibromyalgia, high blood pressure, anxiety, depression, insomnia, diabetes, ADHD, IBS
Mindful Eco Wellness	2022–2024	7	Heart disease, high blood pressure, high cholesterol, prediabetes, diabetes, anxiety, depression, insomnia, chronic pain, obesity
Mindfulness for Your Health	2022–2024	13	Chronic pain, fibromyalgia, high blood pressure, anxiety, depression, insomnia, diabetes, ADHD, IBS
Stress Reduction and Resiliency	2017–2020	8	Stress
Getting to the HEART of a Health Life	2021–2024	9	Heart disease, high blood pressure, prediabetes, diabetes, cholesterol problems, obesity
Healthy Self-care	2020	3	Stress, anxiety, depression, sleep issues
Whole Health Approach to Healthy Weight	2021	2	Heart disease, high blood pressure, high cholesterol, prediabetes, diabetes, anxiety, depression, insomnia, chronic pain, obesity
Yoga 4 Cancer	2020, 2022–2024	8	Cancer survivor support, cancer diagnosis, open to all patients during or after treatment

Abbreviations; ADHD, attention-deficit/hyperactivity disorder; IBS, irritable bowel syndrome.

Figure 2. Number of Group Medical Visits (GMVs) Held per Year at the UW Health Center for Wellness, 2017–2024



Belleville Family Medicine Clinic and UW Health Verona Family Medicine are not shown, as each offered only a single GMV without year-to-year changes.

GMV Programs and Characteristics

The UW Health Center for Wellness typically offers a range of programs each year, including Yoga for Cancer, Goodbye Nicotine, Healing Chronic Pain, Getting to the Heart of a Healthy Life, Mindful Eco-wellness,[16] Living Well with AFib, Kitchen Wisdom, and Mindfulness for Your Health. Sessions last 4 to 8 weeks and average 6 to 12 patients per session. GMVs are divided by season, and scheduling varies based on provider availability and patient needs, with some programs occurring every season and others less frequently. (See https://www.uwhealth.org/treatments/group-medical-visits for a list of current offerings.)

Themes

Analysis of interviews, participant questionnaires, observational notes, and planning materials revealed several key themes (Tables

2 and 3), including a sense of community through group support, innovative program structure, wellness-based content, integrative facilitation of care, clinician satisfaction, and areas for improvement related to support, recruitment, and accessibility.

Table 2. Common Themes and Related Codes From Patient, Clinician, and Administrative Interviews

Theme/Definition	Codes
Community and Group Support	
The supportive environment created in GMVs, where patients and clinicians connect, share experiences, and learn from each other, fosters a sense of belonging and reduces isolation	Peer support, connection learning from others
Innovative Structure	
The unique design of GMVs features longer, interactive sessions that integrate education, peer support, and personalized care, allowing for real-time feedback and active practice of wellness and disease management	Interactive sessions, real-time feedback, peer-to-peer learning and practice
Wellness-based Content	
The integrative approach of GMVs incorporates diverse wellness practices such as stress management, integrative care, and practical health strategies, empowering patients to actively manage their conditions and improve their quality of life	Integrative health practices, personalized wellness tools, active health management
Integrative Facilitation of Care	
The multidisciplinary approach in GMVs involves collaboration between various health care providers to offer comprehensive care that addresses the diverse needs of patients with chronic conditions	Access to diverse expertise, integrated framework, team-based health care
Clinician Satisfaction	
The sense of fulfillment clinicians experienced in GMVs through deeper interactions, shared responsibility, and a collaborative, team-based approach to patient care	Deeper interactions, creative caregiving, collaborative approach
Areas for Improvement	
Key areas needing enhancement in GMVs include better follow-up support, recruitment strategies, and improved accessibility, particularly for underserved populations and through addressing insurance challenges	Recruitment challenges, expanded accessibility, follow-up support

Abbreviation: GMV, group medical visit.

Community and Group Support: Many participants emphasized that the group setting fostered a supportive environment where they could openly share their experiences with others facing similar challenges. This peer support contributed to feelings of connection and reduced the sense of isolation often associated with managing chronic conditions. Patients noted that learning from each other's experiences enhanced their own understanding of and motivation to improve their health.

Innovative Structure: Both patients and clinicians recognized the advantages of the longer, more interactive, and more frequent sessions that GMVs offer compared with standard medical appointments. GMVs provide the space for patients to engage in comprehensive discussions, learn new health behaviors, and actively practice wellness, lifestyle changes, and disease management under clinician guidance with real-time feedback and support. The integration of educational content, peer-to-peer learning and support, and personalized care within the group setting was perceived as a unique strength of the GMV model by clinicians, administrators, and patients alike.

Wellness-Based Content: Patients expressed appreciation for GMVs' wellness-based content, which extended beyond routine medical care to incorporate a range of integrative health practices. Sessions introduced diverse tools and approaches, including stress management techniques, the Whole Health Model,[17] intersectional care frameworks, and integrative practices such as mindfulness, meditation, yoga, and acupuncture. This integrative focus empowered patients by offering practical skills and strategies tailored to their individual needs. Access to such a variety of tools and approaches addressing aspects such as stress, chronic pain, healthy eating, sleep, wellness after cancer treatment, mindfulness, nicotine addiction, heart disease, aging well, and atrial fibrillation, allowed patients to make meaningful changes in their health and lifestyle.

Integrative Facilitation of Care: Clinicians, multidisciplinary experts, and administrators praised the integrated collaborative approach employed in GMVs. The involvement of licensed health care professionals, such as physicians, nurses, and mental health professionals, together with health behavior coaches, mindfulness instructors, and wellness experts, was viewed as a key benefit. This approach allowed for more comprehensive patient care that addressed the complex needs of individuals. Patients also appreciated having access to a range of expertise within a single session, which contributed to a more integrative health care experience.

Clinician Satisfaction: Clinicians reported that the group format allowed for deeper, more meaningful interactions with patients, enhancing job satisfaction. Driven by their synergistic and community-centered nature, the shared environment of GMVs helped reduce the traditional expectation for clinicians serve as the sole source of knowledge, alleviating some of the pressure that comes with one-on-one appointments. Clinicians described the group setting as enabling them to become active participants and learners, benefiting from the collective wisdom of the group. This sense of shared responsibility was further supported by the opportunity to work alongside other health care professionals, easing the burden on individual clinicians and fostering a more creative, team-based approach to care.

Areas for Improvement: Several areas for improvement were identified, particularly related to support, recruitment, and

accessibility. Support was a concern, with patients, clinicians, health coaches, and administrators emphasizing the need for additional follow-up opportunities to help patients sustain the benefits and skills gained through GMVs. Participants also recognized the need for enhanced support for clinicians and administrators, who face challenges managing GMVs because of the time and resources required. Recruitment emerged as a complex challenge, with respondents highlighting difficulties in identifying and reaching patients who could benefit from GMVs. Patients also reported challenges in learning about GMV opportunities and finding sessions that fit their schedules. Accessibility was identified as another challenge, particularly in efforts to serve vulnerable and underserved populations. Expanding access to rural communities, addressing issues related to insurance coverage and copayments, and increasing telemedicine opportunities were noted as challenges. (Getting to the HEART of a Healthy Life is the only GMV offered virtually at the time of evaluation.)

Table 3. Quotations From Clinicians, Administration, and Patients Regarding Each Theme Found From Patient, Clinician, and Administrative Interviews

Theme	Example Quotation (Participant)
Community and Group Support	"It is meaningful to witness patients being empowered to take charge of their health and make small sustainable changes. I enjoy encouraging and supporting people to be proactive and advocate for their own well-being. As the health coach we work with the group to help each individual understand why they are pursuing a healthier lifestyle. This focus on 'what matters most' allows us to align with their personal motivation for change. As part of the group model, patients engage in meaningful conversations and connect with one another through shared experiences. This relationship building and sharing wisdom with one another is a real benefit to the group model. It is gratifying to see the participants interacting with one another and supporting each other, as part of a group facilitating health and healing." (Health Coach)
	"I think it was huge having other cancer survivors there. You know, you're not going through it alone." (Patient)
Clinician Satisfaction	"We're really good at fixing broken pieces, broken bodies, but there's so much more we could offer to help people be healthy and whole and not just give them information, but let's show them how to do this... I think it's empowering for patients, but it was empowering I think for me to do it too." (Clinician)
	"If I had a one-on-one experience with one patient for an hour and a half, sometimes I would feel kind of drained. I would feel like kind of a lot. And I come out of these group medical visits feeling refreshed, maybe even more so than when I stepped into the group. So, this has really [...] made a positive impact. And I think the other thing that I would say too, is it feels like there is some sense of healing that happens in a group setting that just cannot happen in a one-to-one meeting. And, and I think part of that is the community, part of it is everybody sharing their learned, their lived experiences." (Clinician)
Innovative Structure	"You feel like you've got a timer on [during doctor appointments], but here your guard comes down, and the time is allotted." (Patient)
	"People want to eat healthy food and a lot of people have knowledge about it, some people have NO knowledge about healthy food, but it seems like so many of us have knowledge, but we don't really know how to put that knowledge into action, which is the wisdom where we call it kitchen wisdom, trying to turn that knowledge into something useful." (Clinician)
Wellness-based Content	"It just added more things to my so-called lifelong toolbox." (Patient) "It's neuroplastic pain and how using your mind and different steps can really help you not only manage the pain but actually alleviate it to a huge degree." (Patient)
Integrative Facilitation of Care	"Thinking about the whole person holistically, what are the different things in their life, bring in different aspects of that, and then (bringing in) other mind body techniques that I've learned from mindfulness meditation, yoga, and other things." (Clinician)
	"To have a space where there was connection, right? And connection between providers, connection between providers and patients and between patients themselves. I think that's a big part of it, not feeling alone." (Clinician)
Areas for Improvement	"I think about location. You know, are they driving 2 hours away? And this is a nighttime GMV, it's in the winter. I try to, you know, make that an appropriate step to consider." (Administrator)
	"We are finally creating awareness because I think that's our biggest issue. This UW Health system is so enormous. There are so many things happening all around it and great things happening, but none of us know what the other is doing. It's hard to really get this information out to everybody." (Administrator)

Abbreviation: GMV, group medical visit.

DISCUSSION

Our findings align with prior studies[16] describing the core characteristics of GMVs and contribute new insights into their evolution at UW Health while emphasizing the need for more rigorous, large-scale evaluation.

The observed trends highlight the progressive adaptation and enhancement of GMVs at UW Health. These changes emerged organically from the work of interested clinicians and tended to incorporate more integrative approaches, reflecting a broader movement toward integrated comprehensive care models. This evolution indicates a growing recognition of the need for multidisciplinary, patient-centered care that extends beyond traditional medical appointments. The innovative structure and content of GMVs may go beyond the limitations of conventional care, providing a model that accommodates the complexities of chronic disease management and offers patient empowerment through extended, interactive sessions and diverse wellness practices.

Implications for Clinicians, Patients, and UW Health

For clinicians: The evolution of GMVs at UW Health offers a collaborative and professionally rewarding practice model. Participants described greater job satisfaction resulting from deeper patient interactions, interdisciplinary teamwork, and shared learning within the group setting. They said they value the opportunity to participate actively, learning from both patients and peers, and making real-time adjustments based on immediate feedback. This continuous interaction supports creative problem-solving and

innovative care delivery while reducing burnout through a sense of shared responsibility and mutual learning. Closer communication within the group helped clinicians appreciate the common barriers to care and challenges patients face.

For patients: The evolution of GMVs at UW Health demonstrates a move towards more tailored and supportive care models that can better address patients' diverse needs. GMVs offer a unique model by combining evidence-based education, experiential learning, and peer support within a supportive group setting. Unlike traditional medical appointments, GMVs feature extended sessions that facilitate comprehensive discussions and hands-on practice of health behaviors. This extended format may promote patient engagement and provide additional opportunities for behavior change while fostering a sense of community among participants.

The community aspect of GMVs emerged as a central finding in this evaluation. Patients described the supportive group environment as helping to mitigate feelings of isolation and allowing them to share experiences, learn from one another, and enhance motivation and self-care. Integrative practices such as mindfulness, yoga, and acupuncture add options for care. This multifaceted approach caters to patients' health challenges and preferences and may promote more sustainable lifestyle changes and engagement in self-management. However, patients also reported challenges learning about GMV opportunities and finding sessions that fit their schedules.

The collaborative facilitation of care within GMVs enhances both the depth and breadth of patient care. The presence of multiple experts allows for a more comprehensive view of patient health by integrating different perspectives and areas of expertise. This model contrasts with traditional care settings, in which patients may see specialists separately, potentially leading to fragmented care. The collaborative nature of GMVs may strengthen care coordination while also creating opportunities for shared learning and professional satisfaction among clinicians and other health care professionals.

For UW Health: The continued development of GMVs reflects an institutional commitment to innovative approaches for chronic disease management, preventive care, and patient-centered care delivery. More broadly, the ongoing refinement and expansion of GMVs may contribute to a more adaptable and inclusive health care system capable of addressing the complex challenges of chronic disease and preventive care in a more comprehensive and patient-centered manner. However, recruitment remains a challenge, with both clinicians and administrators noting difficulties in identifying and reaching out to eligible patients who may benefit from GMV sessions.

Limitations

Because this evaluation was conducted within a single health system and reflects clinician-driven implementation of GMVs, the findings may not be generalizable to other settings. Additional evaluation across diverse health systems and patient populations is needed to better understand the transferability and broader impact of this care model.

Future Directions

The evolution of the group medical model presents several opportunities for future growth and refinement. Addressing the identified areas for improvement—including enhancing support mechanisms, refining recruitment strategies, and expanding accessibility—may help optimize the effectiveness and reach of GMVs.

Patients, clinicians, multidisciplinary experts, and administrators all emphasized the need for more follow-up opportunities to help patients sustain the benefits gained from GMV participation. Participants also identified a need for greater organizational support for clinicians and administrators responsible for developing, implementing, and coordinating GMVs, given the time and resources required for these activities.

Expanding accessibility will be vital for future GMVs, particularly for vulnerable and underserved populations. This includes reducing financial barriers related to insurance coverage, billing, and copayments to ensure broader and more equitable access. Future GMV models could increase accessibility for underserved areas by expanding telemedicine options and developing partnerships with local community organizations.[18]

Improving awareness of GMV offerings and strengthening recruitment strategies also may increase participation among patients who could benefit from these programs. Enhancing the capacity of clinics to use GMVs for chronic disease management and health promotion could be a key strategy. By addressing these challenges, health systems may improve the inclusivity and effectiveness of GMVs and expand opportunities for patients to access and benefit from this model of care.

CONCLUSIONS

As GMVs continue to evolve, enhancing support mechanisms, refining recruitment strategies, and expanding access will be crucial for optimizing their impact on chronic disease management. These insights offer valuable learnings for UW Health and other institutions seeking to refine and expand GMVs.

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgements: The authors wish to acknowledge Alyssa Bobo, NBC-HWC, RN, Diane Scherschel, Department of Family Medicine and Community Health, University of Wisconsin-Madison, and the Osher Center for Integrative Health housed within the Department of Family Medicine and Community Health, University of Wisconsin-Madison, whose work was essential for the development of this article. They would also like to thank medical librarian Leslie Christensen for assistance with bibliographic research.

Appendices: Available at www.wmjonline.org.

REFERENCES

1. Ee C, De Courten B, Avard N, et al. Shared medical appointments and mindfulness for type 2 diabetes—a mixed-methods feasibility study. *Front Endocrinol.* 2020;11:570777. doi:10.3389/fendo.2020.570777

2. Cunningham SD, Sutherland RA, Yee CW, et al. Group medical care: a systematic review of health service performance. *Int J Environ Res Public Health.* 2021;18(23):12726. doi:10.3390/ijerph182312726

3. Kelly F, Liska C, Morash R, et al. Shared medical appointments for patients with a nondiabetic physical chronic illness: a systematic review. *Chronic Illn.* 2019;15(1):3-26. doi:10.1177/1742395317731608

4. Kiefer D, Eby K, Zaborek J, Goldstein E. Integrative group visits for sleep disturbance: a brief report. *Glob Adv Integr Med Health.* 2024;13:27536130241260016. doi:10.1177/27536130241260016

5. Heisler M, Burgess J, Cass J, et al. Evaluating the effectiveness of diabetes shared medical appointments (SMAS) as implemented in five veterans affairs health systems: a multi-site cluster randomized pragmatic trial. *J Gen Intern Med*. 2021;36(6):1648-1655. doi:10.1007/s11606-020-06570-y

6. Tunay M, Kurdak H, Özcan S, Özdemir Ç, Özer ZY. Family physician-led group visits for lifestyle modification in women with weight problems: a pilot intervention and follow-up study. *Obes Facts.* 2018;11(1):1-14. doi:10.1159/000486133

7. Edelman D, Gierisch JM, McDuffie JR, Oddone E, Williams JW. Shared medical appointments for patients with diabetes mellitus: a systematic review. *J Gen Intern Med*. 2015;30(1):99-106. doi:10.1007/s11606-014-2978-7

8. Ramdas K, Darzi A. Adopting innovations in care delivery — the case of shared medical appointments. *N Engl J M*ed. 2017;376(12):1105-1107. doi:10.1056/NEJMp1612803

9. Thompson-Lastad A, Gardiner P. Group medical visits and clinician wellbeing. *Glob Adv Health Med.* 2020;9:2164956120973979. doi:10.1177/2164956120973979

10. Gardiner P, Luo M, D'Amico S, et al. Effectiveness of integrative medicine group visits in chronic pain and depressive symptoms: a randomized controlled trial. *PLoS One.* 2019;14(12):e0225540. doi:10.1371/journal.pone.0225540

11. Clancy DE, Dismuke CE, Magruder KM, Simpson KN, Bradford D. Do diabetes group visits lead to lower medical care charges? *Am J Manag Care.* 2008;14(1):39-44.

12. Larson M. How to use group visits to manage obesity. *Fam Pract Manag.* 2019;26(5):20-25.

13. Vindrola-Padros C, Johnson GA. Rapid techniques in qualitative research: a critical review of the literature. *Qual Health Res*. 2020;30(10):1596-1604. doi:10.1177/1049732320921835

14. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res.* 2005;15(9):1277-1288. doi:10.1177/1049732305276687

15. Vaughn P, Turner C. Decoding via coding: analyzing qualitative text data through thematic coding and survey methodologies. *J Libr Adm.* 2016;56(1):41-51. doi:10.1080/01930826.2015.1105035

16. Barrett B, Walters S, Checovich MM, et al. Mindful eco-wellness: steps toward personal and planetary health. *Glob Adv Integr Med Health.* 2024;13:27536130241235922. doi:10.1177/27536130241235922

17. National Academies of Sciences, Engineering, and Medicine. Defining whole health. In: National Academies of Sciences, Engineering, and Medicine. *Achieving Whole Health: A New Approach for Veterans and the Nation.* National Academies Press; 2023. Accessed March 11, 2025. https://www.ncbi.nlm.nih.gov/books/NBK591719/

18. Thompson-Lastad A. Group medical visits as participatory care in community health centers. *Qual Health Res*. 2018;28(7):1065. doi:10.1177/1049732318759528

Effectiveness of Group Medical Visits for Patient Wellness: A Mixed Method Study Within UW Health

Isabella Rodriguez Cardenas, BS; Sarah Walters, BS; Lisa Simpson, PA; Magnolia Larson, DO; Karina Viloria-Rodriguez, MD; Kaitlin Tetreault, MB; Alex Pinto, MS; Greta Kuphal, MD; Bruce Barrett, MD, PhD

ABSTRACT

Introduction: Chronic medical conditions affect approximately 129 million Americans. The complexities of chronic illness, coupled with limited health care resources and clinician time, can complicate treatment management, and contribute to poor health outcomes. The effect of group medical visits (GMVs) on patient wellness has not been well established.

Methods: Mixed-methods approach using both quantitative and qualitative data was used to evaluate wellness following completion of GMV programs. Patients completed pre- and post-GMV assessments using the Patient-Reported Outcomes Measurement Information System (PROMIS)-29. GMV programs included Yoga for Cancer, Stress Reduction and Resiliency, Mindful Eco-Wellness, and Mindfulness for Your Health from 2017 to 2024. The PROMIS-29 is a validated health questionnaire that assesses 7 domains: anxiety, depression, fatigue, sleep disturbance, participation in social roles, pain, and physical function. Clinicians and patients also participated in qualitative interviews regarding their GMV experiences.

Results: Among 76 participants who completed pre- and post-GMV PROMIS-29 assessments, fatigue scores improved and participation in social roles increased significantly. Improvements were also observed in anxiety, depression, sleep disturbance, and physical function, although these changes were not statistically significant. Themes identified from interviews with 15 clinicians and 10 patients included patient empowerment, sense of community, patient satisfaction, integrative care, and trust.

Discussion: Improvements in PROMIS-29 domains suggest that GMVs may have the potential to enhance patient health and wellness. The themes discovered portray a positive outlook on GMVs, with mindfulness practices and the sense of community that is cultivated within a group setting highlighted as especially important.

Conclusions: GMVs were associated with improvements in fatigue and participation in social roles and were viewed favorably by patients and clinicians. Although additional controlled studies are needed, GMVs may represent a promising approach to supporting wellness among patients living with chronic conditions.

• • •

Author affiliations: University of Wisconsin School of Medicine and Public Health (UWSMPH), Madison, Wisconsin (Rodriguez Cardenas); Department of Family Medicine and Community Health, UWSMPH, Madison, Wisconsin (Walters, Simpson, Larson, Viloria-Rodriguez, Tetreault, Pinto, Kuphal, Barrett).

Corresponding author: Bruce Barrett, MD, PhD; 610 N Whitney Way, Suite 200, Madison, WI 53705; email bruce.barrett@fammed.wisc.edu; ORCID ID 0000-0002-3953-4718

INTRODUCTION

Chronic conditions are prevalent in the United States. About 129 million people have at least 1 major chronic illness, including cancer, diabetes, heart disease, and hypertension.[1] The complex nature of such conditions poses challenges for treatment management. Among these challenges are limited health care resources and time constraints, which can hinder deeper discussions that promote comprehensive patient education and the incorporation of meaningful self-management strategies. This often leads to nonadherence to medical advice, poor health outcomes, and reduced well-being among patients.

Emerging evidence has shown that group medical visits (GMVs) show promise for managing chronic illness. For example, a prospective cohort study of 60 patients attending a physician-led GMV for weight management in women with overweight or obesity reported a significant decrease in mean body weight, an increase in high-density lipoprotein (HDL) cholesterol, and decreases in heart rate and blood pressure among the 30 patients who completed the program.[2] A randomized study of postdischarge patients with chronic obstructive pulmonary disease (COPD) concluded that, compared with controls, GMV participants experienced fewer acute exacerbations.[3] Similarly, a multisite randomized trial conducted among patients with diabetes at 5 Veterans Affairs health systems found that those who attended GMVs had improved hemoglobin A1c levels; however, the study did not assess patient-oriented health or wellness

outcomes.[4] Although the current literature has evaluated GMVs as an intervention for specific diseases or conditions such as diabetes, overweight and obesity, and COPD, it is unclear whether GMVs are effective for improving overall health outcomes and patient well-being.

GMVs were introduced at the University of Wisconsin (UW) Health system in 1999 to facilitate stress reduction and improve wellness. Early successes gradually piqued the interest of more clinicians, leading to a broader range of GMV options. To date, UW Health has hosted at least 20 GMVs focusing on healing, nutrition, sleep, fitness, weight loss, and mindfulness practices. These GMVs provide a space for education, group sharing, hands-on learning with interdisciplinary health experts, and support for lifestyle changes that may encourage alternative approaches to treatment. This study investigated the effectiveness of GMVs in improving the overall health and well-being of UW Health patients living with chronic conditions such as cancer, addiction, heart disease, chronic pain, insomnia, irritable bowel syndrome, and stress.

METHODS

A mixed-methods approach was employed, consisting of both quantitative (pre- and post-intervention surveys) and qualitative (individual interviews) methods aimed at assessing GMVs, which generally were aimed at reducing stress; improving lifestyle behaviors such as nutrition, physical activity, and sleep habits; and developing new wellness skills, including mindfulness practices.

The GMVs evaluated in this study were held at UW Health clinics from 2017 to 2024, and patients with various chronic conditions were recruited. In general, GMV courses ran for 4 to 7 weeks, with weekly sessions lasting up to 2 hours. GMV class sizes typically range from 6 to 14 participants. Although patients were expected to attend all sessions, occasional absences and dropouts occurred.

For several GMVs, patients completed validated health questionnaires at baseline and upon completion of the program. The most commonly used measure was the Patient-Reported Outcomes Measurement Information System (PROMIS)-29, a highly validated and widely accepted self-report measure of general health.[5] The PROMIS-29 assesses 7 health domains: anxiety, depression, fatigue, sleep disturbance, participation in social roles, pain, and physical function. These data were available from patients who attended a variety of GMVs, including Yoga for Cancer, Stress Reduction and Resiliency, Mindful Eco-Wellness, and Mindfulness for Your Health. Data were pooled across GMVs and assessed for group-level changes. Mann-Whitney U tests were used to assess differences between pre- and post-GMV PROMIS-29 median domain scores. Participants with more than 25% missing items on their questionnaires were excluded from the analyses. To evaluate and respond to missingness when at least 75% of intended data were available, we used Little's Missing Completely at Random (MCAR) test, and when its assumptions were met, we imputed remaining missing data using multiple imputation by chained equations (MICE).[6,7]

Table 1. PROMIS-29 Health Domains Median Scores Before and After Group Medical Visit Courses

Health Domains	Median (IQR) Pre-GMV	Median (IQR) Post-GMV	*P* value[a]
Physical function	18 (14–20)	19 (16–20)	.116
Anxiety	8 (5–10)	7 (5–9)	.069
Depression	6 (4–9)	5 (4–8)	.203
Fatigue	10 (7–14)	8 (7–12)	.034[b]
Sleep disturbance	10 (8–13)	9 (7–11)	.127
Participation in social roles	13 (11–16)	16 (13–18)	.001[c]
Pain	7 (4–12)	7 (4–9.25)	.514

Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; GMV, group medical visits; IQR, interquartile range.

[a]*P* values derive from Mann-Whitney tests comparing medians.
[b]$P \leq .05$; [c]$P \leq .01$.

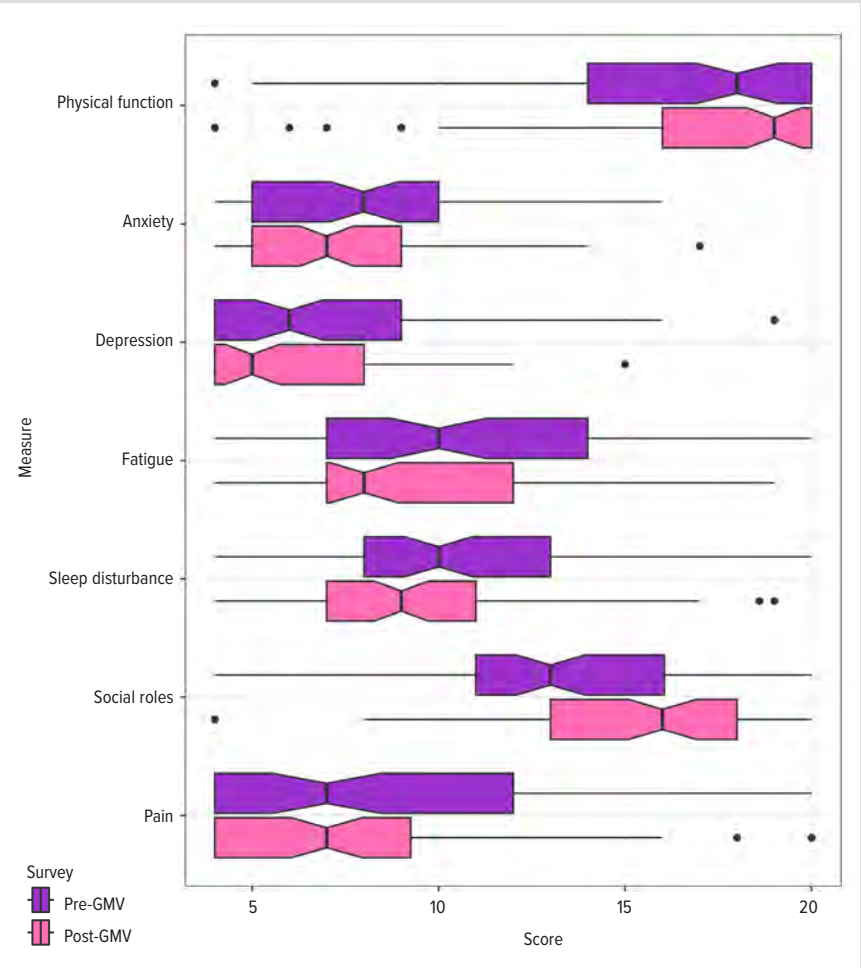
Qualitative methods included semistructured interviews conducted with GMV clinician leaders, administrators who coordinate GMVs, and patients who participated in GMVs. After completion of the Mindfulness for Your Health, Yoga for Cancer, and Mindful Eco-Wellness GMV courses, patients were approached and asked whether they were willing to be interviewed about their GMV experiences. Participation was voluntary. Interview guides were developed in consultation with UW Health GMV leaders and sought respondents' impressions regarding the potential benefits of GMVs. All interviews were recorded and transcribed. Each transcript was analyzed by at least 3 coauthors using conventional content analysis techniques to identify common themes.[8] Each reviewer read the transcripts independently, searching for themes related to potential GMV effectiveness. Guest et al reported that the first 6 to 7 interviews tend to yield most themes, although 11 to 12 interviews are often required to achieve thematic saturation.[9] Themes presented here were developed through consensus during multiple discussions.

This work was deemed exempt from Institutional Review Board oversight because it focused on program evaluation and quality improvement rather than research. Nevertheless, all interviewed patients were informed that participation was completely voluntary and would in no way influence their health care. Information that could be used for personal identification was not collected.

RESULTS

The quantitative component of this study included 16 GMV cohorts representing 122 participants. Of these, 76 participants completed both pre- and post-GMV PROMIS-29 surveys with less than 25% missing data. Among the 76 participants, 12 were missing 1 of 29 items and 2 were missing 2 of 29 items. Of the 7 domains assessed by the PROMIS 29, 2 showed statistically significant improvements between pre- and post-GMV median scores

Figure. Distribution of PROMIS-29 Health Domain Median Scores Among Group Medical Visit Cohorts



Abbreviation: PROMIS, Patient-Reported Outcomes Measurement Information System; GMV, group medical visit.

Data come from 16 group medical visit cohorts from 2017 to 2024, n = 76. Vertical lines represent median, notches are 95% CI, and the box's length corresponds to interquartile range. Includes multiple imputation with chained equations data.

Table 2. Explanations of Common Themes Found in 23 Clinician and Patient Interview Transcripts

Themes[a]	Explanation
Patient autonomy and empowerment	Describes patient education and promoting agency for patients to make informed decisions about their life in regard to health
Sense of community	Refers to the camaraderie and trust among patients and clinicians that is built over the course of GMVs; reduction of loneliness
Patient satisfaction	Patients expressed how helpful GMVs were at teaching mindfulness skills, providing extra resources to address quality of life, and giving them a space to express their concerns
Integrative care	Addressing areas that impact health such as nutrition, movement, sleep, spirituality, purpose, and social connections while incorporating mindfulness practices and holistic therapies
Trust	Creating relationships, bonding, more time to get to know each other in a safe space

Abbreviations: GMV, group medical visit.

[a]Themes come from conventional content analysis of interview transcripts reviewed by at least 3 coauthors.

(Figure 1). Median fatigue scores decreased by 2 points ($P = .034$), and participation in social roles scores increased by 3 points ($P = .001$) (Table 1). The domains of physical function, anxiety, depression, and sleep disturbance also improved, although the changes were not statistically significant. Pain did not change.

Ten patients and 15 clinicians participated in the qualitative interviews. The patient participants had completed the Mindfulness for Your Health (4-week), Mindful Eco-Wellness (7-week), or Yoga for Cancer (6-week) GMVs. The clinician participants had led the Mindfulness for Your Health, Kitchen Wisdom, Goodbye Nicotine, Yoga for Cancer, Stress Reduction and Resiliency, Healing Waters, Living Well with Afib, Healing Chronic Pain, Getting to the HEART of a Healthy Life, Mindful Eco-Wellness, Healthy Aging, or Fitness and Lifestyle Challenge GMVs. In total, 23 transcripts (65 975words) were discussed by 7 reviewers in 7 meetings, with at least 3 reviewers assigned to each transcript. Following independent transcript review and group discussion, the common themes that emerged were patient empowerment, sense of community, patient satisfaction, integrative care, and trust (Table 2). Representative quotations supporting these themes were extracted from the interview transcripts and selected by consensus (Table 3).

DISCUSSION

Treatment of chronic conditions may place a substantial burden on patients and health care systems, which can lead to inadequate attention to general health and well-being. In contrast to the reductionist approach of disease-specific diagnosis and treatment, GMVs offer an integrative approach that addresses multiple facets of patient-oriented health and wellness. These shared medical visits are clinician-guided and incorporate an educational component that includes hands-on learning with the guidance of health experts. GMVs provide time and space for more comprehensive education and allow for meaningful dis-

cussion of self-care and self-management strategies. In this study, we investigated the potential effectiveness of GMVs in improving patient wellness using quantitative and qualitative methods and data from multiple GMVs conducted within the UW Health system.

Our quantitative results suggest that GMVs were associated with statistically significant reductions in fatigue and improvements in participation in social roles. Positive trends were also observed for anxiety, depression, sleep disturbance, and physical function, suggesting that a larger study might detect statistically significant benefits in these domains. The lack of improvement in the pain domain may stem from the fact that none of the GMVs included in this pre-post assessment specifically focused on pain management.

The improvements in the health domains of the PROMIS 29 questionnaire are encouraging and suggesting of the potential for GMVs to improve wellness; however, they are not sufficient to prove effectiveness. Limitations of this study include the absence of a control condition, a modest sample size, missing data, and participant recruitment limited to UW Health patients in Dane County, Wisconsin. Because these data are self-reported and were collected without blinding or a control group, the results may be susceptible to biases such as social desirability bias and other forms of self-report bias. The significant differences in median scores were approximately 2 to 3 points on a 20-point scale, which may or may not be clinically meaningful. A systematic review of PROMIS-29 minimal important change (MIC) values found that, for nonsurgical interventions, a MIC of 2 to 6 points is a reasonable approximation.[10] The statistically significant differences observed in the assessed health domains generally fall within this range, suggesting potential clinical significance.

Nevertheless, further investigation is warranted, including randomized trials involving larger number of participants and multiple clinical sites. Even if future randomized trials demonstrate effectiveness, questions will remain regarding whether the benefits of GMVs outweigh the associated financial, resource allocation, and other potential costs. Ultimately, meta-analyses of randomized trials and cost-effectiveness using measures such as quality-adjusted life-years (QALYs) will be needed.

The themes and supporting quotations arising from qualitative interviews may help explain and contextualize the quantitative findings and may also guide future research. For example, the statistically significant improvement in participation in social roles assessed by the PROMIS-29 corresponds with the theme of sense of community that emerged from the interviews. Unlike conventional one-on-one physician-patient care, GMVs leverage the

Table 3. Clinician and Patient Interview Quotes Supporting Common Themes

Theme	Quotation
Patient autonomy and empowerment	
Healing Chronic Pain	"I try to allow a lot of space for patients to talk, to share their experience and really try to help them feel like they're active participants and involved in what's going on." (clinician)
Stress Reduction and Resiliency	"I think that has been really impactful for people setting health goals, like short-term SMART goals I think has been really helpful as something concrete to move forward." (clinician)
Yoga for Cancer	"That pamphlet you had at home made me think a lot because it was directed towards yourself. What can you do? How are you gonna do it? What do you want to happen in 6 months? It just gets you thinking so you can put all your ducks in a row and say this is how it's gonna roll instead of living your days wondering what's gonna happen." (patient)
Sense of community	
Healthy Sleep	"It was interactive for people, and they learned skills that wouldn't be taught elsewhere… And then the second thing is the peer-to-peer inner interactions, then having a discussion among everyone about what others think." (clinician)
Mindful Eco-wellness	"What a group excels at is the ability to riff off each other's thoughts…if you were directing a focus group and there were 10 of us in the room, you would get a very different outcome when people's thoughts are bounced off each other…Groups are much better at mental health and they're much better at health behaviors." (clinician)
Mindfulness for Your Health; Kitchen Wisdom	"There's this sense of agency where yes, you're giving them some knowledge, but then you're watching how they integrate that and how they support each other." (clinician)
Patient satisfaction	
Stress Reduction and Resiliency	"People showed up and came back, and people loved it." (clinician)
Mindfulness for Your health; Kitchen Wisdom	"They found out I had high blood pressure…it wasn't a preexisting thing and would have probably come out down the line." (patient)
Integrative care	
Healing Chronic Pain	"Thinking about the whole person holistically, what are the different things in their life, bring in different aspects of that, and then other mind body techniques that I've learned from mindfulness meditation, yoga, and other things." (clinician)
Healthy Sleep	"The third thing is integrative health, which has a bunch of different treatments to it from talking about sleep, talking about nutrition and the exercise community. I'm particularly interested in dietary supplements and herbal medicines." (clinician)
Mindful Eco-wellness	"I think learning mindfulness practice and awareness is the main cornerstone of it all…That allows them to break free of the habits that they've been conditioned into." (clinician)
Trust	
Mindfulness for Your Health; Kitchen Wisdom	"I think I feel more at the same level as the participants; when I'm in a group, the relationship seems more casual. " (clinician)
Yoga for Cancer	"…she's looking for a better way and still is looking for a better way to help us feel like there are people in our corner. So that was wonderful." (patient)

Themes come from conventional content analysis of interview transcripts reviewed and discussed by at least 3 coauthors over 7 review sessions.

strengths of having multiple patient perspectives. Several clinicians noted that one of the most valuable aspects of their GMVs was the peer-to-peer interaction among participants. Similarly, the theme of integrative care emerged as both patients and clinicians spoke about the multifaceted nature of health and illness and the importance of considering psychological, social, and spiritual health in addition to physical health. These findings may inform future research by identifying potential pathways to be investigated. Future randomized trials could assess both health outcomes and potential mechanisms of action. For example, the patient empowerment and participation in social roles may represent pathways to improved health and could be evaluated as mediators or moderators of the relationship between GMV participation and health outcomes.

A strength of this study is its mixed-methods design, which yielded consistencies between qualitative and quantitative findings. Interviews with clinicians and patients identified themes that support a whole-health outlook on patient care through community involvement and integrative practices. The quotations supporting these themes suggest that both clinicians and patients valued their experiences in GMVs. Virtually all interview respondents perceived GMVs as effective. The sense of community theme was particularly prominent across interviews, and patients expressed satisfaction with being a part of a community, which is reflected in the improvements in PROMIS-29 health domains—especially in participation in social roles. This finding is notable because it addresses the feelings of isolation commonly experienced by patients living with chronic conditions.

CONCLUSIONS

Group medical visits were associated with improvements in fatigue and participation in social roles among patients with chronic conditions and were viewed favorably by both patients and clinicians. Qualitative findings suggest that patient empowerment, community, trust, and integrative care may contribute to these benefits. Although the results support the potential value of GMVs as a whole-health approach to chronic disease management, larger controlled studies are warranted to determine the effectiveness, mechanisms, and cost-effectiveness of GMVs across diverse patient populations and clinical settings.

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgements: The authors would like to thank the Summer Student Research and Clinical Assistantship program at the University of Wisconsin School of Medicine and Public Health for providing students with opportunities to enrich their research experiences. They would also like to thank medical librarian Leslie Christensen for assistance with bibliographic research and administrative assistant Nathaniel Javid for assistance with final formatting and submission.

REFERENCES

1. Benavidez GA, Zahnd WE, Hung P, Eberth JM. Chronic disease prevalence in the US: sociodemographic and geographic variations by Zip Code Tabulation Area. *Prev Chronic Dis.* 2024;21:E14. doi:10.5888/pcd21.230267

2. Tunay M, Kurdak H, Özcan S, Özdemir Ç, Özer ZY. Family physician-led group visits for lifestyle modification in women with weight problems: a pilot intervention and follow-up study. *Obes Facts.* 2018;11(1):1-14. doi:10.1159/000486133

3. Zhang Y, Sun H, Zhang X, Liang J, Zheng X. Group visits improve health in patients with COPD in post-discharge transition period. *Altern Ther Health Med*. 2022;28(2):32-39.

4. Heisler M, Burgess J, Cass J, et al. Evaluating the effectiveness of diabetes shared medical appointments (SMAs) as implemented in five Veterans Affairs health systems: a multisite cluster randomized pragmatic trial. *J Gen Intern Med*. 2021;36(6):1648-1655. doi:10.1007/s11606-020-06570-y

5. Hays RD, Spritzer KL, Schalet BD, Cella D. PROMIS-29 v2.0 profile physical and mental health summary scores. *Qual Life Res.* 2018;27(7):1885-1891. doi:10.1007/s11136-018-1842-3

6. Little RJA. A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc*. 1988;83(404):1198-1202. doi:10.1080/01621459.1988.10478722

7. Royston P, White IR. Multiple imputation by chained equations (MICE): implementation in Stata. *J Stat Softw.* 2011;45(4):1-20. doi:10.18637/jss.v045.i04

8. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277-1288. doi:10.1177/1049732305276687

9. Guest G, Namey E, Chen M. A simple method to assess and report thematic saturation in qualitative research. *PLoS One*. 2020;15(5):e0232076. doi:10.1371/journal.pone.0232076

10. Terwee CB, Peipert JD, Chapman R, et al. Minimal important change (MIC): a conceptual clarification and systematic review of MIC estimates of PROMIS measures. *Qual Life Res.* 2021;30(10):2729-2754. doi:10.1007/s11136-021-02925-y

Persistent Racial, Ethnic, and County-Level Disparities in Invasive Cervical Cancer Incidence in Wisconsin, 1998–2022

Madelyn Frey, MPH;* Laurie Lapp, MD, MPH;* Lena Swander, MPH; Ran C. Zhang, MD, MPH; Laura Jacques, MD

ABSTRACT

Background: Invasive cervical cancer continues to disproportionately affect racially and ethnically minoritized populations and individuals living in rural areas. We analyzed trends in cervical cancer incidence by race, ethnicity, and geography in Wisconsin from 1998 through 2022.

Methods: Cervical cancer incidence rates (per 100 000 individuals with a cervix) were analyzed by race/ethnicity and county using data from the Wisconsin Cancer Reporting System.

Results: Overall incidence declined 28%, from 8.2 to 5.9 cases per 100 000, but declines were not evenly distributed across populations. Compared with non-Hispanic White individuals, non-Hispanic Black individuals had nearly twice the incidence rate throughout the study period. Although Hispanic individuals experienced the largest relative decline (40.8%, 15.7 to 9.3 per 100 000), incidence remained higher among non-Hispanic White individuals. Milwaukee County, Wisconsin's most socially vulnerable county, had among the highest incidence rates and slowest decline over time (19.8%).

Discussion: Because cervical cancer is largely preventable, the persistence of substantial disparities in Wisconsin highlights structural inequities that warrant urgent attention.

BACKGROUND

Invasive cervical cancer is largely preventable through vaccination and screening.[1] Incidence rates in the United States declined significantly after the introduction of Pap smear screening in the 1970s, high-risk human papilloma virus (hrHPV) testing in 2003, and HPV vaccination in 2006 (quadrivalent) and 2014 (nonavalent).[2-5] While overall incidence rates have declined since the early 2000s, rates have plateaued over the last decade, and more than 13 000 new invasive cervical cancer cases and 4000 deaths were projected in the United States (US) in 2025.[2] Additionally, declines have not been shared equally across populations, and vulnerable groups, including racially minoritized groups, socioeconomically disadvantaged individuals, uninsured and underinsured individuals, and individuals living in rural areas, continue to bear a disproportionate burden of new cases.[6-8] Addressing these disparities is particularly important as the World Health Organization (WHO) has established a global goal of eliminating cervical cancer as a public health problem by 2030.[9]

Wisconsin has some of the most disparate health care outcomes in the nation,[10] yet cervical cancer incidence and outcomes in the state remain underexamined. This research brief provides a descriptive overview intended to highlight areas of concern and inspire more in-depth analyses. We report rates of invasive cervical cancer incidence in Wisconsin from 1998 (5 years before US Food and Drug Administration approval of hrHPV testing) through 2022, with a focus on differences by race, ethnicity, and county.

METHODS

Invasive cervical cancer data were obtained from the Wisconsin Cancer Reporting System (WCRS), and national data were obtained from the National Cancer Institute (NCI) SEER Incidence Database.[11] Analyses were conducted using SEER*Stat Version 9.0.32.0 (National Cancer Institute). Incidence rates were calculated using SEER Site Recode for invasive cervical cancer and were expressed as observed cases per 100 000 individuals

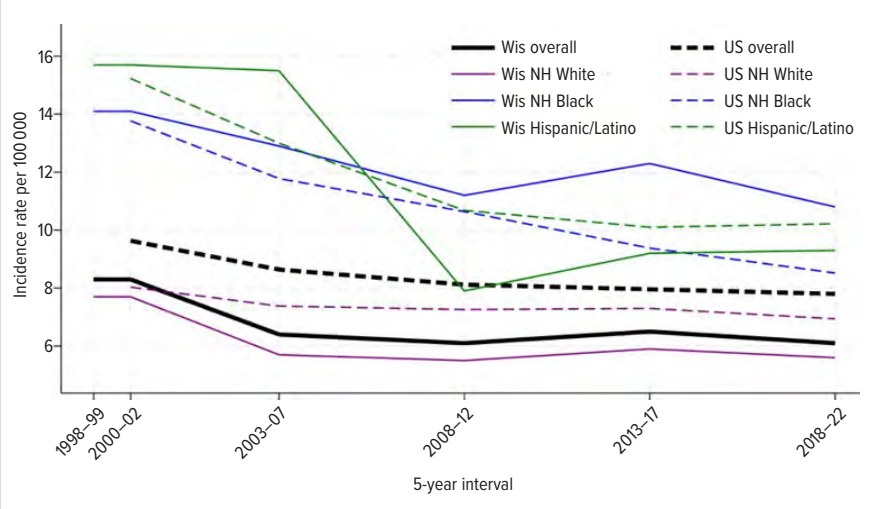
• • •

Author affiliations: University of Wisconsin School of Medicine and Public Health (UWSMPH), Madison, Wisconsin (Frey, Lapp, Zhang, Jacques); Wisconsin Department of Health Services, Madison, Wisconsin (Jacques, Swander); Department of Obstetrics and Gynecology, UWSMPH, Madison, Wisconsin (Jacques, Zhang). *Denotes co-first authors.

Corresponding author: Laura Jacques, MD, 1010 Mound St, Madison, WI 53715; email Laura.jacques@wisc.edu; ORCID ID 0000-0003-2343-8358

with a cervix, age-adjusted to the 2000 US standard population (Census P25-1130), over 5-year intervals. For inclusivity and brevity, the term "individuals" refers to people with a cervix, acknowledging that not all individuals at risk for cervical cancer identify as female. The term "cervical cancer" is used throughout this manuscript to refer to invasive cervical cancer. Incidence rates were stratified by race/ethnicity and county of diagnosis. Rates based on fewer than 16 cases were suppressed to discourage misinterpretation of unstable data and to protect patient confidentiality. WCRS data were imported into Stata version 18 to generate descriptive tables and figures. WCRS data are categorized by sex assigned at birth.

Figure 1. Age-Adjusted Invasive Cervical Cancer Incidence per 100 000 by Race/Ethnicity in Wisconsin and United States, 1998-2022



Abbreviations: Wis, Wisconsin; NH, non-Hispanic; US, United States.

RESULTS

Overall

The overall burden of cervical cancer in Wisconsin decreased 28.0%, from 8.2 to 5.9 cases per 100 000, and from 1138 cases in 1998-2002 to 921 cases in 2018-2022. The sharpest decline occurred between 1998-2002 and 2003-2007, when the incidence rate decreased 22.0% (8.2 to 6.4 per 100 000) (Figure 1).

By Race and Ethnicity

Declines in cervical cancer burden in Wisconsin were not evenly distributed across racial and ethnic groups. Among non-Hispanic White individuals, cervical cancer incidence was the lowest of any measured racial/ethnic group and remained stable throughout the study period. Rates declined from 7.7 to 5.6 per 100 000 (27.3%) from 1998 through 2022, and the sharpest decline occurred between 1998-2002 and 2003-2007 (26%; 7.7 to 5.7per 100,000). From 2003-2007 onward, rates plateaued (5.6 to 5.9 per 100 000).

Non-Hispanic Black individuals in Wisconsin had higher cervical cancer incidence rates than the statewide average and nearly twice the rate of non-Hispanic White individuals during every 5-year interval from 1998 to 2022. The percent difference between non-Hispanic Black individuals and non-Hispanic White individuals in Wisconsin increased from 83.1% higher in 1998-2002 to a peak of 119.6% higher in 2013-2017, before declining modestly to 92.9% higher in 2018-2022 (Figure 1).

Hispanic individuals experienced the largest relative decline in cervical cancer incidence in Wisconsin, decreasing 40.8% (15.7 to 9.3 per 100 000) between 1998-2002 and 2018-2022. The sharpest decline occurred between 2003-2007 and 2008-2012, when incidence decreased 49.0% (15.5 to 7.9 per 100 000). However, incidence recently increased, rising 17.7% from 7.9 per 100 000 in 2013-2017 to 9.3 per 100 000 in 2018-2022. Hispanic individuals in Wisconsin also experienced a disproportionately high incidence of cervical cancer, with the most recent rate 39.8% higher than that of non-Hispanic White individuals (Figure 1).

Cervical cancer incidence data for non-Hispanic American Indian/Alaska Native individuals were suppressed because of case counts fewer than 16 for 1998-2002 and 2018-2022. During the intervals for which data were available, non-Hispanic American Indian/Alaska Native individuals had the highest rates of cervical cancer incidence of any racial/ethnic group, with incidence rates of 14.4, 19.9, and 14.4 cases per 100 000 cases in 2003-2007, 2008-2012, and 2013-2017, respectively (Appendix).

By County

Among Wisconsin's 3 most populous counties (Milwaukee, Dane, and Waukesha), Milwaukee County had the highest cervical cancer incidence rate during every 5-year interval from 1998 through 2022, peaking at 10.1 per 100 000 in 1998-2002 and declining 19.8% to 8.1 per 100 000 in 2018-2022. Dane County had the second-highest rate during each interval except 2003-2007, when it had the lowest rate among the 3 counties (4.1 per 100 000). Incidence rates declined 31.9%, from 7.2 per 100 000 in 1998-2002 to 4.9 per 100 000 in 2018-2022. Incidence rates in Waukesha County declined 43.1% (6.5 to 3.7 per 100 000) over the study period and remained below the statewide average during every interval measured (Figure 2).

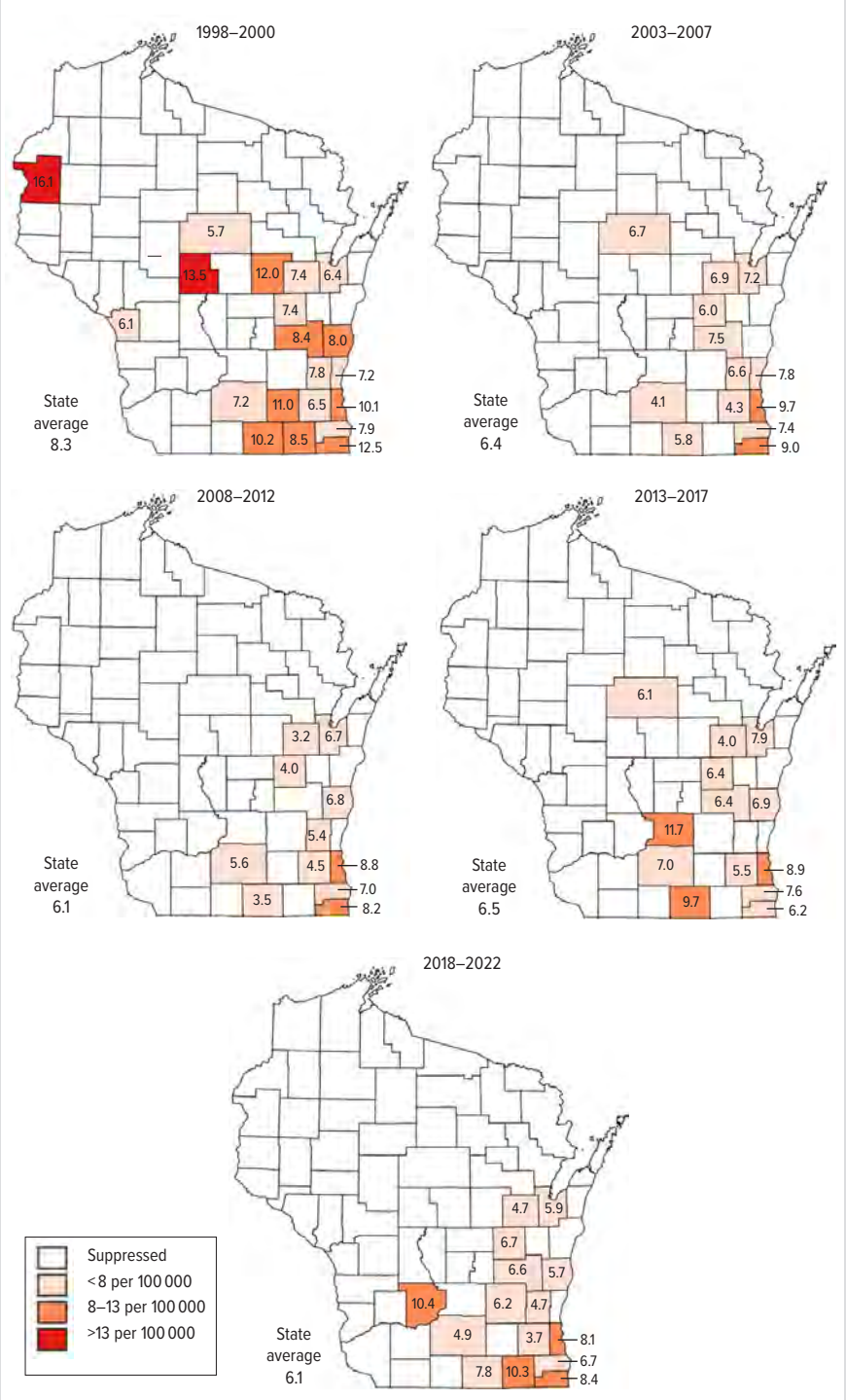
DISCUSSION

We found that while overall Wisconsin cervical cancer incidence rates are lower than US rates, notable disparities exist by race, ethnicity, and county of residence. While the state has experi-

enced an overall decline in incidence since 1998, non-Hispanic Black individuals continue to experience rates nearly double those of non-Hispanic White individuals, and this disparity has widened over time. In contrast, the national disparity between non-Hispanic Black individuals and non-Hispanic White individuals persisted throughout the 1998-2022 time frame but narrowed substantially (Figure 1). Notably, this widening disparity in Wisconsin has occurred during a period of major public health innovation, including the introduction of hrHPV testing and the quadrivalent and nonavalent HPV vaccine.[2-5]

This inequity is unlikely to be explained by differences in vaccination uptake. Statewide data demonstrate that HPV vaccination rates among non-Hispanic Black adolescents are equal to or higher than those among non-Hispanic White adolescents.[12] Differences in cervical cancer screening are also unlikely to explain the disparity, as non-Hispanic Black individuals were as likely or more likely than non-Hispanic White individuals to report having had a Pap test within the last 3 years on every Behavioral Risk Factor Surveillance System (BRFSS) survey conducted from 2002 through 2020.[13] The increase in racial and ethnic disparities in Wisconsin despite comparable vaccination coverage and Pap smear screening contributes to a growing body of evidence suggesting that disparities in preventable diseases such as cervical cancer may reflect systemic racism, including the structures, policies, and institutions that systematically advantage some populations over others.[14,15]

Figure 2. Heat Map of Age-Adjusted Invasive Cervical Cancer Incidence per 100 000 by Wisconsin County, 5-year Intervals (1998-2022)



Data for the 3 most populous counties in Wisconsin–Milwaukee, Dane, and Waukesha–form a natural case study given the substantial differences in socioeconomic context and structural vulnerability across these settings. The Centers for Disease Control and Prevention (CDC) Social Vulnerability Index (SVI), which ranks counties from 0 (least vulnerable) to 1 (most vulnerable) based on factors such as socioeconomic status, minority status, access to housing, and access to transportation, provides a useful measure of the differences.[16] Dane County falls near the state average on key structural indicators, including SVI (0.4), poverty rate (10.0%), and median income ($88,108). In contrast, Milwaukee County consistently ranks as the most vulnerable in the state (SVI, 1.0), has the highest proportion of people living below the poverty line (17.1%)–nearly double the statewide average (10.1%)–and ranks among the lowest Wisconsin counties for median household income ($62,118).[14,15]

Conversely, Waukesha County has maintained an SVI near 0 across all reporting years, has one of lowest poverty rates (5.0%), and ranks among the highest counties for median household income ($104,100).[16,17] It is therefore notable that Milwaukee County, the most structurally disadvantaged county in the state, had the highest cervical cancer incidence in every measured timeframe and the slowest rate of decline. Conversely, Waukesha County, one of the most resourced counties, consistently had the lowest incidence and the most rapid decline among the 3 most populous counties. These patterns underscore the influence of structural vulnerability and socioeconomic conditions on disease burden and warrant further research to better understand underlying drivers and inform development of effective mitigation strategies.

Strengths and Weakness

The strengths of this study include the use of long-term statewide cancer registry data and stratification by race, ethnicity, and geography, allowing for a more nuanced understanding of cervical cancer trends. However, several limitations should be acknowledged. Data categorization methods do not fully capture multiracial or ethnically diverse individuals, potentially masking additional disparities, and the use of binary sex categories may similarly mask disparities among gender and sexual minority populations. Counties with fewer than 16 cases had suppressed rates, limiting assessment of trends in the most rural counties. Additionally, simple comparisons were used to describe changes in cervical cancer incidence across 5-year intervals. Although this approach is straightforward and easily interpretable, it does not permit statistical testing of changes in trend direction or magnitude and may overlook inflection points detectable with more advanced analytic methods. Finally, because WCRS data through 2022 are directly observed and not delay adjusted, recent incidence may be underestimated because of reporting lag. This limitation is particularly important when comparing to WCRS data with national SEER estimates, which are delay adjusted and therefore are not directly comparable.

Future Directions

The aim of this research brief was to provide descriptive data on cervical cancer incidence in Wisconsin as a starting point for future investigation. Several areas warrant further study. First, differences in incidence by race and ethnicity could be examined using regression analyses to determine whether race or ethnicity are statistically significant modifiers of incidence. Second, rurality could not be explored in depth because of data suppression requirements for counties with fewer than 16 cases; future studies could aggregate counties by region or pool data across longer intervals to facilitate comparative analysis. Third, regression models incorporating structural measures such as SVI could provide additional insight into the relationship between community-level vulnerability and cervical cancer incidence. Finally, linking registry data with vaccination and screening measures could clarify whether disparities arise from differential access to, or uptake of, prevention and screening tools.

CONCLUSIONS

Innovation in cervical cancer prevention is accelerating. In-clinic and home-based hrHPV self-collection, extended genotyping, and dual stain cytology will position Wisconsin to meet the WHO goal of eliminating invasive cervical cancer as a public health problem by 2030. However, this rapid progress also creates urgency: if Wisconsin's persistent racial and ethnic disparities are not addressed, these advances may widen, rather than narrow, existing gaps in cervical cancer burden.

Financial disclosures: None declared.

Funding/support: Laura Jacques, MD, was supported by the Wisconsin Department of Health Services Reproductive Health Family Planning Title X Project, FPHPA00656. The collection of cancer incidence data used in this study was supported by the Wisconsin Department of Health Services pursuant to Wis. Stat. § 255.04, Cancer Reporting, and the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries under cooperative agreement NU58DP007146.

Acknowledgements: The ideas and opinions expressed herein are those of the author(s) and do not necessarily reflect the opinions of the State of Wisconsin, Department of Health Services and the CDC or their contractors and subcontractors.

Appendix: Available at www.wmjonline.org

REFERENCES

1. The Lancet Oncology. Global elimination of cervical cancer is achievable-with commitment. *Lancet Oncol.* 2019;20(11):1467. doi:10.1016/S1470-2045(19)30647-3

2. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10-45. doi:10.3322/caac.21871

3. Kim JJ, Burger EA, Regan C, Sy S. Screening for cervical cancer in primary care: a decision analysis for the US Preventive Services Task Force. *JAMA*. 2018;320(7):706-714. doi:10.1001/jama.2017.19872

4. Lei J, Ploner A, Elfström KM, et al. HPV Vaccination and the risk of invasive cervical cancer. *N Engl J Med*. 2020;383(14):1340-1348. doi:10.1056/NEJMoa1917338

5. Stoler MH. The five FDA-approved HPV assays. *MLO Med Lab Obs*. 2015;47(12). Accessed August 3, 2026. https://www.mlo-online.com/home/article/13004462/the-five-fda-approved-hpv-assays

6. Cancer trends progress report: online summary of trends in U.S. cancer control measures: cervical cancer screening. National Cancer Institute. Updated April 2025. Accessed May 22, 2025. https://progressreport.cancer.gov/detection/cervical_cancer

7. Matz M, Weir HK, Alkhalawi E, Coleman MP, Allemani C; US CONCORD Working Group. Disparities in cervical cancer survival in the United States by race and stage at diagnosis: an analysis of 138,883 women diagnosed between 2001 and 2014 (CONCORD-3). *Gynecol Oncol.* 2021;163(2):305-311. doi:10.1016/j.ygyno.2021.08.015

8. Buskwofie A, David-West G, Clare CA. A review of cervical cancer: incidence and disparities. *J Natl Med Assoc*. 2020;112(2):229-232. doi:10.1016/j.jnma.2020.03.002

9. U.S. Preventive Services Task Force. Draft Evidence Review: Cervical Cancer: Screening. Agency for Healthcare Research and Quality. December 10, 2024. Accessed May 22, 2025. https://www.uspreventiveservicestaskforce.org/uspstf/document/draft-evidence-review/cervical-cancer-screening-adults-adolescents

10. COWS. Wisconsin's extreme racial disparity: vast chasm separates Whites and African Americans in the state. High Road Strategy Center; January 2017. Accessed May 20, 2025. https://highroad.wisc.edu/wp-content/uploads/sites/2056/2020/04/2017-Wisconsins-Extreme-Racial-Disparity-2017.pdf

11. National Cancer Institute, Surveillance Epidemiology, and End Results Program. SEER*Explorer: cervix uteri, recent trends in SEER age-adjusted incidence rates, 2000-2023, female by race/ethnicity, delay-adjusted SEER incidence rate, all ages, all stages. Updated April 16, 2025. Accessed April 29, 2025. https://seer.cancer.gov/statistics-network/explorer/

12. Cull Weatherer A, Pritzl SL, Kerch S, Li Z, LoConte NK. Current trends in HPV Vaccine uptake: Wisconsin and United States, 2016-2019. *WMJ*. 2021;120(1):62-65.

13. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System Prevalence & Trends Data: explore by location, nationwide, states – Wisconsin, women's health, pap test, 2002-2020, women aged 21-65 who have had a pap test in the past three years. Updated July 19, 2023. Accessed September 10, 2025. https://www.cdc.gov/brfss/brfssprevalence/

14. Doll KM. Investigating Black-White disparities in gynecologic oncology: theories, conceptual models, and applications. *Gynecol Oncol*. 2018;149(1):78-83. doi:10.1016/j.ygyno.2017.10.002

15. Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. *Lancet*. 2017;389(10077):1453-1463. doi:10.1016/S0140-6736(17)30569-X

16. Agency for Toxic Substances and Disease Registry, Place and Health – Geospatial Research, Analysis, and Services Program. SVI interactive map: overall SVI, United States, Wisconsin: statewide comparison, by county. Updated December 21, 2023. Accessed May 21, 2025. https://www.atsdr.cdc.gov/place-health/php/svi/svi-interactive-map.html

17. QuickFacts: Wisconsin. U.S. Census Bureau. Accessed June 6, 2025. https://www.census.gov/quickfacts/fact/table/WI/PST045222.

Chlorhexidine Gluconate as a Conducting Medium Is Noninferior to Ultrasound Gel in Ultrasound Image Quality: A Blinded, Randomized Comparative Study

Hariharan Shankar, MD; Frank Zachary, MD; Craig Cummings, MD; Ryan Davidovich, MD

ABSTRACT

Background: Ultrasound imaging is increasingly used by physicians for both diagnostic and image-guided procedures. A coupling medium is used to facilitate transmission of ultrasound waves from the transducer to tissues by eliminating air interference. The ideal coupling medium would be inexpensive, provide effective transmission, and neither introduce infection nor damage the skin or transducer. Ultrasound gel, a commonly used coupling medium, has the potential to transmit infection. This blinded, randomized study assessed the noninferiority of ultrasound image quality using chlorhexidine gluconate with isopropyl alcohol as coupling medium compared with ultrasound gel.

Methods: Sixty different locations were imaged on 2 healthy volunteers. The order of use of the 2 coupling media was randomized at each location without changing the imaging site or ultrasound settings. The images were then coded to facilitate blinding. Two blinded reviewers evaluated the coded images using a comparative rating scale.

Results: Chlorhexidine gluconate demonstrated a slightly improved image quality (mean 2.53; 95% CI, 2.46-2.60) compared with ultrasound gel (mean, 2.42; 95% CI, 2.35-2.50) ($P = .04$).

Conclusions: The commonly used skin antiseptic chlorhexidine gluconate with isopropyl alcohol demonstrated noninferior image quality compared with ultrasound gel and may represent a more economical alternative for ultrasound-guided interventions, with the potential to reduce infectious complications.

INTRODUCTION

Ultrasound imaging has become a commonly used imaging modality because of its portability and dynamic visualization. While generally considered one of the safer imaging modalities, it is not without risks. Ultrasound transducers perform the dual function of generating and receiving ultrasound waves. As the waves travel through tissues, they undergo a decrease in intensity and amplitude called attenuation, with different tissues having different attenuation coefficients, allowing appreciation of the subtleties in the reflected image. Acoustic impedance is the resistance offered by tissues to ultrasound waves. The difference between the acoustic impedances of adjacent media determines the amount of ultrasound wave energy reflected.[1] When the difference is greater, more waves are reflected back to the transducer. Because air has an acoustic impedance significantly lower than that of tissues, ultrasound waves are reflected, resulting in loss of penetration through the skin. Ultrasound conducting or coupling media minimize this effect by narrowing the acoustic impedance difference between air and skin, thus allowing for effective transmission of ultrasound waves from the transducer through the skin.[1]

The ideal conducting medium would be cost-effective, provide good transmission, and neither introduce infection nor damage the skin or transducer. Multiple conducting media have been studied, including sterile water, olive oil, hand sanitizer, and cornstarch, in addition to ultrasound gel (USG),[2] which has been widely used for many decades. It is available in both single-use sterile sachets and multiuse bottles. However, concerns persist regarding the potential

• • •

Author affiliations: Department of Anesthesiology, Clement Zablocki VA Medical Center, Medical College of Wisconsin, Milwaukee, Wisconsin (Cummings, Shankar, Zachary); US Anesthesia Partners, Nashville, Tennessee (Davidovich).

Corresponding author: Hariharan Shankar, MD, 5000 W National Ave, Milwaukee, WI 53295; email hshankar@mcw.edu; ORCID ID 0000-0002-1567-3887

for nosocomial infections associated with multiuse bottles despite its being labeled as bacteriostatic.[3,4] Studies have shown that even with the use of sterile USG, skin contamination can occur with certain bacteria, possibly because of the development of resistance or degradation of the parabens.[5] Various parts of ultrasound equipment have been shown to be susceptible to contamination and bacterial growth, and environmental bacteria have been identified in heated USG.[6] There is also concern of contact dermatitis associated with additives in USG, particularly parabens.[7]

Chlorhexidine gluconate (CHG), or the commercially available ChloraPrep solution, is a commonly used broad-spectrum antimicrobial biguanide used for skin antisepsis. It contains 2% weight/volume chlorhexidine gluconate and 70% volume/volume isopropyl alcohol. Clinical practice guidelines recommend the use of alcohol combined with another agent, such as CHG, for surgical-site antisepsis.[8] As CHG is routinely used before ultrasound-guided procedures, we hypothesized that it could also serve as a coupling medium and provide ultrasound image quality similar to that of USG.

Figure. Ultrasound Transverse View of the Anterior Neck Using Chlorohexidine Gluconate (A) and Ultrasound Gel (B)

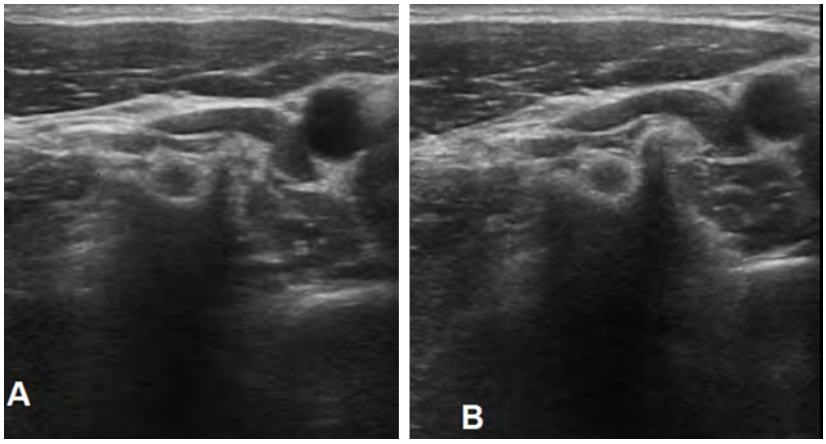


Table. Sample Size Calculation

Probability of Tie	Intracluster Correlation Between Raters			
	0.7	0.8	0.9	1
55%	77.8%	75.7%	73.7%	71.8%
60%	81.9%	80.0%	78.0%	76.2%
65%	86.2%	84.4%	82.6%	80.9%
70%	90.4%	88.9%	87.4%	85.9%

METHODS

The study was approved by the Human Studies Institutional Review Board. Two healthy volunteers underwent ultrasound examinations at different anatomical locations commonly used for ultrasound-guided interventions. Ultrasound settings were kept constant throughout the study to allow accurate comparison. At each location, CHG and USG were used as the conducting medium in random order. Randomization was performed using sealed envelopes. The investigator performing the ultrasound examinations was not blinded to the conducting medium. This resulted in 60 images obtained using CHG and 60 images with USG, for a total of 120 images. Once obtained, the images were numbered and coded to deidentify the medium used before evaluation.

Two reviewers, blinded to the medium used for each image, evaluated image quality. The images were rated on a 3-point scale, with a score of 3 representing superior image quality.

The Table shows the estimated power achieved by the study at a 5% significance level with 58 pairs of ultrasound images obtained with the 2 media, each evaluated by 2 raters, if the images obtained with the 2 media have equivalent quality, ie, P(worse)389 = P(better). The power calculation is based on formulas for a noninferiority test with 1 rater, modified to include a variance inflation factor of [1+(m-1) ρ] for m raters with between-rater correlation ρ. The power of the study depends on the extent of agreement between the 2 raters and the proportion of ties ("same" calls); therefore, a range of plausible scenarios is presented. The selected sample size was based on a 60% probability of ties and a correlation of 0.8 to achieve 80% power. Agreement between the 2 raters was quantified using weighted κ and reported with a 95% confidence interval.

RESULTS

The raters commented that it was not possible to differentiate which image were obtained using CHG versus USG as the conducting medium. They graded image quality as comparable between CHG and USG, with a mean score of 2.53 (95% CI, 2.46–2.60) for CHG and a mean score of 2.42 (95% CI, 2.35–2.50) for USG ($P = .04$). CHG had an interrater reliability of 0.59 compared with 0.54 for USG (Figure).

DISCUSSION

This study demonstrates that CHG provides image quality comparable to that of USG as a coupling medium. We have used CHG as a coupling medium for more than a decade at our institution without any CHG-related adverse events during more than 10000 ultrasound-guided procedures with good results.

In a blinded randomized study, Williams II et al compared image quality and time required to visualize carotid artery and internal jugular vein using saline and USG and found them to be

comparable.[3] Saline is likely to flow away from the site under the influence of gravity, requiring continuous irrigation. In a blinded, randomized, crossover study involving 34 patients, corn starch and commercial USG showed no difference in image quality Although inexpensive, corn starch raises concerns regarding infection risk during ultrasound-guided interventions.[4]

With the primary goal of reducing cost, investigators prepared different formulations using aloe vera as the main ingredient, with additives including parabens, a polymer, triethanolamine, and disodium ethylenediaminetetraacetic acid (EDTA). They found that these formulations had acoustic impedance and quality similar to those of USG.[9] Another study compared 9 commonly available liquids, including water, shampoo, lotion, hand sanitizer, maple syrup, olive oil, soap, and sunscreen, with USG and found comparable image quality for all products except sunscreen; however, sterility remained a limitation.[2]

Because of its antimicrobial properties, hand sanitizer may offer advantages and cost savings compared with sterile USG sachets.[10] To reduce infection risk, one study compared nonsterile USG and USG fortified with 0.5% chlorhexidine and 70% ethyl alcohol in 20 volunteers undergoing ultrasound imaging. Swabs obtained from various sites, including the skin, transducer, and gel, yielded no bacterial growth in the fortified-USG group.[11]

The potential benefits of CHG as a coupling medium include slightly enhanced image quality and potentially reduced costs and infection risk. One disadvantage is the need for reapplication as it evaporates, necessitating maintenance of a fluid coupling medium. In addition, because of its alcohol content, CHG is not considered safe for use during radiofrequency ablation or electrocautery because of the associated fire hazard.

CONCLUSIONS

This study provides preliminary evidence demonstrating the noninferiority of ultrasound image quality with CHG compared with USG as coupling medium for ultrasound-guided interventions. In addition, the use of CHG may decrease infectious complications because of its antimicrobial properties. Larger studies are needed to evaluate the cost-effectiveness of CHG and its potential to reduce infection risk.

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgements: The authors would like to thank Zan Khan for his contribution to data collection. This study was presented as an abstract at the annual meeting of the American Society of Regional Anesthesia and Pain Medicine, April 11-13, 2019, in Las Vegas, Nevada.

REFERENCES

1. Shankar H, Pagel PS. Potential adverse ultrasound-related biological effects: a critical review. *Anesthesiology*. 2011;115(5):1109-1124. doi:10.1097/ALN.0b013e31822fd1f1

2. Wray JN, Soucy ZP, Daniel NJ, et al. Comparison of commonly carried liquids against commercial ultrasound gel for use in the backcountry setting. *Wilderness Environ Med*. 2023;34(2):135-142. doi:10.1016/j.wem.2022.12.005

3. Williams GW 2nd, Cai C, Artime CA, Teima D, Emerald A, Rajkumar KP. Evaluation of saline versus gel as contact medium for ultrasonographic image quality. *J Clin Ultrasound*. 2019;47(9):540-545. doi:10.1002/jcu.22750

4. Binkowski A, Riguzzi C, Price D, Fahimi J. Evaluation of a cornstarch-based ultrasound gel alternative for low-resource settings. *J Emerg Med*. 2014;47(1):e5-e9. doi:10.1016/j.jemermed.2013.08.073

5. Oleszkowicz SC, Chittick P, Russo V, Keller P, Sims M, Band J. Infections associated with use of ultrasound transmission gel: proposed guidelines to minimize risk. *Infect Control Hosp Epidemiol*. 2012;33(12):1235-1237. doi:10.1086/668430

6. Westerway SC, Basseal JM, Brockway A, Hyett JA, Carter DA. potential infection control risks associated with ultrasound equipment - a bacterial perspective. *Ultrasound Med Biol*. 2017;43(2):421-426. doi:10.1016/j.ultrasmedbio.2016.09.004

7. Lee EB, Lobl M, Ford A, DeLeo V, Adler BL, Wysong A. What is new in occupational allergic contact dermatitis in the year of the covid pandemic? *Curr Allergy Asthma Rep*. 2021;21(4):26. doi:10.1007/s11882-021-01000-3

8. Seidelman JL, Mantyh CR, Anderson DJ. Surgical site infection prevention: a review. *JAMA*. 2023;329(3):244-252. doi:10.1001/jama.2022.24075

9. Afzal S, Zahid M, Rehan ZA, et al. Preparation and evaluation of polymer-based ultrasound gel and its application in ultrasonography. *Gels*. 2022;8(1):42. doi:10.3390/gels8010042

10. Sutton E, Bullock WM, Khan T, Eng M, Gadsden J. Hand sanitizer as an alternative to ultrasound transmission gel. *Reg Anesth Pain Med*. 2016;41(5):655-656. doi:10.1097/AAP.0000000000000435

11. Okere P, Iloanusi N, Itanyi U, Ezea M. Low-cost antimicrobial fortification of ultrasound coupling gel:aAn ergonomic innovation to combat sonology-acquired nosocomial infections. *Malawi Med J*. 2019;31(1):45-49. doi:10.4314/mmj.v31i1.8

Improving Utilization of Sputum Culture in Patients Hospitalized with Pneumonia: A Quality Improvement Initiative

Catherine S. Taghizadeh, BS; Jennifer Zimmerman, DO; Faran Ahmad, MD; Richard Swaney, DO; Alexander Hall, PhD; Jeffrey Macaraeg, MD; Jennifer Anthone, PharmD; Manasa Velagapudi, MBBS

ABSTRACT

Background: Sputum cultures are essential for guiding targeted antibiotic therapy; however, they are often underutilized. This quality improvement initiative aimed to enhance sputum culture ordering through an antimicrobial stewardship pharmacist-led intervention.

Methods: A retrospective review of pneumonia hospitalizations from January 2021 through December 2022 evaluated the impact of a policy change allowing antimicrobial stewardship pharmacists to order sputum cultures. Statistical analyses compared preintervention and postintervention sputum culture ordering rates, adjusting for patient demographics, hospital admission location, and other covariates.

Results: Sputum culture orders increased from 36% before the intervention to 50% after the intervention, with a 29% higher likelihood of sputum culture ordering after the intervention (risk ratio, 1.29; 95% CI, 1.19–1.38; $P < .001$).

Conclusions: This intervention demonstrates the potential for antimicrobial stewardship programs to improve adherence to guideline-based practices through pharmacist-led initiatives.

BACKGROUND

In the National Hospital Care Survey, pneumonia accounted for 130 657 qualifying pneumonia hospitalizations across the United States in 2016, with a 35% in-hospital mortality rate.[1] Along with increased morbidity and mortality, pneumonia is associated with significant clinical and economic burdens resulting from prolonged hospitalization and high medical costs. Methods for diagnosing community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) include sputum cultures, antigen tests, blood cultures, polymerase chain reaction, and invasive techniques such as thoracocentesis, transthoracic needle aspiration, and bronchoalveolar lavage.[2]

The American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) 2019 guidelines for community-acquired pneumonia recommend performing a sputum culture for patients with severe pneumonia and for all inpatients being treated empirically for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa* (*P aeruginosa*). Specifically, for intubated CAP patients unable to produce lower respiratory tract specimens and those who previously received treatment for MRSA or *P aeruginos*a, immediate sputum cultures are recommended.[3] Noninvasive sputum cultures have been found to be useful for identifying the pathogenic bacteria responsible for pneumonia, guiding timely and accurate antibiotic selection, and supporting successful treatment outcomes.[4,5]

Previous literature has demonstrated that sputum culture use is associated with improved intensive care unit (ICU) mortality, decreased antibiotic usage, fewer adverse effects, reduced cost, and shortened hospital length of stay.[1,6,7] Despite controversy surrounding sputum culture use due to concerns about sample representativeness and contamination, previous studies have reported increased ICU and hospital mortality among pneumonia patients without sputum culture collection.[6] When compared with invasive bronchoalveolar lavage for definitive diagnosis, sputum cultures are less time-consuming, more cost-effective, and have a 96.5% positive predictive value (PPV).[8] Previous quality improvement (QI) projects have reported improved compliance with established pneumonia performance indicators after implementation of a sputum culture order set, as well as improvements in overall CAP prognosis. Recent research on multidisciplinary, stewardship-led interven-

• • •

Author affiliations: Creighton University School of Medicine, Phoenix, Arizona (Taghizadeh); Department of Internal Medicine, Creighton University School of Medicine, Omaha, Nebraska (Ahmad, Macaraeg, Swaney, Velagapudi, Zimmerman); Department of Clinical Research and Public Health, Creighton University, Omaha, Nebraska (Hall); Creighton University Medical Center at Bergan Mercy, Omaha, Nebraska (Anthone).

Corresponding author: Catherine Taghizadeh, email CST40631@creighton.edu; ORCID ID 0009-0004-3522-6074

tions to improve sputum culture utilization is limited.[9,10] Based on evidence supporting the role of sputum culture in pneumonia treatment and prognosis, this QI initiative aimed to enhance sputum culture collection through an antimicrobial stewardship pharmacist-led intervention at Catholic Health Initiatives (CHI) Health Creighton University Medical Center in Omaha, Nebraska.

Table 1. Overall Patient Characteristics

Patient Characteristics	Overall (N = 3614) Frequency (%)	Preintervention Frequency (%)	Postintervention Frequency (%)	*P* value
Age (Median, IQR)	68 (57–70)	67 (55–78)	70 (60–79)	< .001
Female	1694 (47%)	1002 (47%)	692 (46%)	.60
English language	3336 (92%)	1953 (92%)	1383 (93%)	.57
Hispanic ethnicity	284 (8%)	179 (8%)	105 (7%)	.15
Missing	123 (3%)	62 (3%)	61 (4%)	
Department				0.004
Intensive care unit	668 (18%)	425 (20%)	243 (16%)	
Medical/surgical unit	2946 (82%)	1696 (80%)	1250 (84%)	

Table 2. Sputum Test Ordered (N = 3614)

N = 3614	Risk Ratio (95% CI)	*P* value	Adjusted Risk Ratio (95% CI)	*P* value
Postintervention vs Preintervention	1.30 (1.21–1.40)	< .001	1.29 (1.19–1.38)	< .001
Medical/surgical unit vs intensive care unit	1.26 (1.16–1.37)	< .001	1.25 (1.15–1.37)	< .001
Male vs female	1.05 (0.97–1.13)	.25	1.02 (0.95–1.11)	.55
Other vs English	1.05 (0.91–1.21)	.47	1.13 (0.95–1.35)	.12
Other vs Hispanic	1.04 (0.90–1.20)	.61	1.10 (0.92–1.32)	.28
Age – 5 years	1.00 (0.98–1.01)	.44	0.99 (0.98–1.01)	.35

METHODS

A retrospective chart review was conducted of adult patients admitted to CHI Health Creighton University Medical Center with CAP or HAP from January 1, 2021, through December 31, 2022. Patients transferred to another facility or who died within 48 hours of admission were excluded. This QI project was reviewed by our local Institutional Review Board (IRB) and was determined not to constitute human subjects research (reference No. 2001933-01); therefore, IRB approval was not required.

Intervention

On November 1, 2021, a system-wide initiative allowed antimicrobial stewardship pharmacists to order sputum cultures, a role previously limited to physicians. The intervention was initiated following approval by the hospital's Clinical Policy Committee and endorsement by the Quality Improvement Committee. Implementation steps included developing a concise clinical rationale and presenting it at 3 multidisciplinary QI meetings, engaging internal medicine residents and hospitalists as QI champions to facilitate adoption, and implementing a system-wide policy change enabling stewardship pharmacists to order sputum cultures.

The postintervention period was defined as January 1, 2022, onward to account for implementation adjustments. The data for this 2-month implementation period from November-January has been censored.

Analysis

Descriptive patient characteristics are reported as frequencies and percentages for categorical variables and as medians and interquartile ranges for continuous variables. Patient characteristics were compared between preintervention and postintervention periods using chi-square tests for categorical variables and Mann-Whitney tests for continuous variables. Log-binomial regression was used to estimate the adjusted likelihood of having a sputum culture ordered before versus after the intervention. Covariates included patient age at admission, sex, Hispanic ethnicity (yes/no), hospital admission location (medical-surgical unit vs ICU), and patient primary language (English vs other). Results are presented as unadjusted and adjusted relative risks (RR) with 95% confidence intervals (CIs). All analyses were conducted using Statistical Analysis Software (SAS), version 9.4 (SAS Institute Inc), with statistical significance defined as 2-sided $P < .05$.

RESULTS

A total of 3614 patients diagnosed with pneumonia during the study period were included in the analysis. Of these, 2121 (59%) were diagnosed during the preintervention period, 1694 (47%) were women, and the median age at admission was 68 years. The majority of patients (82%) were admitted to a medical-surgical (med/surg) unit.

Overall, patient admission characteristics appeared similar between the preintervention and postintervention periods, suggesting that the underlying patient populations were comparable. However, a slightly higher proportion of patients were admitted to the med/surg unit in the postintervention period ($P = .004$), and patients in the postintervention period were slightly older ($P < .001$) (Table 1).

Sputum culture orders increased from 36% in 2021 to 42% in 2022, reaching 50% by 2023, highlighting the positive impact of the intervention on clinical practice. After adjustment for all covariates, the likelihood of sputum culture ordering was 29% higher in the postintervention period than in the preintervention period (RR, 1.29; 95% CI, 1.19–1.38; $P < .001$). Admission location was also a significant predictor, with patients admitted to

the med/surg unit having an estimated 25% greater likelihood of sputum culture ordering than patients admitted to the ICU (RR, 1.25; 95% CI, 1.15–1.37; $P < .001$). No other predictors were statistically significant (Table 2).

DISCUSSION

Our findings demonstrated a significant short-term increase in sputum culture orders for pneumonia patients following the implementation of a system-wide QI initiative.

Additionally, our analysis revealed that patients admitted to the med/surg unit had a 25% higher likelihood of having a sputum culture ordered compared with those admitted to the ICU. This finding aligns with prior studies, including a 2014 QI initiative among intubated pneumonia patients, which found that emergency department physicians rarely ordered sputum cultures—a practice associated with increased ICU mortality and reduced antibiotic de-escalation.[7] These results suggest that further QI initiatives targeting ICU and emergency department providers could enhance adherence to evidence-based guidelines and ultimately improve patient outcomes.

There are limited data regarding sputum culture ordering among patients with CAP and HAP. This may be due to ongoing controversy surrounding the routine use of sputum cultures; despite their role in determining antibiotic susceptibility patterns and guiding treatment, they are often considered insufficiently accurate for diagnostic purposes. While some QI efforts have focused on decreasing mortality by increasing sputum culture utilization, there is little evidence evaluating the role of nonphysicians, such as antimicrobial stewardship pharmacists, in driving these improvements. Our system-wide initiative offers insight into how nonphysician-led interventions can influence adherence to best practices in pneumonia management.[6,9,10] Our success may be attributed to several implementation strategies, including leveraging existing stewardship infrastructure, encouraging early stakeholder involvement, and clearly communicating the clinical rationale. The decision to empower pharmacists through a policy change required minimal resources and was broadly acceptable to physicians, facilitating rapid adoption. Although the intervention did not undergo multiple formal Plan-Do-Study-Act cycles, it represents a foundational model on which future, more iterative, and data-driven QI efforts can build. Disseminating not only outcomes but also implementation strategies and contextual factors may help address gaps in the literature regarding successful QI interventions.

Our study highlights the role of a robust antimicrobial stewardship program in successfully implementing guideline-based interventions. By promoting targeted therapy, such programs not only improve diagnostic accuracy and antibiotic selection but also help mitigate the growing threat of antibiotic resistance.

However, like other QI projects, our study has several limitations. Its quasi-experimental design limits the ability to establish direct causality, and statistical adjustments for clustering effects—such as the influence of individual pharmacists managing multiple patients—were not incorporated. The impact of the COVID-19 pandemic on ordering practices was also not evaluated. Additionally, we did not quantify pharmacist time dedicated to the intervention or assess its cost-effectiveness, both of which could provide valuable insights into its economic impact. Furthermore, the generalizability of our findings may be limited in institutions without established antimicrobial stewardship programs, and we did not assess the impact of this intervention on patient outcomes.

Despite these limitations, our findings support the feasibility of low-cost, sustainable QI initiatives that drive meaningful changes in clinical practice. Future efforts should focus on identifying barriers to sputum culture utilization in ICU settings and developing tailored interventions to promote adherence to best practices in pneumonia management. Expanding evaluations of stewardship programs will be critical in demonstrating their long-term benefits in optimizing antimicrobial use, reducing resistance, and improving patient care.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Peters ZJ, Ashman JJ, Schwartzman A, DeFrances CJ. National Hospital Care Survey demonstration projects: examination of inpatient hospitalization and risk of mortality among patients diagnosed with pneumonia. *Natl Health Stat Report.* 2022:167:1-9. doi: 10.15620/cdc:112080

2. Kim B-G, Kang M, Lim J, et al. Comprehensive risk assessment for hospital-acquired pneumonia: sociodemographic, clinical, and hospital environmental factors associated with the incidence of hospital-acquired pneumonia. *BMC Pulm Med.* 2022;22(1):21. doi:10.1186/s12890-021-01816-9

3. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med.* 2019;1;200(7):e45-e67. doi:10.1164/rccm.201908-1581ST.

4. Naidus EL, Lasalvia MT, Marcantonio ER, Herzig SJ. The diagnostic yield of noninvasive microbiologic sputum sampling in a cohort of patients with clinically diagnosed hospital-acquired pneumonia. *J Hosp Med.* 2018;13(1):34-37. doi:10.12788/jhm.2868

5. Cukic V, Hadzic A. The most common detected bacteria in sputum of patients with community-acquired pneumonia (CAP) treated in hospital. *Med Arch*. 2016;70(5):354-358. doi:10.5455/medarh.2016.70.354-358

6. Mahal Y, Smith K, Riker R. Failure to obtain admission sputum culture is associated with higher mortality and fewer ventilator-free days for intubated pneumonia patients: a quality improvement project. *Crit Care.* 2014;18(suppl1):S94. 34th International Symposium on Intensive Care and Emergency Medicine abstract P261. doi:10.1186/cc13451

7. Ariyoshi N, Lassan J, Devendra G. Clinical impact of sputum culture in critically ill patients with non-ventilator-associated nosocomial pneumonia. *Chest*. 2016;150(4)(suppl):227A. CHEST 2016 Annual Meeting Abstracts. doi:10.1016/j.chest.2016.08.240

8. Dubourg G, Abat C, Rolain JM, Raoult D. Correlation between sputum and bronchoalveolar lavage fluid cultures. *J Clin Microbiol*. 2015;53(3):994-996. doi:10.1128/JCM.02918-14

9. Gonzalez CE, Johnson TN, Evans S, et al. Assessing compliance with established pneumonia core measures at a comprehensive cancer center. *J Healthc Qual.* 2015;37(4):232-244. doi:10.1111/jhq.12066

10. An TJ, Myong J-P, Lee Y-H, et al. Continuing quality assessment program improves clinical outcomes of hospitalized community-acquired pneumonia: A nationwide cross-sectional study in Korea. *J Korean Med Sci.* 2022;37(30):e234. doi:10.3346/jkms.2022.37.e234

A Qualitative Analysis on the Implementation of a Community-Based Free Sunscreen Dispenser Program

Alyssa M. Jobe, BS; Drake Seibert, BA; Simran Bedi, BS; Jacqueline T. Cooper, MD; Sophia Neman, MD; Sarah Seiter, MD; Akorfa Adobor, BS; Karolyn A. Wanat, MD

ABSTRACT

Background: Skin cancer is the most common malignancy in the United States, underscoring the need for effective prevention strategies. The Community Sun Protection Program (CSPP), a medical student-run initiative, aims to improve access to sunscreen through the provision of free sunscreen dispensers.

Objectives: This study evaluated the impact of a sunscreen dispenser initiative and identified factors that may inform future community sunscreen dispenser programs.

Methods: The CSPP provided 13 sunscreen dispensers to 8 community partners in Milwaukee County, Wisconsin. After at least 1 summer of dispenser use, community site managers were interviewed, and responses were transcribed for thematic analysis.

Results: Community site managers identified 3 primary themes: improved accessibility, positive community engagement, and increased educational opportunities related to sun safety.

Conclusions: These findings highlight the value of a collaborative public health intervention aimed at improving sun safety awareness and access to preventive resources.

BACKGROUND

Skin cancer is the most common malignancy in the United States, and survival rates for metastatic melanoma remain poor.[1] Daily and long-term sunscreen use has been demonstrated to decrease the risk of melanoma and nonmelanoma skin cancers, with the effect being greatest among individuals with a history of blistering sunburns, lighter skin tones, and numerous nevi.[2-4] While skin cancer is rare in people of color, it often presents at a later stage, and the 5-year survival rate among Black individuals is 70% compared with 94% in White individuals.[5] Therefore, it is important for all patients, regardless of skin color, to wear sunscreen. Decreasing barriers to sunscreen use is an important public health intervention to reduce the risk of skin cancer.

Despite the known positive effects of chronic sunscreen use, there are several reported barriers to its use, including cost, education, and accessibility.[6] In 2014, the US Surgeon General declared skin cancer a major public health issue and recommended that Americans use sun protection while outdoors.[7] As part of that initiative, health care organizations were encouraged to partner with communities to implement preventive resources and education aimed at reducing skin cancer.

In Wisconsin, melanoma incidence and mortality rates are higher than the national average and continue to increase in Milwaukee County.[8] The Community Sun Protection Program (CSPP) is a medical student-run, community-based program that provides free sunscreen dispensers to promote sunscreen use and improve access to sun protection in Milwaukee County. The CSPP was created in collaboration with the Medical College of Wisconsin Department of Dermatology including funding and general program oversight with community partnerships and equipment managed by a medical student team.

This study evaluated the CSPP by assessing its strengths and challenges to inform recommendations for future community sunscreen dispenser projects.

METHODS

The CSPP provided 13 sunscreen dispensers to 8 community partners within Milwaukee County over 3 consecutive summers.

• • •

Author affiliations: Medical College of Wisconsin (MCW), Wauwatosa, Wisconsin (Adobor, Bedi, Cooper, Jobe, Neman, Seibert, Seiter, Wanat); Department of Dermatology, Medical College of Wisconsin, Wauwatosa, Wisconsin (Wanat).

Corresponding author: Karolyn A. Wanat, MD, 8701 W Watertown Plank Rd, Milwaukee, WI 53226; email kwanat@mcw.edu; ORCID ID 0000-0001-6262-2559

Community partners were selected based on their responsiveness to outreach and the goal of reaching a diverse population. Sites included the county zoo, a public pool, a golf course, 3 outdoor educational centers, a beer garden operated by Milwaukee County Parks, and a community center.

Each dispenser is a freestanding, automatic, touch-free dispenser with a support pole and base (Figure). Each dispenser contains 1000 mL of sun protection factor (SPF) 30 broad-spectrum hybrid sport sunscreen. Each dose is 1.5 mL. The sunscreen is water resistant for 80 minutes, zinc-based, and free of para-aminobenzoic acid (PABA), avobenzone, and oxybenzone. Refills were available on request. In addition, informative placards with an optional survey were attached to each dispenser (Figure).

After Institutional Review Board approval, interviews were conducted via phone with each site manager after at least 1 summer of dispenser use. A phone script with a preapproved set of questions was utilized. Responses were transcribed and analyzed thematically. Data were interpreted using grounded theory methodology.[9]

Figure. Automatic Freestanding Sunscreen Dispenser and Educational Placard

Placard includes unique QR code for user survey.

RESULTS

Four community site managers were interviewed in Fall 2022. One site manager declined to be interviewed. Three site managers were not eligible for interviews because they did not have at least 1 full summer of dispenser use. All managers interviewed described their overall perspective of the dispenser program as "positive" and identified the availability of free sunscreen as the most important aspect of the program. Themes identified and described in the Table were accessibility, positive community engagement, and education, respectively. Other positive themes identified during interviews included innovation, novelty, excitement, and usefulness.

DISCUSSION

The goal of the CSPP is to provide free sunscreen throughout Milwaukee County, and this study evaluated factors that affected the use of sunscreen dispensers within the community.

Themes

Accessibility: Cost was the most influential factor identified by the site managers interviewed. This aligns with literature identifying cost as a significant barrier to sunscreen access emphasizing the need for low-cost, convenient sunscreen initiatives.[7] Our findings suggest that site managers perceive cost as a barrier not only for individual users but also for their organizations, which recognize the benefits of sunscreen use but may have limited resources to provide sunscreen independently. By offering free sunscreen dispensers and routine refills, the CSPP reduced this burden on community partners. This was particularly beneficial for organizations with limited budgets, such as government-funded institutions, including the community center. As a result, the initiative expanded access to sunscreen in community settings that otherwise might not have been able to provide this resource. Placement of dispensers in outdoor, sun-exposed locations also supported sunscreen use when individuals forget or choose not to bring their own.

Positive Community Impact and Engagement: Community members and site managers all expressed positive perceptions of the sunscreen dispensers. As noted by the pool manager, patrons felt cared for knowing their community was providing a resource for their benefit. Community members requested refills from site managers and inquired about sunscreen type, brand, and ingredients, which program managers viewed as evidence of strong community engagement.

A strength of this small-scale pilot program was the direct relationship with each site, allowing for a close partnership with the academic dermatology department. Medical students helped manage the dispensers and communicated directly with site managers to improve the program. These close partnerships are essential for improving health outcomes through evidence-based interventions.

Education: While formal interactions positively influence health education, the impact of informal conversations is often overlooked in community-based health interventions. One study noted that casual conversations can fill knowledge gaps by sharing health information, encouraging adoption of new and positive behaviors, and leveraging personal connections and trust.[10] This community engagement approach can help address educational gaps in real time.

Site managers identified educational conversations on topics such as skin cancer risk among people of color, appropriate sunscreen use, and characteristics of quality sunscreen, includ-

Table. Summary of Postintervention Interview Themes and Comments

Description	Evidence	Supporting Comment (Dispenser Location)
Theme: Accessibility		
Increased availability of sunscreen alleviated barriers (eg, cost, inconvenience)	All respondents reported access to free sunscreen as the important factor for engaging with the program	"Receiving the dispenser free of charge was important because we are limited in our funding. Having this apparatus and having this maintained wouldn't be in our budget for the summer. I knew it was important to have." (Community Center) "A lot of people don't apply sunscreen, and being in the Midwest it can get quite hot and sun can definitely burn your skin so it's great that they have the opportunity to use the sunscreen free of charge." (Golf Course)
Theme: Positive Community Impact and Engagement		
Provision of sunscreen positively fected users and facilities	All respondents noted community members approaching them and their employees to express positive feedback and excitement.	"An amazing form of engagement that needs to happen more…bridges the af- gap from not just a recreational facility but also it shows the community that we… care about the public. (Pool) "When it was out, people said, 'Didn't you used to offer sunscreen?' People clearly enjoyed this resource." (Beer Garden) "We appreciated how the kids can use this sunscreen before going on their field trips to the nature center." (Community Center)
Theme: Education		
Sunscreen dispensers and accompanying resources provided education on safe sun practices	Initiated informal educational conversations on necessity of sun safe practices	"People felt that sunscreen is not something they think about putting on on a daily basis unless they go to a beach…" (Community Center) "…maybe an educational pamphlet of some sort about sunscreen would be good." (Pool)

ing broad-spectrum protection and SPF. Through these conversations, the program identified educational gaps that may be addressed through future outreach efforts. An educational pamphlet was created to address common sunscreen misconceptions and provide information about the sunscreen available in the dispensers, along with contact information for additional questions or concerns.

Challenges and Limitations

Due to the nature of a self-service dispenser, we were unable to accurately monitor sunscreen use. Location of application (eg, face, arms, legs, chest), amount of sunscreen used, and reapplication are all important considerations for effective sunscreen use. BrightGuard, the sunscreen vendor, estimates approximately 650 uses per 1000-mL bag of sunscreen, allowing only an estimate of dispenser use. This assumption also requires that each bag be used completely and without any waste.

Partnership with community site managers is essential for monitoring dispenser use. Some site managers were able to directly monitor dispenser use because of its location within their facility; however, no formal recording of use patterns or user behaviors was performed. For sites with consistent observation, managers provided descriptions of user behaviors, including generalized demographic characteristics, such as frequent use by young adult at the pool location during swim meets. Because many community partners do not collect detailed demographic data on visitors, these observations provided only a limited understanding of user demographics.

A limitation to program expansion is the need to establish a dedicated point of contact at each new community partner site. Potential locations including public beaches and local parks have been proposed to capture a larger user population; however, successful implementation depends on identifying an individual who can assume responsibility for dispenser oversight. Many larger public locations lack a consistent manager to oversee issues such as weather-related damage, graffiti, and routine maintenance.

Future Goals

The Community Sun Protection Program continues to expand within and around Milwaukee County. As the program grows, it is seeking partnerships in neighborhoods of lower socioeconomic status, where cost may represent a greater barrier to sunscreen use. Future site selection efforts also will focus on populations known to have lower sunscreen use, including men, people of color, and Hispanic individuals. The CSPP continues to seek funding to support maintenance of existing dispensers and purchase additional units.

CONCLUSIONS

This study evaluated community partners' perceived perceptions of a free sunscreen dispenser program. Community partners identified increased accessibility, positive community impact, and enhanced education through formal and informal interactions as the most important outcomes of this partnership. These findings highlight the value of collaborative public health interventions for improving sun safety awareness and access to preventive resources.

Financial disclosures: None declared.

Funding/support: The purchase of dispensers was funded by the Department of Dermatology at the Medical College of Wisconsin. The purchase of sunscreen refills was funded by the Department of Dermatology and the student-led Dermatology Interest Group at the Medical College of Wisconsin.

REFERENCES

1. US Department of Health and Human Services. Skin cancer as a major public health problem. In: *The Surgeon General's Call to Action to Prevent Skin Cancer*. Office of the Surgeon General (US); 2014:1-9.

2. Ghiasvand R, Weiderpass E, Green AC, Lund E, Veierød MB. Sunscreen use and subsequent melanoma risk: a population-based cohort study. *J Clin Oncol.* 2016;34(33):3976-3983. doi:10.1200/JCO.2016.67.5934

3. Green A, Williams G, Neale R, et al. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet*. 1999;354(9180):723-729. doi:10.1016/S0140-6736(98)12168-2

4. Green AC, Williams GM, Logan V, Strutton GM. Reduced melanoma after regular sunscreen use: randomized trial follow-up. *J Clin Oncol.* 2011;29(3):257-263. doi:10.1200/JCO.2010.28.7078

5. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10-45. doi:10.3322/caac.21871

6. Weig EA, Tull R, Chung J, Brown-Joel ZO, Majee R, Ferguson NN. Assessing factors affecting sunscreen use and barriers to compliance: a cross-sectional survey-based study. *J Dermatolog Treat*. 2020;31(4):403-405. doi:10.1080/09546634.2019.1587147

7. US Department of Health and Human Services. Calls to Action. In: *The Surgeon General's Call to Action to Prevent Skin Cancer.* Office of the Surgeon General (US); 2014:46-64.

8. National Institutes of Health, National Cancer Institute, Centers for Disease Prevention and Control. State Cancer Profiles: Wisconsin (2018-2022). Accessed May 27, 2024. https://statecancerprofiles.cancer.gov/index.html

9. Chun Tie Y, Birks M, Francis K. Grounded theory research: a design framework for novice researchers. *SAGE Open Med*. 2019;7:2050312118822927. doi:10.1177/2050312118822927

10. Burm S, Boese K, Faden L, et al. Recognising the importance of informal communication events in improving collaborative care. *BMJ Qual Saf.* 2019;28(4):289-295. doi:10.1136/bmjqs-2017-007441

Bridging the Gap: Enhancing Pediatric Readiness in Wisconsin's Community Emergency Departments

Maureen Luetje, DO; Carissa Brunner, MPH; Lorin R. Browne, DO; Michael K. Kim, MD

ABSTRACT

Background: Quality pediatric emergency care across the United States is inconsistent. Geographic distance, lack of resources and education can affect the care. This project set out to improve pediatric readiness in at least 20 Wisconsin emergency departments (EDs) statewide.

Methods: The program developed a pediatric readiness guide, recruited EDs to participate, and implemented pediatric readiness interventions within the EDs. Each ED completed the National Pediatric Readiness Project (NPRP) Assessment at the start of the program and a postimplementation assessment at the end, with the goal to improve ED pediatric readiness scores by 10% or more.

Results: Over 36 months, 23 EDs from diverse settings participated in the program. The median [IQR] NPRP score increased from 60.2 (51.5-74.2) to 81.1 (74.7-87.8). Nineteen EDs improved by over 10%.

Discussion: The targeted intervention improved pediatric readiness in 20 EDs from diverse settings and emphasizes the role of leadership and structured guidance to improve care provided to children in Wisconsin.

BACKGROUND

Over the past 20 years, recognition of inequities in pediatric emergency care quality within US emergency departments (EDs) has grown significantly, particularly in trauma care,[1] medical care,[2] and access based on geography.[3,4] Following a joint call to action from the American Academy of Pediatrics[5] and the American College of Emergency Physicians,[6] initiatives have focused on equipping community EDs to provide quality emergency care to children. The National Pediatric Readiness Project[7] (NPRP), a longstanding quality initiative supported by national Emergency Medical Services for Children (EMSC) and the organizations, aims to improve the pediatric readiness of US EDs. The NPRP has conducted 2 national assessment surveys (2013 and 2021), resulting in the engagement of over 1000 EDs in quality improvement collaboratives, and established a registry covering 83% of EDs nationwide. The NPRP survey provides an objective measure of ED pediatric readiness ranging from 0 to 100, with higher scores indicating greater readiness. It comprises 6 domains: (1) Administration and Coordination of Care; (2) Physicians, Advanced Practice Providers, Registered Nurses, and Other Health Care Professionals; (3) Quality Improvement; (4) Pediatric Patient Safety; (5) Policies, Procedures, and Protocols; and (6) Equipment, Supplies, and Medications. The findings from the 2013 and 2021 national assessments indicated persistent gaps in education, policies, guidelines, and personnel for pediatric readiness.[8] Since then, studies have demonstrated that higher NPRP assessment scores are associated with lower mortality among children presenting with severe illness[2] and injury.[9]

In the 2021 NPRP assessment, participating Wisconsin EDs had a median score of 68 of 100, closely aligning with the national median score of 69.5 but indicating room for improvement. In 2016, more than 304 000 (82.2%) pediatric visits occurred in Wisconsin community EDs, whereas only 66 000 (17.8%) occurred in tertiary pediatric EDs, according to Wisconsin Hospital Association data.[10] With only 2 tertiary care children's hospitals in Wisconsin, this represents a key opportunity to col-

• • •

Author affiliations: Children's Corporate Center, Milwaukee, Wisconsin (Browne; Luetje); Children's Health Alliance, West Allis, Wisconsin (Brunner); Department of Emergency Medicine, University of Wisconsin School of Medicine and Public Health (Kim).

Corresponding author: Michael Kim, MD, FAAP, 800 University Bay Dr, Suite 325, Madison, WI 53704; email mkkim@medicine.wisc.edu; ORCID ID 0009-0008-8860-367X

laborate with rural and community EDs, as well as critical access hospitals, to improve pediatric emergency care. The Wisconsin Pediatric Readiness Program (WPRP) was launched in 2021. The primary goals were to develop a Pediatric Readiness Implementation Guide to support the health care workforce and to pilot its use in at least 20 EDs while achieving at least 10% improvement in assessment scores.

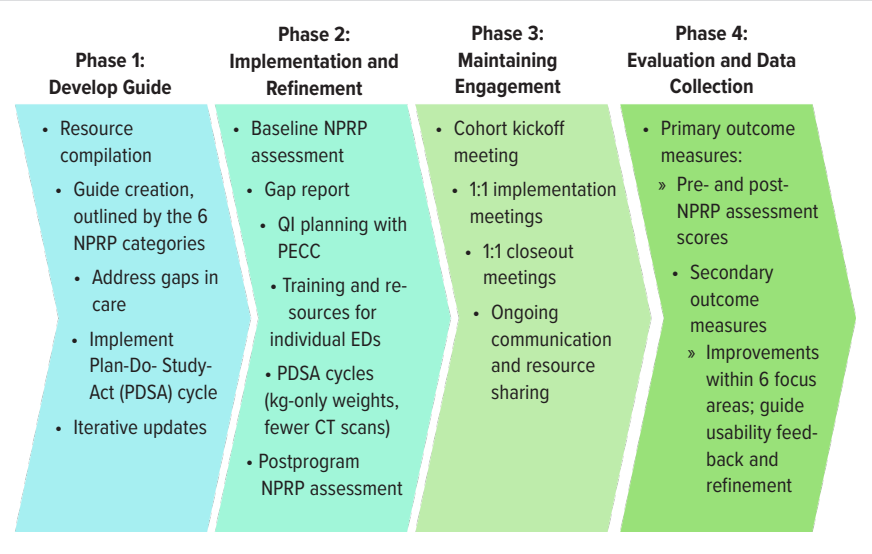
METHODS

The Implementation Guide was developed during the first year with input from ED staff, professional organizations, and public health stakeholders. Designed as a practical resource, it helps EDs assess readiness, identify gaps, and apply quality improvement strategies to enhance pediatric care.

EDs were recruited based on interest and availability. Each ED designated a pediatric emergency care coordinator (PECC) to lead implementation with support from the grant team. Using the Implementation Guide, the program team provided ongoing individualized support through one-on-one meetings and tailored resources to address each site's unique needs. Three board-certified pediatric emergency medicine physicians were designated as subject matter experts for the program. Using the Implementation Guide as the framework, support was provided through regular contact with the subject matter experts to review each NPRP gap analysis at the start of the program. A one-on-one meeting was held with each PECC and subject matter expert to identify existing resources and gaps while prioritizing site-specific goals for improvement.

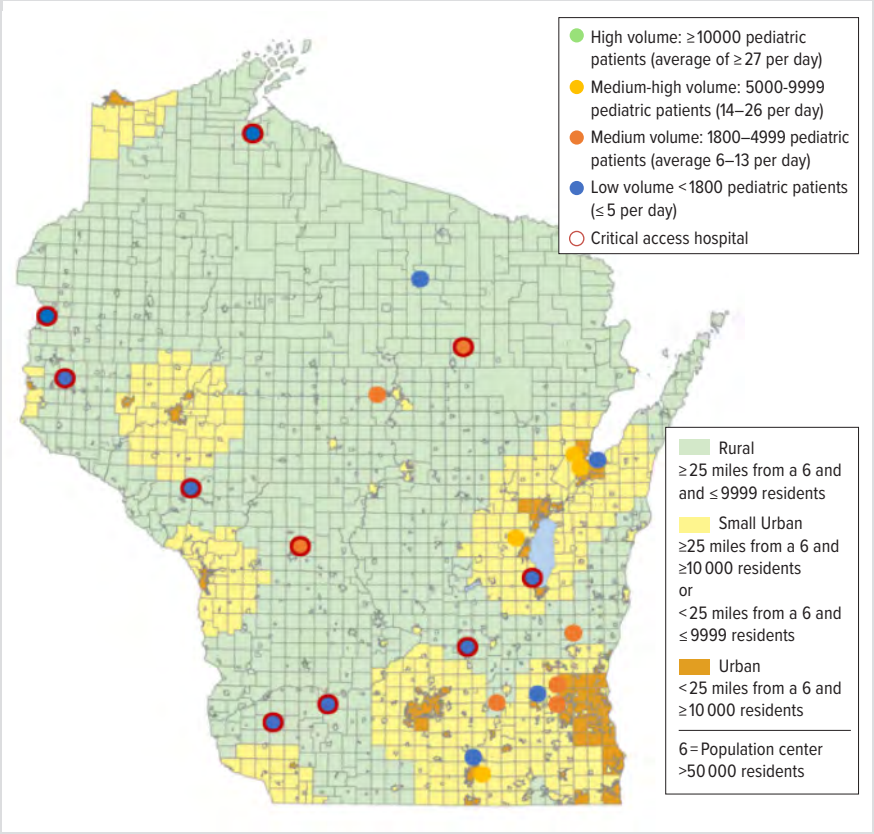
Throughout the program, support was available by email and virtual meetings with the program lead and subject matter experts. An online resource repository was developed, and additional resources were added as topics and questions evolved. At the end of the participation period, each site completed a postimplementation assessment, and the gap report was reviewed and discussed with the subject

Figure 1. The Four Phases of the Pediatric Readiness Program Cycle and Its Key Elements Outlined



Abbreviations: NPRP, National Pediatric Readiness Project; PDSA, plan-do-study-act; QI, quality improvement; PECC, pedicatric emergency care coordinator; ED, emergency department; CT, computed tomography.

Figure 2. Map Indicating Location of All Enrolled Emergency Departments With Volume and Rural Status



Map indicators represent the emergency departments that completed the Pediatric Readiness program: Aspirus–Langlade Hospital, Aspirus–Rhinelander (St. Mary's), Aspirus Wausau Hospital, Aurora–BayCare, Aurora–Oshkosh, Aurora–Summit Bellin Memorial Hospital–Green Bay, Beloit Memorial Hospital, Fort HealthCare, Froedtert–Menomonee Falls, Froedtert–West Bend, Grant Regional Health Center, Gundersen Tri-County Hospital, HSHS–St Vincent Hospital, Mercyhealth–Janesville, Prairie Ridge Health, ProHealth Waukesha Memorial Hospital, St Croix Regional Medical Center, SMM Health Ripon Community Hospital, Tamarack Health Ashland Medical Center, Tomah Health, Upland Hills Health, and Western Wisconsin Health.

matter experts during a closeout meeting. The key phases of the intervention are outlined in Figure 1.

The primary outcome measure was improvement in NPRP assessment scores before and after implementation. Secondary outcome measures included progress in the 6 NPRP domains and feedback on the Implementation Guide. Qualitative data were collected throughout the program to guide further refinement of the Implementation Guide.

Descriptive statistics are reported as counts and percentages, and nonparametric data are reported as medians with interquartile ranges (IQRs). The 2-sided Wilcoxon signed-rank test was used, with a significance threshold of $P<.05$ to evaluate whether postintervention scores were significantly higher than preintervention scores across participating sites. The proportion of sites achieving the predefined benchmark of at least 10% improvement in scores was also calculated and compared with a null hypothesis of 50% using a binomial test.

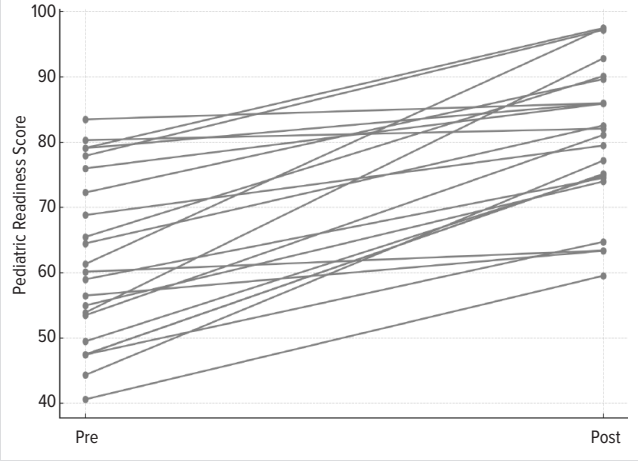
RESULTS

WPRP was launched on July 1, 2021, with 25 EDs initially participating and 23 EDs completing the program by October 2024. Two EDs completed initial NPRP assessment but did not complete the program. The participating EDs represented a range of sizes, geographic locations, and patient volumes (Figure 2). Of the 23 EDs, 12 were considered low-volume EDs, 10 were designated as critical access hospitals, and 12 were designated as rural. The median preintervention readiness score among participating EDs was 60.2 (IQR, 51.5-74.2), and the median postintervention score was 81.1 (IQR, 74.7-87.8). The Wilcoxon signed-rank test demonstrated a statistically significant median improvement in readiness scores across sites ($P<.001$). All participating EDs improved their pediatric readiness score, with individual gains ranging from 2.5 to 36.2 points (Figure 3). Nineteen sites (82.6%) achieved the predefined benchmark of at least a 10% improvement. A binomial test showed that this success rate was significantly greater than expected ($P=.0013$).

Four EDs made improvements in all 6 domains, whereas 17 EDs focused on Policies, Procedures and Protocols, 16 on Administration and Coordination of Care, and 12 on Provider Credentialing/Competency. Two domain elements contributed the greatest score gains: designation of a PECC (+209 points across all sites) and fulfillment of pediatric equipment needs (+163 points across all sites).

Postintervention survey responses indicated that participants valued the WPRP for highlighting strengths, identifying gaps, and increasing staff confidence. Participants emphasized the importance of ongoing quality improvement, education, and leadership support. The primary barriers cited were limited time, competing responsibilities, limited pediatric expertise, and occasional delays in EMSC communication. Desired support included group discussions, guidance regarding education and competencies, and assistance in securing pediatric physician champions. PECCs identified credentialing, patient safety, and quality improvement as top priorities for future readiness efforts. Participants strongly encouraged other rural EDs to join the program, start small, and leverage available resources to improve pediatric care and demonstrate measurable progress.

Figure 3. Pre- and Post-Pediatric Readiness Score by Site



DISCUSSION

Geographic distance from tertiary care centers, hospital resource limitations, and delays in access to pediatric specialists significantly affect pediatric emergency care in Wisconsin.[4,11,12] Low preintervention pediatric readiness scores in this program reflect these challenges and emphasize the need for continued support and outreach to EDs statewide.

WPRP not only met but exceeded its goal of improving pediatric readiness scores, demonstrating the effectiveness of a structured, evidence-based approach coupled with personalized coaching. A key factor in the program's success was the PECCs. These champions foster collaboration, address identified gaps, and drive implementation within their EDs. Recognizing their importance is essential to sustaining and expanding pediatric readiness efforts statewide.

Critical access hospitals and rural EDs typically have fewer resources and specialty capabilities than urban hospital systems.[13] They also tend to have lower pediatric readiness scores than urban EDs.[14] WPRP specifically targeted these EDs in an effort to reduce resource gaps and strengthen pediatric readiness. Continued focus on critical access hospitals and rural EDs may help maximize pediatric readiness improvement efforts throughout Wisconsin.

Despite its successes, WPRP faced notable challenges. Assigning and retaining PECCs proved difficult because of limited resources, lack of protected time allocation, staff turnover, and competing priorities. Sustaining participation was also a concern, underscor-

ing the need for long-term engagement and organizational commitment. Time, staffing, leadership support, and funding will need to be prioritized in future pediatric readiness efforts. One limitation of this project was the lack of a control group, which limits causal inference; however, the magnitude of improvement suggests meaningful impact.

WPRP demonstrates that targeted, personalized interventions can successfully improve pediatric readiness, even in resource-limited settings. Sustaining these improvements will require continued investment and integration into broader health care systems. More specifically, continued engagement of participating EDs through quality-improvement projects, educational conferences, and meetings will likely help maintain and further improve pediatric readiness. Financial sustainability may be enhanced through innovative funding models, formal recognition of PECCs, or incorporation of pediatric readiness into ED quality metrics. Although Wisconsin's infrastructure facilitated implementation, states with different funding mechanisms or regional structures may require adaptation of the model. The success of WPRP provides a framework for future initiatives and reinforces that meaningful change is possible when collaboration, innovation, and leadership align. Ensuring that every child in Wisconsin receives timely, high-quality emergency care, regardless of geography, should remain a priority.

Financial disclosures: None declared.

Funding/support: This program was funded wholly by the Advancing a Healthier Wisconsin Endowment.

Acknowledgements: The authors wish to gratefully acknowledge Erica Kane, Brittany Farrell, Maisie Williams, Leslie Walker, and Anna Verkuilen for their significant contributions to the development of the implementation guide and program.

REFERENCES

1. Remick K, Gaines B, Ely M, Richards R, Fendya D, Edgerton EA. Pediatric emergency department readiness among US trauma hospitals. *J Trauma Acute Care Surg.* 2019;86(5):803-809. doi:10.1097/TA.0000000000002172

2. Ames SG, Davis BS, Marin JR, et al. Emergency department pediatric readiness and mortality in critically ill children. *Pediatrics*. 2019;144(3):e20190568. doi:10.1542/peds.2019-0568

3. Ray KN, Olson LM, Edgerton EA, et al. Access to high pediatric-readiness emergency care in the United States. *J Pediatr.* 2018;194:225-232.e1. doi:10.1016/j.jpeds.2017.10.074

4. Park KY, Eithun BL, Havlena J, et al. Driving time to trauma centers for children living in Wisconsin. *WMJ*. 2021;120(3):174-177.

5. American Academy of Pediatrics, Committee on Pediatric Emergency Medicine and American College of Emergency Physicians, and Pediatric Committee. Care of children in the emergency department: guidelines for preparedness. *Pediatrics*. 2001;107(4):777-781. doi:10.1542/peds.107.4.777

6. American College of Emergency Physicians, American Academy of Pediatrics. Care of children in the emergency department: guidelines for preparedness. *Ann Emerg Med.* 2001;37(4):423-427. doi:10.1067/mem.2001.114067

7. Emergency Medical Services for Children. About. National Pediatric Readiness Project. Updated 2021. Accessed March 26, 2025. https://emscimprovement.center/domains/pediatric-readiness-project/about

8. Remick KE, Hewes HA, Ely M, et al. National assessment of pediatric readiness of US emergency departments during the COVID-19 pandemic. *JAMA Netw Open.* 2023;6(7):e2321707. doi:10.1001/jamanetworkopen.2023.21707

9. Newgard CD, Lin A, Goldhaber-Fiebert JD, et al. Association of emergency department pediatric readiness with mortality to 1 year among injured children treated at trauma centers. *JAMA Surg.* 2022;157(4):e217419. doi:10.1001/jamasurg.2021.7419

10. Wisconsin Hospital Association Information Center. Emergency Department Data Set, 2017 [custom data report]. Wisconsin Hospital Association Information Center; 2017.

11. Bucholz EM, Day RT, Khazanchi R, et al. Geospatial accessibility of pediatric resources by child opportunity, racial and ethnic composition and urbanicity. *Acad Pediatr.* 2025;25(5):102817. doi:10.1016/j.acap.2025.102817

12. Municipal urban-rural classification system. Wisconsin Office of Rural Health. Updated July 2016. Accessed February 14, 2025. https://worh.org/resources/data-maps/defining-rural-wisconsin/municipal-urban-rural-classification-system/

13. Joynt KE, Harris Y, Orav EJ, Jha AK. Quality of care and patient outcomes in critical access rural hospitals. *JAMA*. 2011;306(1):45-52. doi:10.1001/jama.2011.902

14. Rutledge C, Waddell K, Gaither S, Whitfill T, Auerbach M, Tofil N. Evaluation of pediatric readiness using simulation in general emergency departments in a medically underserved region. *Pediatr Emerg Care*. 2024;40(5):335-340. doi:10.1097/PEC.0000000000003056ch_f/5460879?cesid=1hWvpEiKm0H&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dgardasil%2B9%26t%3Dname%26acs%3Dfalse%26acq%3Dgardasil

Thinking Beyond Common Diagnoses: A Case Report of Creutzfeldt-Jakob Disease

Thomas Licata, DO; Won Huh, MD; Michael Bolan, DO

ABSTRACT

Introduction: Prion diseases are rare neurodegenerative disorders characterized by abnormal folding of prion proteins in the brain. Creutzfeldt-Jakob disease (CJD), is the most common prion disease in humans, typically presenting with neuropsychiatric manifestations, including dementia, behavioral abnormalities, and motor dysfunction. Diagnosis can be challenging because its nonspecific presentation overlaps with numerous other potential causes.

Case Presentation: A 60-year-old man presented with altered mental status and progressive neurologic decline. After an extensive diagnostic evaluation, he was diagnosed with probably CJD. Management was primarily supportive and focused on symptom relief and patient comfort. The patient died shortly after the diagnosis was confirmed.

Conclusions: This case highlights the challenges of diagnosing CJD and underscores the value of System 1 and System 2 reasoning in navigating a broad differential diagnosis in patients presenting with altered mental status and rapidly progressive neurologic symptoms.

INTRODUCTION

Prions are small pathogenic agents that induce abnormal folding of prion proteins naturally found in the brain. Creutzfeldt-Jakob disease (CJD) is the most common human prion disease. The average age at symptom onset is 62 years, following a long incubation period.[1] There is no sex predilection,[2] and 85% to 98% of cases occur sporadically, without known risk factors such as environmental exposure. The remaining 5% to 15% are genetically linked, and iatrogenic and variant CJD together comprise less than 1% of cases.[3]

• • •

Author affiliations: Aspirus Wausau Hospital, Wausau, Wisconsin (Bolan; Licata); Wisconsin Northern and Central Graduate Medical Education Consortium, Wausau, Wisconsin (Huh).

Corresponding author: Thomas Licata, DO, email Thomas.Licata@Aspirus.org; ORCID ID 0000-0001-6029-757X

Early symptoms of CJD include impairments in attention, concentration, memory, and judgment. These neuropsychiatric findings rapidly progress to dementia, behavioral abnormalities, and aphasia and apraxia, reflecting deficits in higher cortical function.[4,5] Hypersomnia is frequently observed.[6] Mood disturbances such as depression and apathy are common, while anxiety, euphoria, and affective lability are less common.[7] Psychotic symptoms such as hallucinations also have been reported. On examination, signs of corticospinal tract involvement (eg, hyperreflexia, positive Babinski reflex, muscle spasticity) are present in 40% to 80% of cases. Extrapyramidal signs (eg, hypokinesia, bradykinesia, dystonia, muscle rigidity) are also seen.

Because CJD invariably progresses to death, with a median disease duration of 6 months, death records serve as a reliable measure of incidence. From 2003 through 2015, the age-adjusted mean annual incidence for CJD in the United States was 1.2 cases per million.[2]

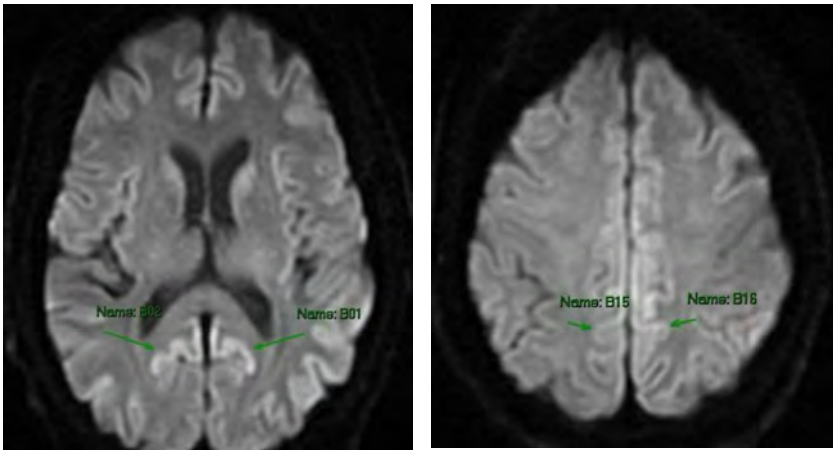
Management of CJD centers on supportive care to maximize patient comfort throughout disease progression.[8] Arriving at the diagnosis can be challenging, however, because of low clinical suspicion when a patient presents with altered mental status, which can arise from neurologic, infectious, systemic, or metabolic etiologies. The emotional and psychomotor disturbances that often accompany altered mental status can further complicate the diagnostic picture, especially in patients with a psychiatric history.[9]

This report describes the case of a middle-aged man with altered mental status and expressive aphasia who tested positive for CJD after the common, and even uncommon, diagnoses had been ruled out.

CASE PRESENTATION

The patient was a relatively healthy 60-year-old man with a past medical history of major depressive disorder with compulsive behaviors controlled with bupropion, attention-deficit/hyperactivity disorder controlled with Adderall, obstructive sleep apnea, and alcohol use disorder in sustained remission for 30 years. His past surgical history was notable only for a cadaver bone graft 20 years prior following failed pin stabilization of a left foot fracture.

Figure. Magnetic Resonance Imaging Evidence of Cortical Ribboning



The patient was transferred to our facility for neurologic evaluation of worsening confusion, visual and auditory hallucinations, and gait instability over a 2-month period. Before transfer, he developed progressive expressive aphasia without evidence of acute stroke or other overt intracranial abnormalities on imaging.

Because of his inability to participate in an interview, the history was obtained primarily from his wife. Three months before admission, he developed ear pain and was diagnosed with bilateral acute otitis media. He was treated with antibiotics. Notably, he also reported headaches accompanying the ear pain, followed by the aforementioned neuropsychiatric symptoms in subsequent months. He exhibited paranoia related to his hallucinations.

The patient lived in a rural environment. He and his wife had recently become more active outdoors, often hiking in wooded areas near their home. For several years, he had been putting out food for a feral cat on his property but had no direct contact with the animal. He worked as a truck driver. He consumed a well-balanced diet without exposure to game or undercooked meats and typically packed meals from home for long truck routes. Despite heavy alcohol consumption in his 20s and early 30s, he had limited his drinking to holidays and special occasions for the past 3 decades.

Examination on the day of admission demonstrated bilateral upper- and lower-extremity hyperreflexia without clonus, as well as waxy flexibility, catalepsy, and repetitive handwaving and finger-tapping motions reminiscent of catatonia. Pupils were 3 mm and reactive without nystagmus. Speech comprehension appeared intact; he was able to provide 1- or 2-word responses to questions, perform simple calculations such as "2+2," and follow basic commands.

Based on his initial presentation, the differential diagnosis notably included indolent (eg, parasitic or fungal) meningitis, autoimmune (including Hashimoto) encephalitis, metabolic encephalitis, Wernicke encephalopathy, rapidly progressive dementia, catatonic state secondary to psychopharmacotherapy, and seizure disorder. High-dose thiamine and folate were initiated out of concern for Wernicke encephalopathy. Continuous electroencephalogram (EEG) was ordered to monitor for abnormal brain wave activity. A lumbar puncture was planned to evaluate for these potential pathologies.

Initial laboratory results were unrevealing: ethanol level 0mg/dL; negative results for COVID-19, influenza A and B, and respiratory syncytial virus; unremarkable complete blood cell count (CBC), with peripheral blood smear showing only mild absolute monocytosis; international normalized ratio of 1.0; urine drug screen positive for amphetamines consistent with prescribed medications; unremarkable comprehensive metabolic panel; ammonia level within normal limits; and vitamin B12 and folate levels within normal limits. Methylmalonic acid (MMA) levels were normal. Syphilis, HIV, and hepatitis C testing results were negative.

Subsequently, the patient's tick-borne panel, including testing for *Babesia*, *Ehrlichia*, *Anaplasma*, and Lyme disease, returned negative results. Testing for *Coccidioides*, *Histoplasma*, *Blastomyces*, and *Bartonella* was also negative. Antinuclear antibody, antineutrophil cytoplasmic antibody, myeloperoxidase, and proteinase 3 testing results were unremarkable.

Thyroid-stimulating hormone, thyroid peroxidase antibody, and thyroglobulin antibody levels were within normal limits. Paraneoplastic and autoimmune encephalopathy panels were negative for CV2 antibody; neuronal nuclear antibodies to Hu, Ri, Yo, and Tr antigens; amphiphysin antibody; contactin-associated protein 2 (CASPR2), leucine-rich glioma-inactivated protein 1 (LGI1) antibody, and γ-aminobutyric acid receptor type B (GABA-B) antibody. Interestingly, the patient's JC virus antibody test was positive despite no history of immunocompromise.

Catatonic features became more prominent during the first 24 hours after admission. During that time, he was verbally unresponsive but appeared to understand conversations, signaling "yes" or "no" with finger movements or blinking. As he became

Table. Patient History Timeline

Prior to Admission
- History of heavy alcohol consumption in 20s-30s and cadaver bone graft for left foot fracture repair

1 year
- Patient moves from Oregon to rural Wisconsin

3 months
- Patient complains of ear pain with headaches ➔ diagnosed with bilateral acute otitis media, treated with antibiotics

2 months
- Patient experiences progressively worsening cognitive changes ➔ begins using walker due to gait instability

Day of Admission (Hospital Day 0)

Events
- Patient transferred for neurology evaluation; experiencing AMS and expressive aphasia; concern for parasite passed in urine

Exam findings
- Bilateral upper and lower extremity hyperreflexia without clonus; waxy flexibility, catalepsy, stupor, stereotypy, minimal speech; receptive language intact, able to follow simple commands; eye movements within normal limits

Imaging
- No acute findings on noncontrast CT head, CTA head/neck, MRI brain with and without contrast

Hospital Day 1

Laboratory results
- Ethanol level: 0; UDS: unremarkable; COVID-19, influenza A/B, RSV: neg; INR: 1.0; parasite exam: neg; syphilis: neg; HIV 1/2: neg; ammonia, CBC, CMP, B12, folate, MMA: within normal limits

Hospital Days 2–5

Events
- LP performed; patient initiated on Solu-Medrol 1 g daily x3 doses, valproate 500 daily x 3

Imaging
- Repeat MRI brain: restricted diffusion in cortex of occipital and parietal lobes bilaterally; patchy and ill-defined signal alteration in subcortical and deep white matter bilaterally; not significantly changed from prior MRI.

Laboratory results
- CSF chemistry: incl protein; CSF acid-fast bacilli, gram stain/culture, fungal culture: neg; TSH/FT4, TPO Ab, anti-thyroglobulin Ab: unremarkable; ANA titer: within normal limits; CSF meningitis panel:[a] neg

Hospital Days 6–7

Events
- AMS-induced oropharyngeal dysphasia ➔ diet status changed to nothing by mouth, first NG tube attempt; IVIG initiated for possible autoimmune encephalitis

Laboratory results
- *Blastomyces*, *Histoplasma*, *Coccidioides*: neg; *Bartonella*: neg; West Nile virus: neg; Lyme: neg; *Babesia*, *Ehrlichia*, *Anaplasma*: neg; ANCA, MPO/PR3 Ab, CASPR2 Ab, LGI1 Ab, GABA-B Ab: neg

Imaging
- CT chest/abd/pelvis: neg for occult malignancy

Hospital Day 9

Laboratory results
- CSF JC virus: pos

Hospital Day 12–13

Events
- Second NG tube attempt; PICC line placed

Laboratory results
- CV2 Ab, neuronal nuclear Abs, amphiphysin Ab: neg

Hospital Day 14

Events
- Third NG tube failure ➔ TPN initiated; concern for developing dysautonomia consistent with advancing prion disease

Hospital Day 16

Laboratory results
- CSF 14-3-3: pos; CSF RT-QuIC: pos; CSF T-tau protein: >20 000

Day of Discharge (Hospital Day 17)

Events
- Patient discharged with plan to transition to hospice ➔ succumbs to CJD the following day

[a]CSF meningitis panel included testing for *Escherichia coli*, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae*, cytomegalovirus, enterovirus, herpes simplex virus 1 and 2, human herpesvirus 6, human parechovirus, varicella-zoster virus, and *Cryptococcus neoformans*.

Abbreviations: Ab, antibody; AMS, altered mental status; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; CBC, complete blood count; CASPR2, contactin-associated protein 2; CJD, Creutzfeldt-Jakob disease; CMP, comprehensive metabolic panel; CSF, cerebrospinal fluid; CT, computed tomography; CTA, computed tomography angiography; FT4, free thyroxine; GABA-B, γ-aminobutyric acid receptor type B; INR, international normalized ratio; IVIG, intravenous immune globulin; LGI1, leucine-rich glioma-inactivated protein 1; LP, lumbar puncture; MMA, methylmalonic acid; MPO, myeloperoxidase; MRI, magnetic resonance imaging; neg, negative; NG, nasogastric; PICC, peripherally inserted central catheter; pos, positive; PR3, proteinase 3; RSV, respiratory syncytial virus; RT-QuIC, real-time quaking-induced conversion; TPN, total parenteral nutrition; TPO, thyroid peroxidase; TSH, thyroid-stimulating hormone; UDS, urine drug screen.

increasingly lethargic, EEG demonstrated triphasic waves in the 1.0- to 1.5-Hz range within the left hemisphere. Repeat magnetic resonance imaging (MRI) of the brain with and without contrast demonstrated cortical ribboning that had not been observed on outside imaging studies (Figures 1 and 2). Lumbar puncture was completed without clear evidence of infection, with negative bacterial and viral meningitis panels (see Table for pathogens tested). Cerebrospinal fluid (CSF) analysis demonstrated only mild abnormalities in glucose (74 mg/dL; reference range, 50-70 mg/dL) and protein (82 mg/dL; reference range, 15-45 mg/dL), findings consistent with an encephalitic process.

The official EEG interpretation reported "generalized background abnormalities indicative of diffuse encephalopathy, periodic discharges diffuse with left hemispheric predominance typically seen in the setting of acute neuronal injury indicative of cortical excitability and can also be noted in chronic focal epilepsy."

The official repeat MRI interpretation reported "mildly restricted diffusion in the cortex of the occipital and parietal lobes bilaterally, which is greatest medially. Primary differential considerations include encephalitis, status epilepticus, Wernicke's encephalopathy, and metabolic encephalopathy. Hypoxic-ischemic encephalopathy is relatively less likely in this clinical context… patchy and ill-defined signal alteration in the subcor-

tical and deep white matter bilaterally not significantly changed, with radiological interpretation suggesting small-vessel disease chronic in nature, migraine headaches, and nonspecific gliosis."

In response to the severity of the patient's neurologic findings, empiric treatment was with methylprednisolone (Solu-Medrol) 1 g daily for 3 days and valproate (Depakote) 500 mg 3 times daily was initiated. Prion testing was ordered in light of EEG and MRI abnormalities and nondiagnostic lumbar puncture results.

By hospital day 6, the patient was deemed unable to safely swallow following speech-language pathology evaluation. He repeatedly self-dislodged multiple nasogastric (NG) tubes, and, because he did not improve with steroid and valproate therapy, so intravenous immune globulin was initiated while awaiting prion test results.

On hospital day 10, an abdominal x-ray obtained because of abdominal distension suggested moderate ileus formation. An NG tube was placed again for suction, and the patient was transitioned to total parenteral nutrition. Unstable blood pressure, heart rate, and respiratory rate raised concern of dysautonomia.

On hospital day 15, he developed Cheyne-Stokes breathing patterns and intermittent episodes of various arrhythmias on telemetry.

On hospital day 16, CSF prion test results returned positive 14-3-3 protein and real-time quaking-induced conversion (RT-QuIC) assay results, with CSF total tau protein >20 000pg/mL (reference range, 0-1149 pg/mL), indicating probable CJD. At his wife's request, he was transitioned to hospice care and died within 72 hours of the diagnosis.

DISCUSSION

Per the Centers for Disease Control and Prevention diagnostic criteria,[10] definite sporadic CJD is diagnosed by standard neuropathological techniques, immunocytochemical methods, Western blot confirmation of protease-resistant prion protein (PrP), or identification of scrapie-associated fibrils. Probable sporadic CJD is diagnosed by (1) the presence of a neuropsychiatric disorder plus a positive RT-QuIC assay in CSF or other tissues, or (2) rapidly progressive dementia plus at least 2 of following clinical features: myoclonus, visual or cerebellar signs, pyramidal or extrapyramidal signs, or akinetic mutism, together with at least 1 supportive test result, including periodic sharp-wave complexes on EEG, a positive CSF 14-3-3 assay in patients with disease duration of less than 2 years, or characteristic MRI abnormalities involving the caudette nucleus, putamen, or at least 2 cortical regions (temporal, parietal, or occipital) on diffusion-weighted imaging or fluid-attenuated inversion recovery sequences.

Our patient met criteria for probable sporadic CJD based on his rapidly progressive dementia, positive CSF RT-QuIC result, and positive CSF 14-3-3 assay. At the start of his diagnostic journey, however, he presented as a patient with altered mental status and a focal neurologic deficit, a common presentation in the hospital setting. The evolution of his presentation illustrates how Systems 1 and System 2 reasoning can be used to prioritize high-mortality and high-morbidity conditions before proceeding through the differential diagnosis in a stepwise manner based on clinical likelihood.

System 1 thinking describes fast, intuitive, and reflexive decision-making.[11] In medicine, it often manifests as pattern recognition in the acute setting to quickly identify conditions requiring urgent or emergent intervention and thereby prevent substantial morbidity or death. In our patient, System 1 thinking guided our initial evaluation for stroke and other acute intracranial abnormalities using noncontrast computed tomography (CT) of the head, MRI of the brain with and without contrast, and CT angiography of the head and neck. It also informed the initial laboratory and bedside evaluation of rapidly reversible or time-sensitive causes of altered mental status, including electrolyte abnormalities, substance intoxication or withdrawal, Wernicke encephalopathy, and hypoglycemia. Comprehensive metabolic panel, complete blood cell count with differential, ethanol level, urine drug screening and point-of-care glucose testing were obtained as part of this evaluation. Following exclusion of vitamin B12 deficiency, hyperammonemia, tick-borne disease, and sexually transmitted infections through normal B12 and MMA levels, normal ammonia level and arterial blood gas results, negative Lyme and tick-borne disease testing, and negative syphilis and HIV serologic results, the differential diagnosis expanded to include less common conditions. This shift marked a transition from System 1 thinking to the slower, more deliberate, and methodical process of System 2 thinking.

System 2 reasoning built upon the initial impressions generated by System 1 thinking as patient's symptoms evolved. Although features of catatonia were observed early in the hospitalization, the progression from aphasia to an increasingly comatose state over a matter of days made a primary psychiatric etiology less likely. Similarly, despite his rural residence and propensity for the outdoors, CSF studies demonstrating an isolated protein elevation diminished concern for fungal or parasitic meningitis. Instead, these CSF findings, together with the formal EEG and repeat MRI interpretations, shifted the leading diagnostic considerations toward encephalopathy and focal seizure activity.

In hindsight, the triphasic waves identified on EEG prompt the question of why this characteristic finding of CJD[1,3,10] did not immediately raise suspicion for the diagnosis. One possible explanation is anchoring bias. Because the EEG was obtained primarily to evaluate altered mental status rather than a suspected prion disease, the interpretation may have been influenced by the more common causes of altered mental status encountered in the hospital setting. Similarly, the MRI report did not emphasize the hyperintense corticol signal abnormalities along the gyri, a characteristic feature of CJD known as the cortical ribbon sign.[3] This observation may likewise reflect anchoring bias, whereby interpretation remained focused on more common diagnostic considerations.

This case highlights the role of dual-process reasoning and potential cognitive biases that can occur in a complex diagnostic scenario. It also illustrates the significance of clinical context in diagnostic interpretation. Diagnostic studies are only as informative as the context in which they are interpreted. Ultimately, neurologic consultation and reconsideration of the patient's evolving symptoms were instrumental in establishing the diagnosis of probable sporadic CJD. Although earlier recognition would not have altered management or outcome, more detailed communication of the clinical concern to radiology (eg, altered mental status with concern of meningitis as well as irregular EEG containing triphasic spikes) may have facilitated earlier recognition of imaging and EEG findings suggestive of CJD.

Of note, our patient underwent cadaveric bone grafting during ankle reconstruction 20 years before his CJD diagnosis. Cadaveric dura mater grafts have been implicated in cases of iatrogenic CJD.[1,12] However, given the nature of the patient's prior procedure and the rarity of iatrogenic CJD, a sporadic etiology is considerably more likely, although the absence of definitive confirmatory testing precludes complete exclusion of an iatrogenic origin.

Another noteworthy aspect of this case was the diagnosis of acute otitis media 3 months before hospitalization. Whether this represented an unrelated condition or an early manifestation of the patient's evolving neurologic disease remains uncertain. Given the nonspecific nature of early CJD symptoms and the retrospective nature of this observation, any association should be interpreted cautiously.

CONCLUSIONS

Prion diseases, particularly Creutzfeldt-Jakob disease (CJD), are fatal neurodegenerative disorders that pose complex diagnostic challenges. This case of a 60-year-old man highlights the importance of maintaining a broad differential diagnosis and pursuing comprehensive evaluation in patients with rapidly progressive neurologic decline. The rapid progression and uniformly fatal nature of CJD underscore the need for heightened clinical awareness, timely recognition, and appropriate supportive care in managing this rare condition.

This case also highlights the potential influence of cognitive bias on diagnostic decision-making and emphasizes the value of careful clinical contextualization when interpreting diagnostic studies. Although the patient's prior history of cadaveric bone grafting raises a theoretical question regarding disease transmission, the available evidence supports a diagnosis of probable sporadic CJD. Further investigation into rare transmissible causes of prion disease remains warranted as understanding of these disorders continues to evolve.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Haywood AM. Transmissible spongiform encephalopathies. *N Engl J Med*. 1997;337(25):1821-1828. doi:10.1056/NEJM199712183372508

2. Maddox RA, Person MK, Blevins JE, et al. Prion disease incidence in the United States: 2003-2015. *Neurology*. 2020;94(2):e153-e157. doi:10.1212/WNL.0000000000008680

3. Belay ED, Holman RC, Schonberger LB. Creutzfeldt-Jakob disease surveillance and diagnosis. *Clin Infect Dis*. 2005;41(6):834-836. doi:10.1086/432726

4. Krasnianski A, Bohling GT, Heinemann U, et al. Neuropsychological symptoms in sporadic Creutzfeldt-Jakob disease patients in Germany. *J Alzheimers Dis*. 2017;59(1):329-337. doi:10.3233/JAD-161129

5. Rabinovici GD, Wang PN, Levin J, et al. First symptom in sporadic Creutzfeldt-Jakob disease. *Neurology*. 2006;66(2):286-287. doi:10.1212/01.wnl.0000196440.00297.67

6. Landolt HP, Glatzel M, Blättler T, et al. Sleep-wake disturbances in sporadic Creutzfeldt-Jakob disease. *Neurology*. 2006;66(9):1418-1424. doi:10.1212/01.wnl.0000210445.16135.56

7. Krasnianski A, Bohling GT, Harden M, Zerr I. Psychiatric symptoms in patients with sporadic Creutzfeldt-Jakob disease in Germany. *J Clin Psychiatry*. 2015;76(9):1209-1215. doi:10.4088/JCP.13m08915

8. Appleby BS, Yobs DR. Symptomatic treatment, care, and support of CJD patients. *Handb Clin Neurol.* 2018;153:399-408. doi:10.1016/B978-0-444-63945-5.00021-0

9. Veauthier B, Hornecker JR, Thrasher T. Recent-onset altered mental status: evaluation and management. *Am Fam Physician*. 2021;104(5):461-470.

10. Clinical overview of Creutzfeldt-Jakob disease. Centers for Disease Control and Prevention. Accessed January 2025. https://www.cdc.gov/creutzfeldt-jakob/hcp/clinical-overview/diagnosis.html

11. Kahneman, D. *Thinking, Fast and Slow.* 1st ed. Farrar, Straus and Giroux; 2011.

12. Centers for Disease Control (CDC). Rapidly progressive dementia in a patient who received a cadaveric dura mater graft. *MMWR Morb Mortal Wkly Rep*. 1987;36(4):49-55.

De Novo Hepatocellular Carcinoma in Primary Sclerosing Cholangitis Post-Liver Transplant: The Case for Surveillance

Anneleise Frie, MD; Adnan Said, MD, MS

ABSTRACT

Introduction: While recurrent primary sclerosing cholangitis and de novo malignancies such as skin cancer are common after liver transplantation, de novo hepatocellular carcinoma (HCC) after liver transplantation for primary sclerosing cholangitis is exceedingly rare.

Case Presentation: A 72-year-old man with ulcerative colitis underwent liver transplantation for primary sclerosing cholangitis. Thirty years later, abdominal imaging incidentally revealed cirrhotic liver morphology with a new, bulky, and locally invasive hepatic mass. Biopsy confirmed stage IIIA hepatocellular carcinoma, which was treated successfully with Y-90 radioembolization segmentectomy.

Discussion: Immunosuppression-related malignancies are prevalent in long-term liver transplant survivors, and HCC recurrence can occur in patients transplanted for HCC. However, de novo HCC is rare in liver transplant recipients with primary sclerosing cholangitis and has primarily been reported in patients with viral hepatitis.

Conclusions: Vigilant screening for allograft fibrosis, cirrhosis, and malignancy using emerging modalities in long-time liver transplant survivors warrants consideration.

INTRODUCTION

Malignancy beyond 1 year post-liver transplant occurs at rates approximately twice those in the general population, driven by prolonged immunosuppression, recurrent or de novo liver diseases, and lifestyle factors such as tobacco or alcohol use.[1] Up to 20% of patients transplanted for hepatocellular carcinoma (HCC) develop recurrence,[2] while among patients transplanted for primary sclerosing cholangitis (PSC), the 10-year cumulative risk of malignancy is 21%, primarily due to colorectal cancer or cholangiocarcinoma.[3] The prevalence of de novo HCC after liver transplantation in patients with PSC is rare but has been observed in patients with viral hepatitis, metabolic liver disease with advanced fibrosis/cirrhosis, older donor age, male sex, and exposure to environmental carcinogens.[4,5] However, de novo HCC after liver transplantation in patients with PSC is rare, with only a few reported cases occurring in patients with recurrent liver disease (including 1 case without fibrosis) or secondary causes such as hepatitis C infection.[6,7]

CASE PRESENTATION

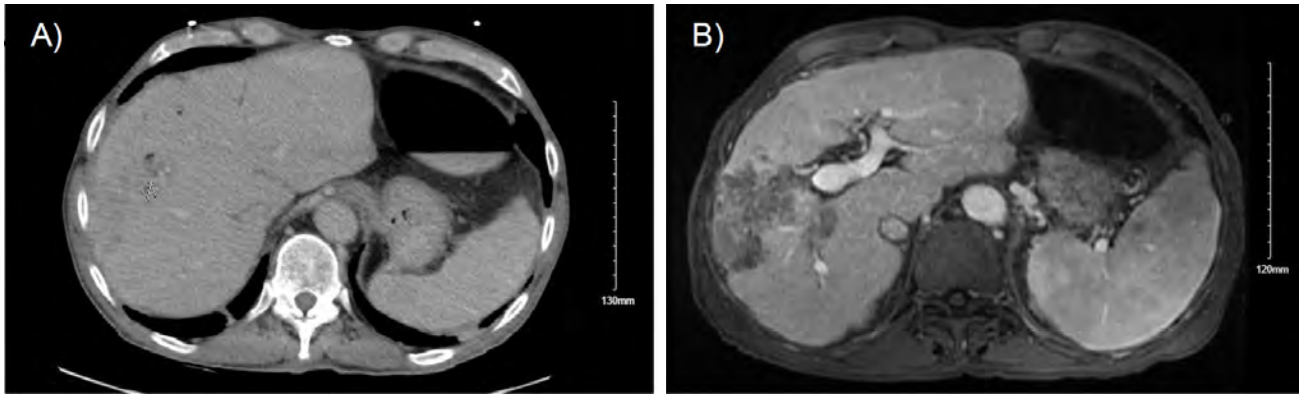
We present the case of a 72-year-old man with ulcerative colitis who received an orthotopic liver transplantation in 1994 for PSC and cirrhosis. Following transplantation, he maintained excellent allograft function on immunosuppression with prednisone, tacrolimus, and mycophenolate. His course was complicated by mucinous adenocarcinoma of the colon, treated with curative total colectomy and ileal pouch creation in 1998; elevated alkaline phosphatase in 2014, for which magnetic resonance cholangiopancreatography (MRCP) findings were unrevealing; and Crohn's disease of the ileal pouch, controlled with vedolizumab since 2021. Computed tomography (CT) of the abdomen in 2021 incidentally revealed hepatic fissural prominence and undulation of the liver surface without a focal lesion. He continued routine follow-up in hepatology and inflammatory bowel disease clinics.

In May 2024, nearly 29 years posttransplant, he was hospitalized for viral pneumonia. Laboratory testing showed mild anemia (hemoglobin 12.5 g/dL), thrombocytopenia (platelet count,

Author affiliations: Department of Medicine, University of Wisconsin Hospitals and Clinics, Madison, Wisconsin (Frie); Division of Gastroenterology and Hepatology, Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin (Said).

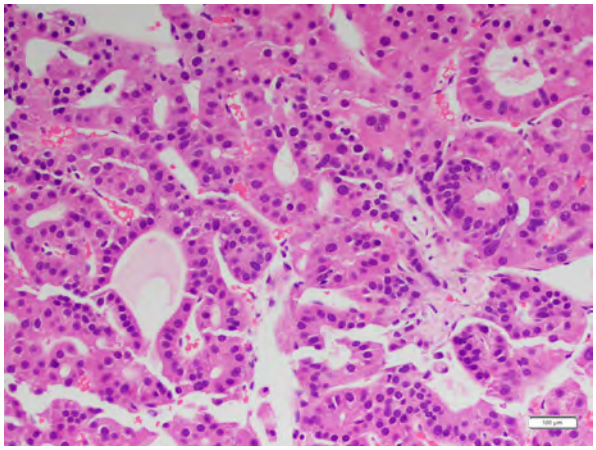
Corresponding author: Anneleise Frie, MD, 600 Highland Ave, Madison, WI 53792; email afrie@uwhealth.org; ORCID ID 0009-0005-0470-5985

Figure 1. Computed Tomography and Magnetic Resonance Imaging of the Abdomen



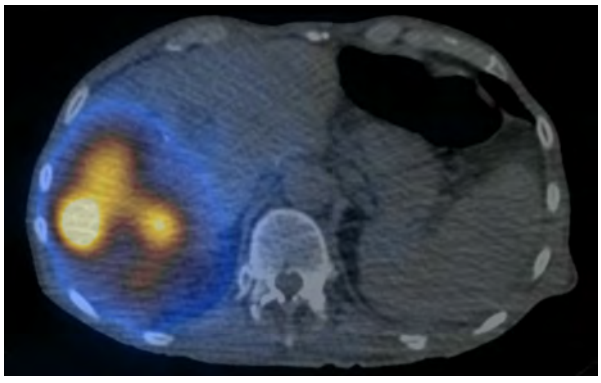
A) CT indicates a new portal venous thrombus. Low attenuation of the liver seen peripheral to the thrombus is concerning for underlying mass.
B) MRI indicates a 7.3 x 5.5-cm infiltrative mass in the right hepatic lobe with multiple satellite lesions.

Figure 2. H&E Stain of Liver Mass Showing Moderately Differentiated Hepatocellular Carcinoma With Predominant Pseudoacinar Pattern



Abbreviation: H&E, hematoxylin and eosin.

Figure 3. Liver Biopsy Specimen Showing Moderately Differentiated Hepatocellular Carcinoma



131 × 10^3/μL), elevated alkaline phosphatase (166 U/L), and stable liver function test results. Viral polymerase chain reaction testing was negative, and no significant alcohol use was identified. CT of the abdomen revealed cirrhotic liver morphology and a lesion concerning for a hepatic mass. Magnetic resonance imaging (MRI) confirmed a 7.3 x 5.5-cm infiltrative mass in the right hepatic lobe with associated portal vein thrombus (Figure 1). Biopsy pathology (Figure 2) confirmed moderately differentiated HCC with a pseudoacinar pattern, and immunohistochemical staining corroborated HCC rather than metastatic colorectal cancer or cholangiocarcinoma.

Because safe resection was not feasible, a multidisciplinary tumor board recommended yttrium-90 (Y-90) transarterial radioembolization segmentectomy (Figure 3), which he tolerated well. Follow-up MRI demonstrated stable posttreatment changes 11 months after diagnosis. Adjunctive chemotherapy remains under consideration.

DISCUSSION

This case presents a rare instance of de novo HCC nearly 30 years after liver transplantation for PSC. Although de novo HCC after liver transplantation for PSC is rare, our patient highlights its potential emergence in the setting of subclinical recurrent PSC. Cholangiocarcinoma and metastatic colorectal cancer were more likely diagnostic considerations given his history of PSC and colorectal cancer. Accurate diagnosis required high-quality MRI and image-guided biopsy with pathologic evaluation..

Survival beyond 20 years after liver transplantation is increasingly common. Patients undergoing liver transplant for PSC have reported life expectancies of 9 to 20 years,[3] with >69% surviving beyond 10 years.[8] As patients with PSC have longer survival than non-PSC liver transplant recipients,[9] This extended survival underscores the need for proactive screening for posttransplant

liver disease, risk factor mitigation, and enhanced malignancy surveillance in this subpopulation.

Recurrent and de novo liver disease after liver transplantation are common and warrant close evaluation. Clinically significant PSC recurrence after liver transplantation ranges from 18% to 37%, with risk factors including concurrent inflammatory bowel disease, acute cellular rejection, male recipients, intact colon prior to liver transplant, cholangiocarcinoma prior to liver transplant, or cytomegalovirus,[8] several of which were present in our patient. MRI/MRCP findings in 2014 showed no evidence of recurrent PSC. Because subtle signs of liver disease were present on imaging in 2021, subclinical recurrence of PSC after 2014 is likely. Similarly, de novo metabolic dysfunction-associated liver disease has been shown to affect >70% of patients 5 years after liver transplantation, with risk factors including metabolic syndrome, calcineurin inhibitor or corticosteroid use, alcohol use, and genetic factors.[10] Given the high prevalence of recurrent and de novo liver diseases after liver transplantation, screening for and diagnosing progression to advanced fibrosis or cirrhosis is crucial.

Currently, no routine screening exists for hepatic malignancy after liver transplantation unless cirrhosis is identified. The most recent International Liver Transplantation Society/Spanish Society of Liver Transplantation consensus conference and the American Association for the Study of Liver Diseases guidelines recommend individualized malignancy screening based on viral infection status, burden of immunosuppression, and estimated cancer risk (eg, abdominal imaging every 6 to 12 months for HCC screening in patients who develop allograft cirrhosis).[11,12] Increasing uptake of newer screening modalities such as elastography[13] may allow earlier identification of posttransplant liver disease and guide targeted HCC screening in higher-risk patients. Screening protocols using biannual imaging (abdominal CT, MRI, or bone scan with nuclear tracing) for transplant recipients have demonstrated improved survival.[14,15] Thus, among long-term transplant recipients, elastography or even routine CT or MRI every 3 to 5 years after transplantation may improve detection of liver disease, fibrosis, and malignancy; however, formal cost-effectiveness and benefit analysis are needed.

The occurrence of HCC 30 years after liver transplantation for PSC highlights the potential for asymptomatic allograft liver disease, particularly allograft fibrosis or cirrhosis. Given the increasing longevity of liver transplant recipients, there is a growing need to maintain a high index of suspicion for recurrent or de novo liver disease and malignancy. Although current guidelines recommend individualized approaches to malignancy screening after transplantation, emerging literature suggests a potential benefit from more proactive screening strategies, including elastography.

CONCLUSIONS

Our patient's asymptomatic recurrent PSC and de novo HCC detected decades after liver transplantation underscore the need for proactive screening for late-onset disease, allograft fibrosis, and malignancy in long-term transplant survivors. Because his HCC was identified incidentally at a relatively early stage, allowing treatment with Y-90 radioembolization, this case suggests that routine screening for recurrent liver disease, fibrosis, and malignancy in long term liver transplant survivors may be beneficial.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Chandok N, Watt KD. Burden of de novo malignancy in the liver transplant recipient. *Liver Transpl.* 2012;18(11):1277-1289. doi:10.1002/lt.23531

2. Straś WA, Wasiak D, Łągiewska B, et al. Recurrence of hepatocellular carcinoma after liver transplantation: risk factors and predictive models. *Ann Transplant.* 2022;27:e934924. doi:10.12659/AOT.934924

3. Mouchli MA, Singh S, Loftus EV Jr, et al. Risk factors and outcomes of de novo cancers (excluding nonmelanoma skin cancer) after liver transplantation for primary sclerosing cholangitis. *Transplantation*. 2017;101(8):1859-1866. doi:10.1097/TP.0000000000001725

4. Trevisani F, Garuti F, Cucchetti A, Lenzi B, Bernardi M. De novo hepatocellular carcinoma of liver allograft: a neglected issue. *Cancer Lett.* 2015;357(1):47-54. doi:10.1016/j.canlet.2014.11.032

5. El-Domiaty N, Saliba F, Sebagh M, et al. De novo hepatocellular carcinoma in a non-cirrhotic allograft 27 years after liver transplantation: a case report. *Am J Transplant.* 2021;21(5):1953-1958. doi:10.1111/ajt.16476

6. Tamè M, Calvanese C, Cucchetti A, Gruppioni E, Colecchia A, Bazzoli F. The onset of de novo hepatocellular carcinoma after liver transplantation can be both of donor and recipient origin. A case report. *J Gastrointestin Liver Dis*. 2015;24(3):387-389. doi:10.15403/jgld.2014.1121.243.gpp

7. Allaire M, Sérée O, Coilly A, et al. De novo primary liver cancer after liver transplantation: a French national study on 15803 patients. *Exp Clin Transplant.* 2018;16(6):779-780. doi:10.6002/ect.2018.0222

8. Pena Polanco NA, Levy C, Martin EF. Cholestatic liver diseases after liver transplant. *Clin Liver Dis.* 2017;21(2):403-420. doi:10.1016/j.cld.2016.12.011

9. Lucey MR, Furuya KN, Foley DP. Liver transplantation. *N Engl J Med.* 2023;389(20):1888-1900. doi:10.1056/NEJMra2200923

10. Saeed N, Glass L, Sharma P, Shannon C, Sonnenday CJ, Tincopa MA. Incidence and risks for nonalcoholic fatty liver disease and steatohepatitis post-liver transplant: systematic review and meta-analysis. *Transplantation*. 2019;103(11):e345-e354. doi:10.1097/TP.0000000000002916

11. Salcedo M, Vinaixa C, Javle M, Trapero-Marugán M, Bustamante J, Line PD. Evaluation and management of liver transplant candidates with prior nonhepatic cancer: guidelines from the ILTS/SETH consensus conference. *Transplantation*. 2022;106(1):e3-e11. doi:10.1097/TP.0000000000003997

12. Lucey MR, Terrault N, Ojo L, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transpl.* 2013;19(1):3-26. doi:10.1002/lt.23566

13. Ginès P, Castera L, Lammert F, et al. Population screening for liver fibrosis: toward early diagnosis and intervention for chronic liver diseases. *Hepatology*. 2022;75(1):219-228. doi:10.1002/hep.32163

14. Lee DD, Sapisochin G, Mehta N, et al. Surveillance for HCC After liver transplantation: increased monitoring may yield aggressive treatment options and improved postrecurrence survival. *Transplantation*. 2020;104(10):2105-2112. doi:10.1097/TP.0000000000003117

15. Finkenstedt A, Graziadei IW, Oberaigner W, et al. Extensive surveillance promotes early diagnosis and improved survival of de novo malignancies in liver transplant recipients. *Am J Transplant.* 2009;9(10):2355-2361. doi:10.1111/j.1600-6143.2009.02766.x

Lung Adenocarcinoma in Primary Ciliary Dyskinesia: A Case Report of Metastatic Disease and Successful Multimodal Treatment

Vishnu Kommineni, MBBS, MD, MBA; Rathnamitreyee Vegunta, MBBS, MD; Venkata Rokkam, MD; Gurusaravanan Kutti Sridharan, MD

ABSTRACT

Introduction: Primary ciliary dyskinesia (PCD) is a rare genetic disorder characterized by impaired mucociliary clearance. To our knowledge, no cases of lung adenocarcinoma in patients with PCD have been previously reported.

Case Presentation: A 43-year-old White man with PCD presented with persistent cough and dysphonia. Chest imaging revealed a 4-cm mass in the left upper lobe, and positron emission tomography/computed tomography (PET/CT) demonstrated increased uptake in the mass, hilar lymph nodes, and sternum, suggesting metastatic disease. Biopsy of the lung mass confirmed adenocarcinoma, and magnetic resonance imaging of the brain identified a metastatic lesion. He was treated initially with pembrolizumab and stereotactic radiation therapy for a brain metastasis and had a mixed response. Consequently, chemotherapy with carboplatin and pemetrexed was added, resulting in complete response, with no fluorodeoxyglucose-avid lesions on follow-up PET imaging.

Discussion: With only 8 reported cases of lung cancer in patients with PCD, this is, to our knowledge, the first report of lung adenocarcinoma in a patient with PCD successfully treated with chemoimmunotherapy.

Conclusions: Although rare, clinicians should consider lung cancer in patients with PCD who present with persistent symptoms refractory to standard treatment.

INTRODUCTION

Primary ciliary dyskinesia (PCD) is a rare inherited condition characterized by impaired mucociliary clearance due to genetic mutations affecting motile cilia. It primarily follows an autosomal recessive inheritance pattern, although other patterns, including autosomal dominant and X-linked inheritance, also occur. PCD affects approximately 1 in 10 000 to 20 000 live births.[1] Primary lung cancer among patients with PCD is rare.

CASE PRESENTATION

A 43-year-old White man presented with cough, chest pain, headache, and hoarseness that had persisted for several months. He was a never-smoker but chewed tobacco for 10 years before quitting 2 years prior to presentation. He had a history of recurrent bronchiectasis since childhood. Testing for cystic fibrosis and alpha-1-antitrypsin deficiency was negative. Electron microscopy of cilia showed partial absence of the inner dynein arms, leading to a diagnosis of PCD. Pulmonary function testing revealed severe chronic obstructive pulmonary disease (COPD).

A chest x-ray identified a focal opacity in the left upper lobe. Subsequent computed tomography (CT) of the chest revealed severe bilateral bronchiectasis and a 4-cm mass in the left upper lobe. Positron emission tomography/computed tomography (PET/CT) scan showed left hilar lymphadenopathy, sternal metastasis, and the 4-cm mass in the left upper lobe (Figures 1A and 2). A CT-guided biopsy of the lung mass confirmed lung adenocarcinoma. Staging workup with magnetic resonance imaging (MRI) of the brain revealed a 7-mm lesion in the left parietal lobe, leading to a diagnosis of stage IV (T2N1M1b) lung adenocarcinoma (Figure 3). Mutation testing was negative for epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS proto-oncogene 1 (ROS1), and other mutations. Programmed death ligand 1 (PD-L1) testing revealed a tumor proportion score of 95%.

Given the treatment options for oligometastatic non-small cell

• • •

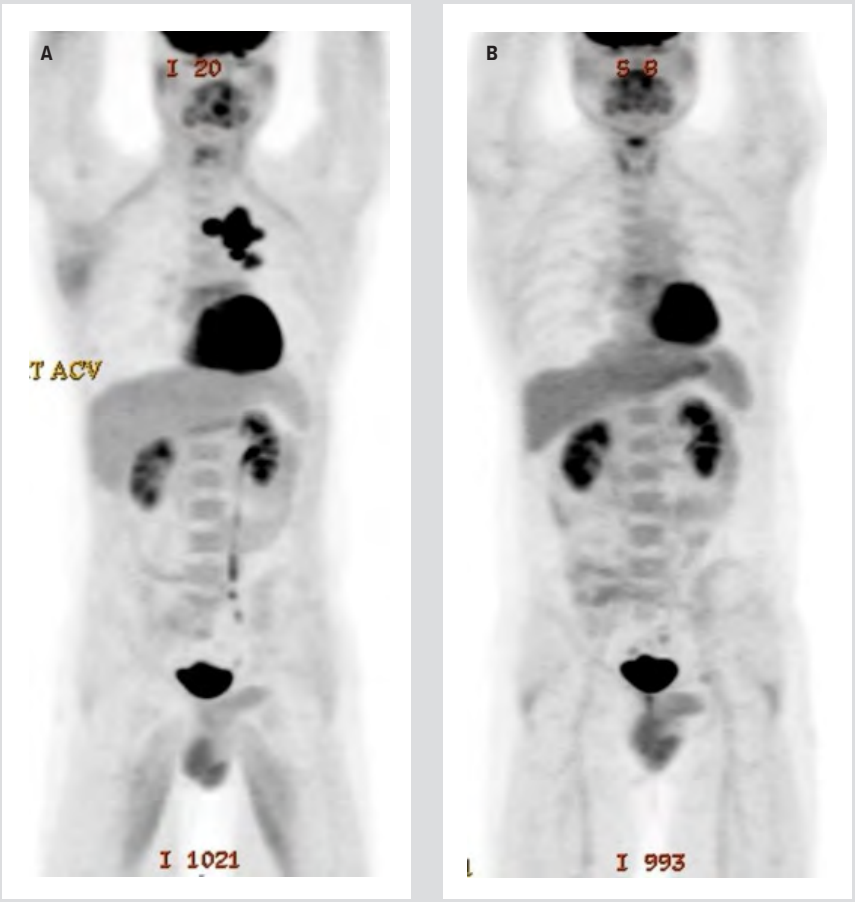
Author affiliations: Hospital Internal Medicine, Mayo Clinic Health System, Eau Claire, Wisconsin (Kommineni); Hematology and Oncology, Westchester Medical Center, Valhalla, New York (Vegunta); Internal Medicine, University of Arizona College of Medicine, Tucson, Arizona (Rokkam, Sridharan).

Corresponding author: Vishnu Kommineni, MBBS, MD, MBA, 1221 Whipple St, Eau Claire, WI 54703; email Kommineni.Vishnuteja@Mayo.edu; ORCID ID 0009-0005-6776-3592

lung cancer, including chemoradiation therapy, chemoimmunotherapy, or immunotherapy alone, the decision was made to treat the patient with immunotherapy alone because of his severe COPD, bronchiectasis, PCD, and high PD-L1 expression. He was started on intravenous (IV) pembrolizumab 200 mg every 3 weeks. After the first cycle of pembrolizumab, his hoarseness improved. He received stereotactic radiation therapy for the brain metastasis. During immunotherapy, he developed hypothyroidism and was started on thyroid hormone replacement therapy.

After 8 cycles of pembrolizumab, a repeat chest CT scan showed a mixed response to therapy, with near resolution of the left lung lesions but new nodules in the right middle lobe (Figure 4). An MRI of the brain showed no evidence of recurrent disease. As the patient had no clinical symptoms, laboratory abnormalities, or imaging findings suggestive of infection or inflammation (eg, ground glass opacities, organizing pneumonia), the decision was made to forego biopsy of the new right middle lobe lesions and add chemotherapy to ongoing immunotherapy. He received carboplatin, pemetrexed, and pembrolizumab every 3 weeks for 4 cycles and tolerated the therapy well, with no infectious complications. A follow-up chest CT after these 4 cycles showed an excellent response to therapy, with no new metastasis.

Figure 1. Positron Emission Tomography Scan Coronal View



A. Initial PET scan with increased uptake in the left upper chest and sternum.
B. Follow-up PET scan after completion of chemoimmunotherapy. Notice resolution of left upper chest lesions seen in Figure 1A.

He subsequently received maintenance treatment with pembrolizumab and pemetrexed for 4 cycles. However, he developed severe psoriasis secondary to immunotherapy, and further treatment was withheld. A follow-up PET/CT scan demonstrated a complete response to therapy, with no fluorodeoxyglucose-avid lesions (Figure 1B). Sixty-six months after initial presentation, he remained under surveillance with no evidence of recurrence.

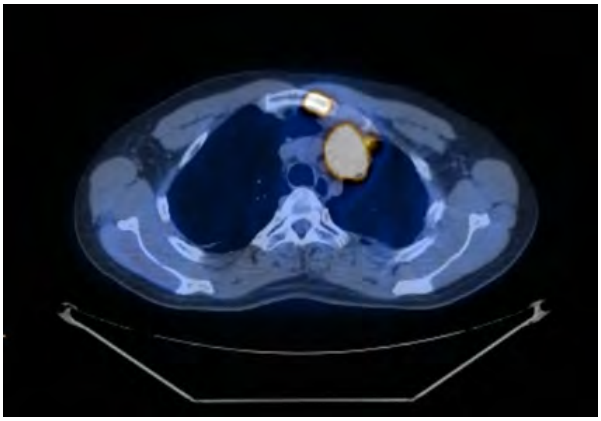
DISCUSSION

PCD is part of a growing group of genetic disorders known as ciliopathies. Mutations in genes encoding the axonemal structure and the cytoplasmic and regulatory proteins involved in the structure and function of motile cilia lead to PCD. Due to the large number of proteins involved in ciliary function and assembly, PCD exhibits substantial genetic heterogeneity. Patients typically present early in life and with a wide range of clinical manifestations caused by impaired mucociliary clearance. These manifestations include neonatal respiratory distress, persistent sinonasal disease, middle ear disease, hearing loss, chronic daily cough, bronchiectasis, and laterality defects. The severity of these symptoms varies according to the specific genotype involved.[1]

Diagnosing PCD is challenging because no single test can definitively confirm or exclude the disease. Historically, transmission electron microscopy (TEM) to assess axonemal ultrastructure has been considered the gold standard; however, limitations of electron microscopy have become apparent with advances in genetic tools.[1] Various subtypes of PCD have been identified based on the ultrastructural and functional ciliary defects. Diagnostic tools include nasal nitric oxide measurement, high-speed video microscopy, TEM, and genetic studies.[1,2] One notable subtype of PCD with situs inversus, chronic sinusitis, and bronchiectasis is Kartagener syndrome.

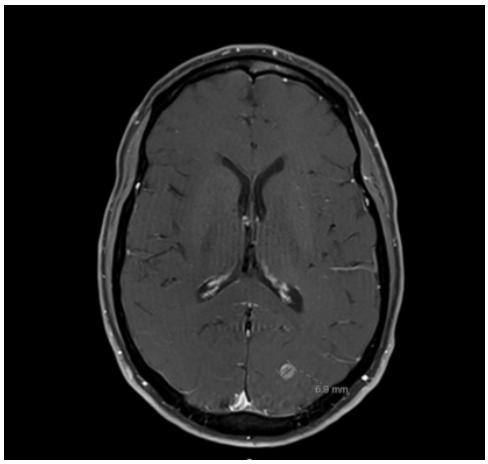
The relationship between PCD and lung cancer is not fully understood. Only 8 cases of lung cancer have been reported in patients with ciliary dyskinesia or Kartagener syndrome. Most of these patients were male (7 of 8) and older than 50 years (6 of

Figure 2. Initial PET/CT in Transverse Plane Showing Increased Uptake in the 4-cm Left Upper Lobe Mass With Left Hilar Lymph Nodes and Sternal Metastasis



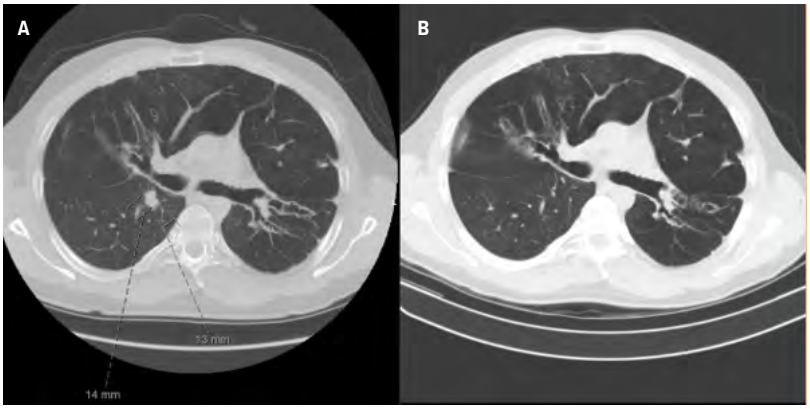
Abbreviation: PET/CT, positron emission tomography/computed tomography.

Figure 3. Magnetic Resonance Imaging of the Brain Showing a 7-mm Metastatic Lesion in the Left Parietal Lobe



8). No predilection for tumor laterality has been observed.[3,4] Squamous cell carcinoma was the most frequently reported histologic subtype (4 of 8 cases). Because most patients with PCD who developed lung cancer had a smoking history (5 of 6 cases), chronic inflammation related to smoking and emphysema has been proposed as a risk factor for squamous cell carcinoma.[5] PCD is associated with recurrent respiratory tract infections and bronchiectasis, both of which contribute to chronic pulmonary inflammation. Chung et al reported an increased risk of lung cancer in patients with bronchiectasis.[6] In a unique case, mucoepidermoid carcinoma was reported in a 39-year-old female never-smoker with Kartagener syndrome, with some evidence suggesting a possible role for congenital lung malformation.[4] Further research is needed to understand the pathophysiology underlying PCD-associated lung cancer across histologic subtypes and its association with never-smokers.

Figure 4. Computed Tomography of the Thorax



A. CT image after 8 cycles of pembrolizumab with new lung nodules in the right middle lobe.
B. CT image of the same section of thorax at the time of diagnosis.

Treatment options for oligometastatic non-small cell lung cancer include chemotherapy with immunotherapy, immunotherapy alone, or chemoradiation therapy. The KEYNOTE-024 trial demonstrated improved progression-free survival and overall survival among patients with PD-L1 expression greater than 50% who received pembrolizumab compared with platinum-doublet chemotherapy.[7] According to National Comprehensive Cancer Network guidelines, the addition of pembrolizumab to platinum-doublet chemotherapy is the preferred first-line treatment for non-small cell lung cancer with PD-L1 expression >1%, no contraindications to PD-1 or PD-L1 inhibitors, and no EGFR exon 19 deletion, EGFR L858R mutation, or ALK, RET, or ROS1 rearrangement.[8] However, treatment should be individualized based on each patient's comorbidities. To our knowledge, this is the first reported case of metastatic lung adenocarcinoma in a patient with PCD successfully treated with a combination of chemotherapy and immunotherapy.

CONCLUSIONS

The possibility of lung malignancy should be considered in patients with PCD who present with persistent respiratory symptoms refractory to standard treatment. Combination chemotherapy and immunotherapy can be administered safely to patients with lung adenocarcinoma and PCD.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Horani A, Ferkol TW. Understanding primary ciliary dyskinesia and other ciliopathies. *J Pediatr.* 2020;230:15-22.e1. doi:10.1016/j.jpeds.2020.11.040

2. Frommer A, Hjeij R, Loges NT, et al. Immunofluorescence analysis and diagnosis of primary ciliary dyskinesia with radial spoke defects. *Am J Respir Cell Mol Biol.* 2015;53(4):563-573. doi:10.1165/rcmb.2014-0483OC

3. Inoue Y, Suga A, Sekido Y, Yamada S, Iwazaki M. A case of surgically resected lung cancer in a patient with Kartagener's syndrome. *Tokai J Exp Clin Med*. 2011;36(2):21-4.

4. Nagai Y, Koyama N, Iwai Y, et al. Pulmonary mucoepidermoid carcinoma arising in a patient with Kartagener syndrome. *BMC Pulm Med*. 2020;20(1):93. doi:10.1186/s12890-020-1133-y

5. Papi A, Casoni G, Caramori G, et al. COPD increases the risk of squamous histological subtype in smokers who develop non-small cell lung carcinoma. *Thorax*. 2004;59(8):679-681. doi:10.1136/thx.2003.018291

6. Chung WS, Lin CL, Hsu WH, Kao CH. Increased risk of lung cancer among patients with bronchiectasis: a nationwide cohort study. *QJM*. 2016;109(1):17-25. doi:10.1093/qjmed/hcu237

7. Reck M, Rodriguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. *N Engl J Med.* 2016;375(19):1823-1833. doi:10.1056/NEJMoa1606774

8. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. *N Engl J Med.* 2018;378(22):2078-2092. doi:10.1056/NEJMoa1801005

Sitosterolemia: A Rare Cause of Severe Hypercholesterolemia in Children

Daniel Beacher, MD; Amy Ott, MS, CGC; Rebecca Plier, RD

ABSTRACT

Introduction: Severe hypercholesterolemia in children is commonly caused by familial hypercholesterolemia (FH); however, sitosterolemia, a rare autosomal recessive disorder, should be considered when FH genetic testing is negative.

Case Presentation: A 4-year-old boy presented with xanthomas on his knees. His total cholesterol was 561 mg/dL. Initially, homozygous FH was suspected, and rosuvastatin was started; however, genetic testing was negative. Subsequent genetic testing identified a homozygous *ABCG8* variant, consistent with sitosterolemia. Rosuvastatin was discontinued, and ezetimibe and dietary plant sterol restriction were initiated, resulting in significant improvement in cholesterol levels and resolution of xanthomas.

Discussion: Sitosterolemia results from impaired ABCG5/8 transporter function, leading to plant sterol accumulation, which can cause hypercholesterolemia, xanthomas, and hematologic abnormalities. Diagnosis is established by demonstrating elevated plant sterol levels or through genetic testing. Treatment involves dietary plant sterol restriction and ezetimibe.

Conclusions: Sitosterolemia, though rare, should be considered in severe hypercholesterolemia when FH genetic testing is negative. This case demonstrates a typical presentation and favorable response to treatment with ezetimibe and dietary modification.

INTRODUCTION

Severe hypercholesterolemia in children is usually defined as a low-density lipoprotein cholesterol (LDL-C) level of ≥ 190 mg/dL.[1] Severe hypercholesterolemia that persists despite a trial of lifestyle modifications is often due to a primary, inherited dyslipidemia, with familial hypercholesterolemia (FH) being most common. Sitosterolemia is another rare cause of severe hypercholesterolemia in children that should be considered if genetic testing for FH is negative. Here, we describe a case of sitosterolemia in a 4-year-old boy, characterized by xanthomas, severely elevated cholesterol, and elevated plant sterol levels in the blood.

CASE PRESENTATION

A 4-year-old boy with no significant past medical history was noted to have yellow cutaneous nodules on his knees at his well-child visit at age 4 years. His physical exam was otherwise normal, with no cardiac murmurs and no evidence of corneal arcus. He was referred to dermatology, and a punch biopsy of the right knee nodule (Figure 1) was performed. Histology of the biopsy showed a mixture of foamy histiocytes, lymphocytes, and other mononuclear cells, along with a few multinucleated giant cells. The differential diagnosis included xanthoma and juvenile xanthogranuloma.

A lipid panel showed severely elevated lipid levels, with an LDL-C of 406 mg/dL and a total cholesterol of 561 mg/dL. The family history was notable for consanguinity; the paternal grandfather and maternal grandfather are brothers. The paternal grandfather died at age 26 from a suspected myocardial infarction. The mother had a history of high cholesterol that was controlled with dietary modifications and is now normal. The father had not had his cholesterol measured.

Given the marked LDL-C elevation, the presence of xanthomas, and the family history, the highest clinical concern was for homozygous FH. The patient was started on the HMG-CoA reductase inhibitor rosuvastatin and was referred for genetic testing. An

• • •

Author affiliations: Pediatric Cardiology, Medical College of Wisconsin, Milwaukee, Wisconsin (Beacher); Pediatric Genetics, MCW, Milwaukee, Wisconsin (Ott); Pediatric Gastroenterology and Nutrition, MCW, Milwaukee, Wisconsin (Plier).

Corresponding author: Daniel Beacher, MD, 8701 W Watertown Plank Rd, Milwaukee, WI 53226; email dbeacher@mcw.edu; ORCID ID 0000-0002-4520-6593

FH genetic testing panel was performed, including sequencing and deletion/duplication analysis of the 4 FH-associated genes (*LDLR*, *APOB*, *PCSK9*, and *LDLRAP-1*). While awaiting results, his rosuvastatin dose was increased without a significant effect on his LDL-C levels (Figure 2). During this time, he remained asymptomatic, and an echocardiogram showed no evidence of cardiac cholesterol deposition or valvular heart disease.

The FH genetic panel ultimately returned negative. Given the persistently elevated cholesterol and lack of significant response to rosuvastatin, an alternative genetic etiology was suspected. A broader genetic testing panel for hereditary dyslipidemia identified a homozygous pathogenic variant *ABCG8* (c.547del; p.Gln183Serfs*9 [NM_022437.2]), consistent with autosomal recessive sitosterolemia. Given this diagnosis, rosuvastatin was discontinued, and he was started on ezetimibe 10 mg daily.

The family underwent extensive dietary counseling to reduce plant sterols intake. A detailed diet history was obtained, and key foods high in plant sterols were identified. The patient was encouraged to avoid these foods, and alternatives were suggested. Foods particularly high in plant sterols and to be avoided in sitosterolemia include vegetable oils (eg, olive, corn, canola), nuts and seeds (eg, almonds, walnuts, cashews, sesame, sunflower), juice or soy milk fortified with plant sterols, kidney beans, lentils, and margarine. Plant sterols may also be present in foods or supplements marketed for heart health and also should be avoided. Most fruits and vegetables contain relatively low amounts of plant sterols; however, those with higher levels (eg, avocados) should also be avoided. Acceptable alternatives low in plant sterols include lean animal proteins (eg, chicken, turkey) and refined grains. Initiation of ezetimibe and dietary modification resulted in significant improvement in LDL-C and total cholesterol (see Figure 2) and resolution of the cutaneous xanthomas.

Cascade genetic testing of the patient's parents showed that both were heterozygous carriers of the variant. Given the autosomal recessive inheritance of *ABCG8*, his sister was at risk of being affected; however, she tested negative for the variant.

The patient remains clinically well and asymptomatic from a cardiovascular standpoint, with no recurrence of xanthomas. Complete blood cell counts occasionally have shown mild anemia (hemoglobin 10.8-11.6 g/dL), with normal platelet counts. Blood was sent for gas chromatography-mass spectrometry (GC-MS) after initiation of ezetimibe and diet changes, and plant sterol levels remained elevated (sitosterol, 12.81 mg/dL [normal ≤ 1.5 mg/dL]; campesterol, 7.77 mg/dL [normal ≤ 0.8 mg/dL]; stigmasterol, 0.6 mg/dL [normal ≤ 0.05 mg/dL]).

Figure 1. Right Knee Nodules

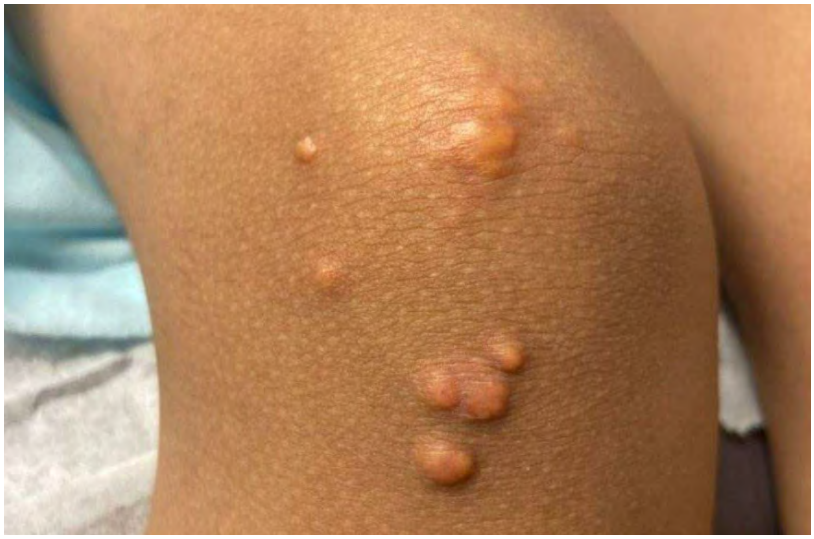
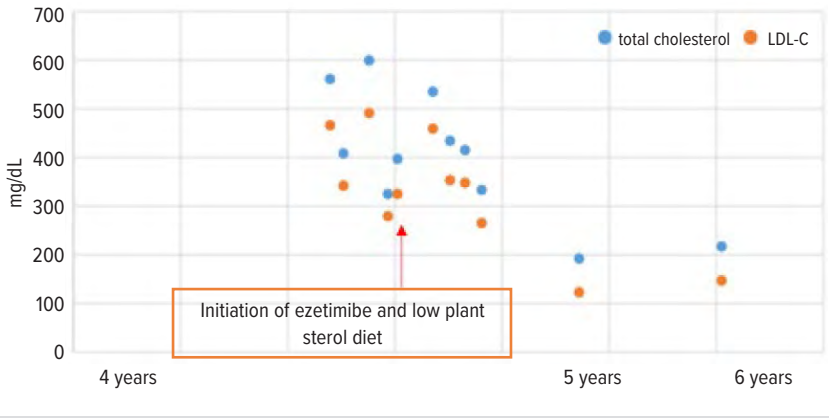


Figure 2. Patient Total Cholesterol and Low-Density Lipoprotein Cholesterol (LDL-C) Levels



DISCUSSION

Sitosterolemia is an extremely rare cause of severe hypercholesterolemia. The exact prevalence is unknown; however, fewer than 200 individuals have been reported in the literature, and the condition is likely underdiagnosed.[2]

The primary abnormality in sitosterolemia is the accumulation

of plant sterols. Plant sterols (most commonly sitosterol, campesterol, and stigmasterol) are structurally similar to animal cholesterol. However, unlike cholesterol, plant sterols are not used in human metabolism; therefore, plasma plant sterol levels are typically very low (<1 mg/dL).[2,3]

Sitosterolemia was first described by Bhattacharyya and Connor in 1974.[4] Subsequent studies have elucidated its molecular basis.[5-8] It is an autosomal recessive disorder caused by homozygous or compound heterozygous loss-of-function variants in *ABCG5* or *ABCG8*, which encode 2 proteins of the ATP-binding cassette family, which ultimately form a heterodimeric transport molecule primarily in the intestine and liver.[9]

Dietary cholesterol and plant sterols are transported from the intestinal lumen into enterocytes by the Nieman-Pick C1-like 1 (NPC1L1) protein. Most plant sterols are then excreted back into the intestinal lumen or biliary tract in the liver via the ABCG5/8 transporter. This transporter also excretes excess cholesterol. Although dietary intake of cholesterol and plant sterols is similar in Western diets, approximately 50% of cholesterol is absorbed into the bloodstream, compared with <5% of plant sterols.[2,3,9]

Accumulated plant sterols are transported in lipoproteins and may contribute to xanthoma formation, potentially at lower serum cholesterol levels than in FH.[10] Xanthomas can appear early in life and sitosterolemia with cutaneous findings has even been reported in breastfed infants.[11] Minor trauma may precipitate xanthoma development, particularly on extensor surfaces (eg, elbows and knees).

There is a heterogeneity in presenting serum cholesterol levels; however, most patients have at least mild elevation, and many have severe LDL-C elevation. Children with sitosterolemia may have higher serum cholesterol levels than adults, possibly due to age-related differences in LDL receptor expression or intrinsic cholesterol synthesis, although the mechanism remains unclear.[11,12] Patients are at risk for premature coronary artery disease,[13] and sudden death has been reported in a 5 year old with coronary ostial occlusion from aortic lipid deposits.[14] Valvular heart disease, particularly involving the aortic valve, may also occur.

There also may be significant hematologic effects in some patients. Circulating plant sterols appear to be toxic and damaging to red blood cells and platelets, and patients can develop hemolytic anemia and/or thrombocytopenia with stomatocytosis and macrothrombocytopenia, as well as splenomegaly.[15] These findings may rarely be the presenting symptom.[16] Routine complete blood cell count monitoring is recommended for all patients with sitosterolemia.

Patients may present with xanthomas, severe hypercholesterolemia, and/or hematologic abnormalities. Due to its rarity and similarity with more common disorders, sitosterolemia is often misdiagnosed. In addition to FH, cerebrotendinous xanthomatosis (CTX) should be considered and can be distinguished by the presence of gastrointestinal symptoms, cataracts, neurologic findings, and absence of hematologic findings.

In pediatric patients, sitosterolemia should be suspected in those with severe hypercholesterolemia unresponsive to standard therapy, those with associated hematologic abnormalities, and/or those with severe xanthomas. This case also underscores the importance of universal lipid screening in children, as recommended by the National Heart, Lung, and Blood Institute Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents.[17] These guidelines recommend screening once during ages 9 to 11 years and again during ages 17 to 21 years, with enhanced screening for high-risk individuals. As many children with inherited hypercholesterolemia disorders—including sitosterolemia—may present solely with dyslipidemia on laboratory testing, universal screening is essential for early diagnosis and detection.

The diagnosis of sitosterolemia can be made clinically based on phenotype and elevated plant sterols levels; however, GC-MS testing may not be widely available. Alternatively, the diagnosis can be confirmed with genetic testing. Although traditionally considered an autosomal recessive disorder, recent research suggests that heterozygous carriers may have increased coronary artery disease risk compared with the general population.[18]

Treatment focuses on limiting plant sterols in the diet as well as use of the NPC1L1 inhibitor ezetimibe. By blocking the NPC1L1 transporter, absorption of both dietary cholesterol and plant sterols is reduced. Small studies have demonstrated safety and efficacy in sitosterolemia, including in children.[19–21]

As noted above, foods high in plant sterols (eg, vegetable oils, nuts, seeds) should be avoided. Plant sterols found in health food products or supplements geared towards heart health also should be avoided. Naturally occurring plant sterols are not routinely listed on nutrition labels; however, they might be listed on products when plant sterols are added for a specific health benefit.

CONCLUSIONS

Sitosterolemia is a rare autosomal recessive disorder characterized by excess absorption and accumulation of plant sterols, with a phenotype that includes hypercholesterolemia, xanthomas, and hematologic abnormalities. Clinicians should consider this diagnosis in patients with severe hypercholesterolemia who are unresponsive to standard therapies, particularly in the presence of hematologic abnormalities or pediatric xanthomas.

Diagnosis can be established by measuring plant sterol levels in the blood and/or confirmed with genetic testing. Children with severe hypercholesterolemia should be referred to a pediatric lipid specialist. This case highlights the importance of considering alternative etiologies in patients who do not respond to standard lipid-lowering therapy.

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgements: As the patient is a minor, the patient's mother provided written consent for publication of this case.

REFERENCES

1. Sniderman AD, Tsimikas S, Fazio S. The severe hypercholesterolemia phenotype: clinical diagnosis, management, and emerging therapies. *J Am Coll Cardiol.* 2014;63(19):1935-1947. doi:10.1016/j.jacc.2014.01.060

2. Kidambi S, Patel SB. Sitosterolaemia: pathophysiology, clinical presentation and laboratory diagnosis. *J Clin Pathol.* 2008;61(5):588-594. doi:10.1136/jcp.2007.049775

3. Liebeskind A, Peterson AL, Wilson D. Sitosterolemia. In: Feingold KR, Adler RA, Ahmed SF, et al., eds. Endotext. MDText.com, Inc.; March 10, 2023. Accessed February 3, 2025. https://www.ncbi.nlm.nih.gov/books/NBK395586/

4. Bhattacharyya AK, Connor WE. Beta-sitosterolemia and xanthomatosis: a newly described lipid storage disease in two sisters. *J Clin Invest*. 1974;53(4):1033-1043. doi:10.1172/JCI107640

5. Lee MH, Lu K, Patel SB. Genetic basis of sitosterolemia. *Curr Opin Lipidol.* 2001;12(2):141-149. doi:10.1097/00041433-200104000-00007

6. Lu K, Lee MH, Hazard S, et al. Two genes that map to the STSL locus cause sitosterolemia: genomic structure and spectrum of mutations involving sterolin-1 and sterolin-2, encoded by ABCG5 and ABCG8, respectively. *Am J Hum Genet.* 2001;69(2):278-290. doi:10.1086/321294

7. Wang J, Joy T, Mymin D, Frohlich J, Hegele RA. Phenotypic heterogeneity of sitosterolemia. *J Lipid Res*. 2004;45(12):2361-2367. doi:10.1194/jlr.M400310-JLR200

8. Berge KE, Tian H, Graf GA, et al. Accumulation of dietary cholesterol in sitosterolemia caused by mutations in adjacent ABC transporters. *Science*. 2000;290(5497):1771-1775. doi:10.1126/science.290.5497.1771

9. Nghiem-Rao TH, Patel SB. Investigating sitosterolemia to understand lipid physiology. *Clin Lipidol.* 2013;8(3):649-658. doi:10.2217/clp.13.60

10. Zhang J, Chen QL, Guo S, et al. Clinical characteristics of sitosterolemic children with xanthomas as the first manifestation. *Lipids Health Dis*. 2022;21(1):100. doi:10.1186/s12944-022-01710-1

11. Park JH, Chung IH, Kim DH, Choi MH, Garg A, Yoo EG. Sitosterolemia presenting with severe hypercholesterolemia and intertriginous xanthomas in a breastfed infant: case report and brief review. *J Clin Endocrinol Metab.* 2014;99(5):1512-1518. doi:10.1210/jc.2013-3274

12. Niu DM, Chong KW, Hsu JH, et al. Clinical observations, molecular genetic analysis, and treatment of sitosterolemia in infants and children. *J Inherit Metab Dis.* 2010;33(4):437-443. doi:10.1007/s10545-010-9126-2

13. Miettinen TA. Phytosterolaemia, xanthomatosis and premature atherosclerotic arterial disease: a case with high plant sterol absorption, impaired sterol elimination and low cholesterol synthesis. *Eur J Clin Invest.* 1980;10(1):27-35. doi:10.1111/j.1365-2362.1980.tb00006.x

14. Mymin D, Wang J, Frohlich J, Hegele RA. Image in cardiovascular medicine: aortic xanthomatosis with coronary ostial occlusion in a child homozygous for a nonsense mutation in ABCG8. *Circulation*. 2003;107(5):791. doi:10.1161/01.cir.0000050545.21826.ad

15. Rees DC, Iolascon A, Carella M, et al. Stomatocytic haemolysis and macrothrombocytopenia (Mediterranean stomatocytosis/macrothrombocytopenia) is the haematological presentation of phytosterolaemia. *Br J Haematol*. 2005;130(2):297-309. doi:10.1111/j.1365-2141.2005.05599.x

16. Su Y, Wang Z, Yang H, et al. Clinical and molecular genetic analysis of a family with sitosterolemia and co-existing erythrocyte and platelet abnormalities. Haematologica. 2006;91(10):1392-1395. Accessed February 3, 2025. https://haematologica.org/article/view/4184

17. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents; National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics*. 2011;128(suppl 5):S213-S256. doi:10.1542/peds.2009-2107C

18. Nomura A, Emdin CA, Won HH, et al. Heterozygous ABCG5 gene deficiency and risk of coronary artery disease. *Circ Genom Precis Med*. 2020;13(5):417-423. doi:10.1161/CIRCGEN.119.002871

19. Othman RA, Myrie SB, Mymin D, et al. Ezetimibe reduces plant sterol accumulation and favorably increases platelet count in sitosterolemia. *J Pediatr.* 2015;166(1):125-131. doi:10.1016/j.jpeds.2014.08.069

20. Salen G, von Bergmann K, Lütjohann D, et al. Ezetimibe effectively reduces plasma plant sterols in patients with sitosterolemia. *Circulation*. 2004;109(8):966-971. doi:10.1161/01.CIR.0000116766.31036.03

21. Lütjohann D, von Bergmann K, Sirah W, et al. Long-term efficacy and safety of ezetimibe 10 mg in patients with homozygous sitosterolemia: a 2-year, open-label extension study. *Int J Clin Pract*. 2008;62(10):1499-1510. doi:10.1111/j.1742-1241.2008.01841.x

A Confirmed Case of Rat Bite Fever

Thomas Kolman, MD; Noor Bhatti, MPH; Shruti Narayan, MA; Akorfa Adobor, BS; Samuel Fischer, MD; Pinky Jha, MD

ABSTRACT

Introduction: Rat bite fever is a rare zoonotic illness that presents with nonspecific symptoms. Rapid identification and treatment are essential to reduce morbidity or mortality.

Case Presentation: A 39-year-old male presented to the emergency department with severe headache and arthralgias. His history was notable for multiple bites and scratches from pet rats. He was admitted for further evaluation after meeting systemic inflammatory response syndrome (SIRS) criteria for sepsis. A meningitis workup was unrevealing. He was treated for presumed rat bite fever with amoxicillin and discharged in improved condition. Several days later, his blood culture grew *Streptobacillus moniliformis*. His symptoms resolved with appropriate antibiotic therapy.

Discussion: Prompt recognition and management are necessary to avoid complications of rat bite fever. A thorough history is crucial to identify uncommon exposures when initial workup is unrevealing.

Conclusions: This report describes a rare, culture-confirmed case of rat bite fever. Because this disease is not nationally reportable, it may be more prevalent than currently recognized and should remain in the differential diagnosis for patients with nonspecific symptoms and known rodent exposure.

INTRODUCTION

Rat bite fever is a rare disease most commonly caused by infection with *Spirillum minus* or *Streptobacillus moniliformis*. Most cases are seen in Japan, where the causative agent is more likely to be *S minus*. In contrast, in Western countries, the causative agent is more likely to be *S monilformis*, a nonmotile, pleomorphic, gram-negative bacillus that forms a characteristic "cotton ball" appearance on growth media.[1] Classically, transmission occurs via infected mucosal secretions from a rodent, giving the disease its name. However, transmission can also occur through rat urine and via contaminated food or water, as well as through household pets (eg, cats and dogs) that may serve as reservoirs for the disease if exposed to an infected rodent.[2]

Symptoms typically arise 2 to 4 weeks following exposure and include fever, which may wax and wane for months, along with migratory polyarthralgias most commonly affecting the knees, ankles, and back.[2] Approximately 75% of patients develop a maculopapular rash on the extremities.[2,3] Symptoms are thought to be due to bacteremia; however, this is difficult to confirm because the organism is challenging to culture.

The actual incidence is unknown because the causative bacteria are fastidious and difficult to grow, often respond to common antibiotic regimens prior to diagnosis, and the disease is not nationally reportable; however, a 2013 case report found that during 2000-2012, only 17 confirmed cases of rat bite fever were identified in California.[4] The general mortality rate of untreated rat bite fever is approximately 13% and can be as high as 53% in *S monilformis* endocarditis; therefore prompt identification and treatment are essential.[1,4]

CASE PRESENTATION

A 39-year-old male presented to the emergency department (ED) with severe arthralgias in the bilateral shoulders, elbows, wrists, and knees, and back, as well as pain, erythema, and warmth of his right third metacarpophalangeal (MCP) joint and left second MCP joint. Approximately 1 week prior to admission, he developed diarrhea and vomiting that persisted for 24 hours and resolved

Author affiliations: Internal Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin (Adobor, Bhatti, Fischer, Jha, Kolman, Narayan).

Corresponding author: Thomas Kolman, 8701 W Watertown Plank Rd, Milwaukee, WI 53226; email tkolman@mcw.edu; ORCID ID 0000-0002-3955-7143

spontaneously. Three days prior to admission, he was removing his pet rats from their cage when one of the rats scratched his back. He was unsure whether the rat bit him at that time but reported a confirmed bite approximately 4 weeks prior to admission. Within hours of being scratched, he developed diffuse arthralgias that progressively worsened until he presented to the ED.

In the ED, the patient was tachycardic (heart rate, 124 beats/min), and mildly hypertensive (systolic blood pressure, 131 mm Hg). His white blood cell count (WBC) was markedly elevated $26.5 \times 10^3/\mu L$ with a neutrophilic predominance. His C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated to 327.4 and 97, respectively. Based on his tachycardia and elevated WBC, he was admitted with sepsis after meeting systemic inflammatory response syndromesepsis (SIRS) criteria.

On admission, he developed a fever of 101.1°F. Physical examination was notable for tenderness to palpation in the bilateral neck, shoulders, elbows, wrists, knees, and MCP joints, along with erythema, edema, and warmth in the right third MCP joint and left second MCP joint, without associated lymphadenopathy. Several well-healed, nonerythematous scratches were noted across his left posterior flank. He was also found to have strength graded 2/5 in the left lower extremity and 1/5 in the right lower extremity. His patellar reflexes were brisk bilaterally, approaching 4+. Laboratory results were significant for a leukocytosis and elevated ESR and CRP (see Table). He subsequently developed a fever of 102.6°F several hours after admission. Head computed tomography (CT) without contrast showed no acute findings. Lumbar puncture demonstrated elevated cerebrospinal fluid (CSF) protein. Blood and CSF cultures were collected and remained negative during hospitalization. Magnetic resonance imaging of the lumbar and thoracic spine, obtained due to new-onset weakness and hyperreflexia, showed no acute findings. Testing for hepatitis A, B, C and HIV was negative.

The patient was started on vancomycin, ceftriaxone, ampicillin, acyclovir, and dexamethasone for empiric meningitis coverage. Given concern for zoonotic infection, doxycycline was also initiated. Meningitis-directed therapy was discontinued following a negative workup, and he was transitioned to oral amoxicillin. He showed clinical improvement and was discharged home in stable condition on amoxicillin 5 days after admission with a presumptive diagnosis of rat bite fever.

However, he re-presented to the ED 5 days after discharge after notification from the hospital that his blood cultures had grown a gram-negative bacterium. He reported no new symptoms aside from persistent back pain, and his physical examination and vital signs were unchanged. He was discharged the following day following repeat blood cultures and no change in antibiotic therapy after infectious disease consultation. Subsequently, his initial cultures confirmed *S moniliformis*, establishing the diagnosis of rat bite fever. Repeat blood cultures remained negative following treatment.

Table. Laboratory Values

Lab	Value	Reference Range
White blood cell count	26 500 cells/uL	4000–11 000 cells/uL
Erythrocyte sedimentation rate	97 mm/hr	0–15 mm/hr
C-reactive protein	327.4 mg/L	<10 mg/L
Cerebrospinal fluid protein	46.9 mg/dL	15–45 mg/dL
HIV-1/HIV-2 antigen/antibody	Negative	Negative
Total anti-hepatitis A (IgG and IgM)	Negative	Negative
Total anti-hepatitis B core (IgG and IgM)	Negative	Negative
Anti-hepatitis C antibody	Negative	Negative

DISCUSSION

Rat bite fever is a rare, systemic, zoonotic illness characterized by recurring fevers and a rash that often affects the palms and soles. Transmission most commonly occurs via a rat bite; however, infection can also result from ingestion of contaminated food or water.[5] Each year, more than 2 million animal bites occur in the United States, yet rat bites account for approximately 1% of these cases. Children younger than 5 years are most affected, and individuals who work in pet stores or conduct research with rats are also at increased risk. Following a rat bite, the estimated risk of infection is approximately 10%.[2]

Although limited data exist regarding the incidence in the United States, a retrospective study analyzing rat-bite injuries between 2001 and 2015 found an ED visit rate of 0.33 per 1 million individuals and a hospitalization rate of 0.20 per 1 million individuals.[6] Another retrospective study examining S moniliformis cultures from 1970 to 1998 found that approximately 83% of suspected rate bite fever cases involved either a rat bite or rodent exposure.[7] Because rat bite fever is not a nationally reportable condition, comprehensive epidemiological data remain scarce, underscoring the need for improved surveillance, standardized reporting, and increased public health awareness.

The Centers for Disease Control and Prevention (CDC) provides information on rat bite fever on its website but notes the disease is not reportable in any state and is not nationally notifiable.[8] The CDC does not specify the reasons; however, it acknowledges that rat bite fever is rare in the United States, which may contribute to its nonreportable illness. According to the CDC, the Council of State and Territorial Epidemiologists determines the list of nationally reportable diseases, in collaboration with the CDC, including diseases for which data allow states and local agencies to tailor programs for disease control and prevention.[9] Surveillance is increased when prevention is feasible (eg, measles) or when a disease is severe and novel (eg, acquired immunodeficiency syndrome, SARS-CoV-2.[9] Because rat bite fever lacks a vaccine and treatment is typically highly effective, it is not prioritized for mandatory reporting.

Rat bite fever is primarily caused by infection with *S moniliformis* but may also be caused by other organisms. Notably, *S*

minus and *S notomytis* are causative agents of similar yet distinct syndromes that share the same name but are far less common in North America.[1,7] *S moniliformis* is a pleomorphic, branching, gram-negative bacillus that is commonly found in the flora of the nasal and oropharyngeal cavities in rodents, most notably rats.[1,7] This pathogen has multiple routes of transmission to humans, including direct exposure to rodent saliva (bites, scratches), handling infected or colonized rats (including close contact such as kissing pet rodents), or ingestion of food or water contaminated with infected rat feces (a condition known as "Haverhill fever").[1] Given the low incidence and mortality rates of rat bite fever, there is limited research on the pathogenesis of *S moniliformis,* although immune complex deposition has been hypothesized to play a role.[1] This pathogen is known to be difficult to culture but may produce characteristic "puffball" or "cotton ball" colonies when grown in thioglycolate broth.[4] More advanced techniques may be required for definitive identification if traditional culture methods are unsuccessful, including gas chromatography, mass spectrometry, and genetic sequencing.[1,7]

Symptoms of rat bite fever typically develop 2 to 4 weeks after exposure. At disease onset, patients commonly experience fever, rigors, headache, nausea, vomiting, and severe myalgias.[1] The fever may recur intermittently and persist for months.[2] As the illness progresses, more than 50% of patients develop migratory polyarthralgias affecting both large and small joints of the extremities, particularly the knees and ankles.[1] Migratory polyarthralgia is often the most persistent feature, lasting for months or even years.

In infections caused by *Streptobacillus,* the site of the bite may appear healed with minimal or no signs of inflammation. Approximately 75% of patients develop a petechial or maculopapular rash, and some may present with tender, hemorrhagic vesicles on the extremities.[2] In contrast, infections due to *S minus* (spirillosis) often involve a more visibly indurated and potentially ulcerated bite site. Lymphadenopathy is more common in spirillosis than in Streptobacillus infections, and approximately half of patients with spirillosis develop a violaceous, red-brown macular rash.[2]

Diagnosis is largely clinical, based on a history of rodent exposure and characteristic findings. Laboratory evaluation may reveal leukocytosis and elevated inflammatory markers. Blood cultures may confirm *S moniliformis* infection; however, the organism is fastidious and may require specialized media.[2]

Patients are advised to avoid contact with rodents and practice proper hygiene, including handwashing after contact and prompt cleaning of bites or scratches. Empiric antibiotic therapy is essential, as delays in treatment increase the risk of complications. For adults, the recommended first-line treatment is intravenous (IV) penicillin G (400 000-600 000 units/day) or IV ceftriaxone 1 g daily for 7 to 10 days.[1] Once the patient improves clinically, a transition can be made to oral penicillin V 500 mg 4 times daily, ampicillin 500 mg 4 times daily, or amoxicillin 500 mg 3 times daily to complete a 14-day course.[2] For penicillin-allergic patients, doxycycline 100 mg orally or intravenously twice daily is an acceptable alternative.[2] With timely and appropriate treatment, the prognosis for rat bite fever is excellent, highlighting the importance of early recognition and intervention.

CONCLUSIONS

This case represents a rare instance of rat bite fever. Although uncommon and difficult to culture, this condition is likely underreported and may present with delayed symptom onset of up to 4 weeks. Exposure history may not be readily elicited, and lesions are often well healed at presentation. Because the causative organisms are typically susceptible to common antibiotics (eg, penicillin, amoxicillin, doxycycline, ceftriaxone), empiric therapy may lead to rapid clinical improvement before a definitive diagnosis is established. This case highlights the importance of a thorough history, particularly regarding animal exposures, including pet ownership. It also underscores the value of careful physical examination, even of seemingly benign findings such as healed scratch wounds. The patient's swift recovery emphasizes the importance of early recognition and prompt treatment to reduce morbidity or mortality associated with this rare but potentially serious disease.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Elliott SP. Rat bite fever and Streptobacillus moniliformis. *Clin Microbiol Rev*. 2007;20(1):13-22. doi:10.1128/CMR.00016-06

2. Gupta M, Bhansali RK, Nagalli S, Oliver TI. Rat-Bite fever. In: *StatPearls*. StatPearls Publishing; 2023.

3. Tandon R, Lee M, Demierre MF, Sulis CA. A 26-year-old woman with a rash on her extremities. *Clin Infect Dis*. 2006;43(12):1585-1586. doi:10.1086/509574 (Authors differ from what was provided.)

4. Adam JK, Varan AK, Pong AL, McDonald EC; Centers for Disease Control and Prevention. Notes from the field: fatal rat-bite fever in a child — San Diego County, California, 2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(50):1210-1211.

5. Miraflor AP, Ghajar LD, Subramaniam S, et al. Rat-bite fever: an uncommon cause of fever and rash in a 9-year-old patient. *JAAD Case Rep*. 2015;1(6):371-374. doi:10.1016/j.jdcr.2015.09.008

6. Kache PA, Person MK, Seeman SM, et al. Rat-bite fever in the United States: an analysis using multiple national data sources, 2001-2015. *Open Forum Infect Dis*. 2020;7(6):ofaa197. doi:10.1093/ofid/ofaa197

7. Graves MH, Janda JM. Rat-bite fever (Streptobacillus moniliformis): a potential emerging disease. *Int J Infect Dis*. 2001;5(3):151-155. doi:10.1016/s1201-9712(01)90090-6

8. Centers for Disease Control and Prevention. Clinical overview of rat bite fever (RBF). May 22, 2024. Accessed July 18, 2025. https://www.cdc.gov/rat-bite-fever/hcp/clinical-overview/index.html

9. Chorba TL, Berkelman RL, Safford SK, Gibbs NP, Hull HF. Mandatory reporting of infectious diseases by clinicians. *MMWR Recomm Rep*. 1990, 39(RR-9):1-17. Accessed July 18, 2025. https://www.cdc.gov/mmwr/preview/mmwrhtml/00001665.htm

Intraventricular Left Anterior Descending Artery in a Patient with Ventricular Tachycardia – Innocent Bystander with Significant Procedural Implications

Jennifer Y. Choi, DO; John Birchak, MD; Divyanshu Mohananey, MD, MSc

ABSTRACT

Introduction: An intra-right ventricular course of the left anterior descending (LAD) artery is a rare coronary anomaly with uncertain clinical and procedural significance. We describe the use of multimodality imaging to characterize this variant in a patient with ventricular tachycardia and to guide the safe performance of catheter ablation.

Case Presentation: A 46-year-old White woman presented with ventricular tachycardia and was found on coronary computed tomography angiography to have an intraventricular course of the mid LAD through the right ventricular cavity. Multimodality imaging, including coronary computed tomography angiography and stress cardiac magnetic resonance imaging, demonstrated no evidence of obstructive coronary artery disease, myocardial ischemia, structural heart disease, or myocardial scar. She was ultimately diagnosed with idiopathic right ventricular outflow tract ventricular tachycardia and underwent successful catheter ablation.

Discussion: An intra-right ventricular course of the LAD is a rare coronary variant. In a large coronary computed tomography angiography study, this anomaly was identified in less than 1% of patients. Although its clinical significance is not well understood, this anatomic variant can have important procedural implications for ventricular tachycardia ablation.

Conclusions: Multimodality imaging is vital in assessing the clinical significance of an anomalous coronary artery and ensuring the procedural safety of ventricular tachycardia ablation.

INTRODUCTION

A typical left anterior descending (LAD) artery courses along the anterior surface of the heart within the anterior interventricular sulcus. We describe a unique anatomic variant in which the LAD enters the right ventricular cavity without significant intramyocardial bridging.

• • •

Author affiliations: Division of General Internal Medicine, Department of Medicine, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Choi); Division of Cardiovascular Medicine, Department of Medicine, MCW, Milwaukee, Wisconsin (Birchak; Mohananey).

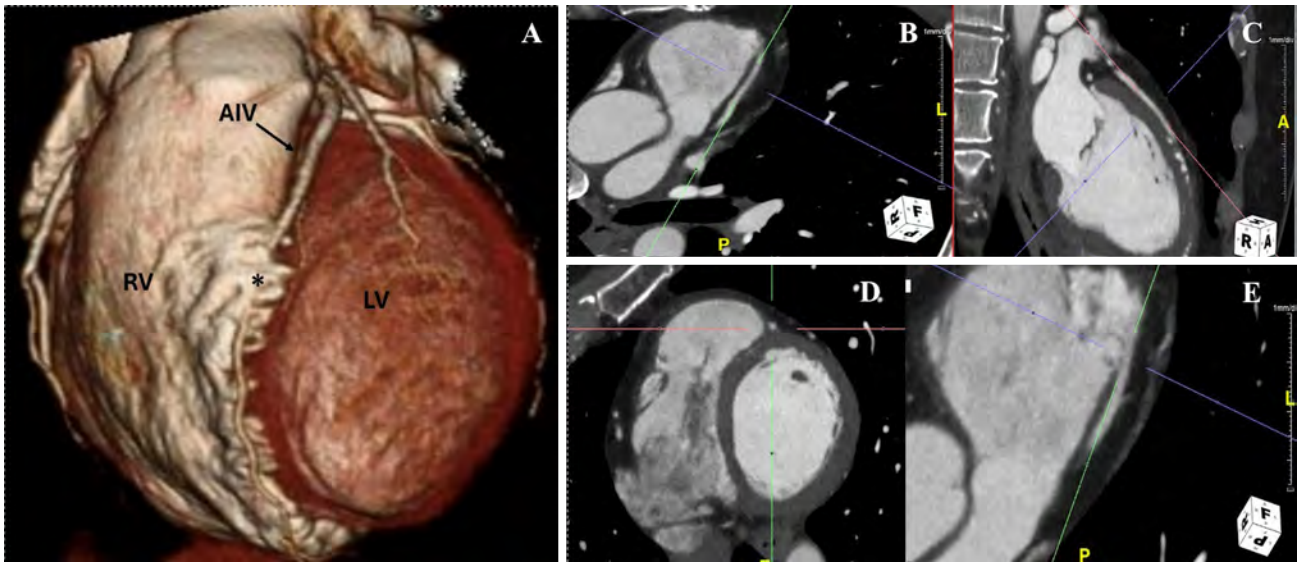
Corresponding author: Divyanshu Mohananey, MBBS, MSc; 8701 W Watertown Plank Rd, Milwaukee, WI 53226; email dmohananey@mcw.edu

CASE PRESENTATION

A 46-year-old woman with a history of hyperlipidemia presented with palpitations and presyncope. While en route to the hospital, she was found to have sustained monomorphic ventricular tachycardia lasting 45 seconds at a rate of 211 beats per minute (bpm) (Figure 2). On arrival at the emergency department, she was in normal sinus rhythm at a rate of 90 bpm. Her other vital signs and physical examination findings were unremarkable. Initial high-sensitivity troponin T was < 4 ng/L. Chest radiography revealed no acute findings. She was started on metoprolol tartrate and amiodarone.

During her hospitalization, transthoracic echocardiography demonstrated normal biventricular size and function. Given the patient's low-to-intermediate pretest probability of obstructive coronary artery disease, a gated coronary computed tomography angiography (CCTA) was performed. The study was negative for coronary artery disease but revealed a mid LAD coursing through the right ventricular cavity before re-emerging distally into the anterior interventricular groove (Figure 1). Although the inferior axis and left bundle branch block morphology of the ventricular tachycardia suggested a right ventricular outflow tract (RVOT) origin, we pursued a cardiac magnetic resonance imaging (CMR) with regadenoson stress to rule out ischemia from potential compression related to the intraventricular course. CMR was negative for vasodilator-induced ischemia and showed no structural abnormalities of either ventricle or any evidence of myocardial scar. The intraventricular course of the LAD was again identified. Therefore, we diagnosed the patient with idiopathic RVOT ventricular tachycardia.

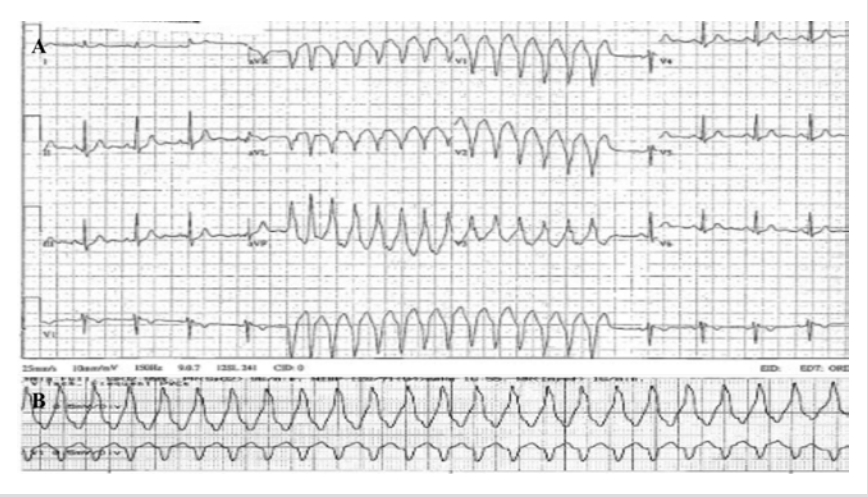
Figure 1. Three-dimensional Gated CCTA Demonstrating the Anomalous Course of the Left Anterior Descending Artery (LAD)



(A) LAD runs in the AIV groove before entering the right ventricular chamber (*) and exits distally in the AIV. Multiplanar reconstruction images show this unique LAD in the orthogonal long axis (B, C) and short axis views (D). The crosshairs have been moved more apically in panel E to demonstrate the LAD inside the right ventricle.
Abbreviations: CCTA, coronary computed tomography angiography; AIV, anterior interventricular; LV, left ventricle.

Given the patient's symptoms and young age, we pursued catheter ablation of the ventricular tachycardia. Based on preprocedural imaging, there was concern that the unusual trajectory of the LAD would be in proximity (<5 mm) to the suspected ventricular tachycardia focus in the RVOT, placing her at increased risk of coronary injury during delivery of radiofrequency ablation lesions.[1] As suspected, the ventricular tachycardia origin was mapped during the procedure to the anterior portion of the RVOT using activation mapping during the arrhythmia and pace mapping. The ablation catheter was maintained at the location of interest, and a coronary angiography confirmed a distance >5 mm between the LAD and ablation site (Figure 3). Radiofrequency ablation was then performed successfully, resulting in suppression of the arrhythmia, and the patient was discharged home.

Figure 2. Twelve-lead ECG and ECG Strip of a Patient With Sustained Monomorphic Ventricular Tachycardia

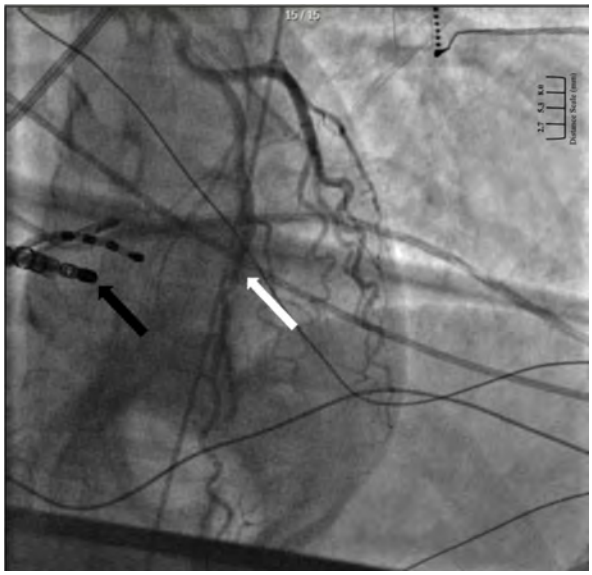


A. 12-lead ECG demonstrating 14 beats of VT with inferior axis and left bundle branch block morphology.
B. ECG strip showing sustained VT for 45 seconds at a rate of 211 beats/minute.
Abbreviations: ECG, electrocardiogram; VT, ventricular tachycardia.

DISCUSSION

An intra-right ventricular course of the LAD is a rare coronary variant. To the best of our knowledge, only 1 study has documented this finding. In a large study of 31748 coronary CTAs, only 17 patients had an intra-right ventricular coronary artery. Interestingly, in all 17 patients, the affected vessel was the LAD.[2] The clinical significance of this anomaly has yet to investigated. Our case highlights the role of multimodality imaging in both diagnosis of RVOT ventricular tachycardia and the procedural safety of ventricular tachycardia ablation.

Figure 3. Fluoroscopic Coronary Angiogram in the Left Anterior Oblique View at 21 Degrees and the Cranial View at 24 Degrees



Left heart catheterization demonstrates the >5 mm distance between the ablation catheter (black arrow) and the left anterior descending artery (white arrow).

CONCLUSIONS

This unique case highlights the utility of multimodality imaging in narrowing the differential diagnosis to RVOT ventricular tachycardia. CCTA was not only effective in ruling out obstructive coronary artery disease, but it was also instrumental in identifying of the intra-right ventricular course of the LAD. Furthermore, stress CMR ruled out cardiomyopathy, myocardial scar, and myocardial ischemia as potential etiologies for ventricular tachycardia. Although this anomaly was unrelated to the patient's ventricular tachycardia, it had important procedural implications, as described above. Knowledge of the anomalous LAD course identified on CCTA prompted coronary angiography and helped guide the procedural team in safely performing ventricular tachycardia ablation.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Enriquez A, Malavassi F, Saenz LC, et al. How to map and ablate left ventricular summit arrhythmias. *Heart Rhythm*. 2017;14(1):141-148. doi:10.1016/j.hrthm.2016.09.018

2. Tyczyński P, Skowroński J, Opolski MP, et al. Intra-Right ventricle course of the coronary arteries on computed tomography angiography. *J Comput Assist Tomogr.* 2020;44(4):586-590. doi:10.1097/RCT.0000000000001021

Purple Fentanyl: A New Face on an Old Enemy

Jennifer Esch, PharmD, MBA, BCPS; Matthew Bougie, PharmD; Alexis Vandehey, PharmD, BCPS

ABSTRACT

Introduction: Overdoses due to novel potent opioids continue to increase across the United States. The availability of colored fentanyl products that may appeal to younger patients is concerning.

Case Presentation: We present the case of an adult male with an unknown ingestion subsequently identified as purple fentanyl. Brorphine is a common component of purple fentanyl and is considered an emerging novel potent opioid.

Discussion: Only limited number of case reports describing brorphine exposure are available, and many clinicians remain unfamiliar with this substance. It is a potent opioid with a presumed long half-life. Clinical presentation is similar to that of other opioid toxidromes, including respiratory depression, miosis, and sedation, and is managed similarly. Patients may require extended monitoring after exposure to brorphine.

Conclusions: Awareness of emerging substances of abuse will enable clinicians to diagnose and treat affected patients more readily.

INTRODUCTION

Overdoses due to novel potent opioids continue to increase. In addition, the increased availability of colored fentanyl products that may appeal to younger patients is concerning. Purple fentanyl, also referred to as rainbow fentanyl, can be a combination of several substances – including fentanyl, carfentanyl, and brorphine – as an opioid base often mixed with methamphetamine or acetaminophen.[1] The bright color of the product may appeal to children and poses a public health hazard. The Drug Enforcement Administration (DEA) has reported an uptick in these "rainbow fentanyl" products, which often resemble prescription medications.[2] In July, 2024, over 23 kg (50 pounds) of purple fentanyl powder was seized from 2 vehicles crossing from Mexico to the United States.[3] While this is only one example, it illustrates the increase in production and need for greater awareness and understanding. In this case report, we focus on the brorphine component of purple fentanyl, as it is a relatively new substance for many clinicians in emergency medicine.

Brorphine is a Schedule I substance with no identified therapeutic use in the United States.[4] It is considered a novel potent opioid (NPO),[5] which are illicit synthetic nonfentanyl compounds introduced to the drug market with increasing frequency in recent years. The motivation to produce NPOs is unclear, but they may have become more popular due to demand for increased potency. Brorphine has been found as both a single agent and in combination with heroin or fentanyl.[6]

CASE PRESENTATION

A 33-year-old male was brought to the emergency department (ED) at our institution by an unknown party in a private vehicle. He had miosis (pinpoint pupils), clammy skin, and was minimally responsive to a sternal rub. Opioid toxicity was suspected; therefore 2 mg of intranasal naloxone was administered. The patient became more responsive and was able to answer some questions but repeatedly stated that the purple fentanyl he had taken must have been stronger than he thought. He began scratching his arms and torso and hitting his head against the wall after naloxone administration. He also exhibited slowed cognition.

Pertinent past medical history included hepatitis C, generalized

• • •

Author affiliations: Aurora BayCare Medical Center, Green Bay, Wisconsin (Esch, Bougie, Vandehey).

Corresponding author: Jennifer Esch, PharmD, MBA, BCPS, 2845 Greenbrier Rd, Green Bay, WI 54311; email Jennifer.esch@aah.org; ORCID ID 0009-0007-4610-236X

Table 1. Vitals and Laboratory Values

Blood pressure	156/86 mmHg	Calcium	9.3 mg/dL
Sodium	140 mmol/L	Temperature	98 °F
Heart rate	87 beats per minute	White blood cell count	7.6 K/mcL
Potassium	4.1 mmol/L	AST	98 units/L
Respiratory rate	18	Hemoglobin	14.4 g/dL
Creatine	0.82 mg/dL	ALT	79 units/L
SpO_2	95%	Platelets	268 K/mcL

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; SpO_2, peripheral oxygen saturation.

anxiety, and intravenous drug use. He had an allergy to codeine, reporting a reaction of hives and shortness of breath. At the time of presentation, he weighed 91 kg and was 1.75 m tall. Home medications included citalopram 20 mg daily and olanzapine 10 mg nightly. The electrocardiogram was nonischemic, and he was monitored on telemetry without evidence of arrhythmia. There was no leukocytosis, anemia, electrolyte abnormality, or change in kidney function. Laboratory results were notable for elevated liver enzyme levels. The patient reported a history of hepatitis C but was not receiving treatment. Pertinent vital signs and laboratory results are listed in Table 1. His urine drug screen was positive for fentanyl, amphetamines, cocaine, and opiates. Naloxone was repeated as needed, and he was admitted for observation. At the time, no ED staff were familiar with purple fentanyl and how it might differ from other opioid-containing drugs.

DISCUSSION

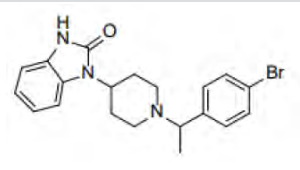
Analytical labs in Europe and the United States have found that positive drug samples containing brorphine are frequently adulterated with other substances, including fentanyl, flualprazolam, cocaine, methamphetamine, tramadol, diphenhydramine, and isotonitazene.[7] Common methods of administration include injection, smoking, snorting, and oral consumption. Pharmacology details are shown in Table 2.

The substance is sold under various names, including purple fentanyl, purple heroin, and purple meth; however, the product may not contain the compounds listed in its name. A report on a series of deaths in the Midwestern United States indicated that a typical user was an adult man with a mean age of 52.[8] This report also highlights that standard screening tests do not detect brorphine, and specialized testing may be required. Illicit substances lack standardized quality control, so the amount of brorphine in different batches can vary substantially.

The unique color of these products may appeal to children, which is concerning because the lethal dose would be much lower than for adults. Although brorphine historically has been identified in middle-aged adults, these color formulations could entice younger populations to experiment. Given the potency of brorphine, even a small ingestion could be fatal in children.

Brorphine is structurally similar to fentanyl.[9] The exact half-life is unknown, but case data demonstrate detectable blood concentrations up to 60 hours after oral ingestion. A patient in 1 report described prolonged euphoria and more intense withdrawal cravings compared with heroin. Pharmacokinetic studies show that it is a potent activator of the μ-opioid receptor, with less activity at the κ-opioid receptor.[10]

Table 2. Brorphine Pharmacology

Mechanism of action	Agonist at the μ-opioid receptor; causes typical effects found with opioid compounds (eg, euphoria, dizziness, loss of consciousness, respiratory depression)[6]
Structure	 • Synthetic opioid with a benzimidazole group that prevents it being regulated as a fentanyl analog[7] • Can be found as a hydrochloride salt, which is water soluble[6]
IUPAC name	1-{1-[1-(4-Bromophenyl)ethyl]piperidin-4- yl}-1,3-dihydro-2H-benzimidazol-2-one
Molecular formula	$C_{20}H_{22}BrN_3O$
Molecular weight	400.32 g/mol
Schedule	• Schedule I controlled substance in the United States • 12 times more potent than morphine[4]
Pharmacokinetics	Brorphine was still detected in a serum sample analyzed 60 hours after admission to a medical facility[9]

Management of Brorphine Overdose

Signs and Symptoms

Patients may present with an opioid toxidrome, including respiratory depression, sedation, unresponsiveness, and miosis.[11] Other reported symptoms include itching and seizures. Case reports also describe rhabdomyolysis and acute kidney injury in patients with detected brorphine levels.[8] Given the polysubstance exposure typically seen in brorphine-containing mixtures, signs of amphetamine overdose also may occur, including anxiety, agitation, hallucinations, hyperthermia, diaphoresis, mydriasis, and seizures.[11] If these substances are co-ingested, the clinical presentation may be confusing due to opposing toxidromes. In 2022, Glidden et al reported that opioid plus methamphetamine exposures resulted in a sympathomimetic toxidrome in 31% of cases and an opioid toxidrome with 32.9% of cases.[12] Common clinical findings included tachycardia (16.1%), bradypnea (11.6%), respiratory depression (26.5%), central nervous system (CNS) stimulation (52.9%), coma/CNS depression (46.5%), acute kidney injury (7.7%), and rhabdomyolysis (16.1%).

Diagnosis

Definitive diagnosis of brorphine overdose requires testing at a lab that can perform an enzyme-linked immunosorbent assay capable

of detecting NPOs.[10] Brorphine can be detected in blood and urine; however, these samples must be sent to specialized facilities, and results may take days.

Clinical diagnosis should not be delayed pending laboratory confirmation and can be based on history, presentation, physical examination, and findings consistent with opioid toxicity (eg, respiratory depression, miosis, clammy skin, seizures, delirium, and bradycardia).

Treatment

Initial management includes ensuring any immediate complications are managed (eg, stabilization of airway, breathing, and circulation). If an opioid toxidrome is suspected, prompt administration of naloxone is recommended and should be repeated as needed until the patient is stable. Because the half-life of brorphine is not well-defined and may be prolonged, patients should be monitored for 12 to 24 hours after stabilization.[13]

In this case, the patient responded to an initial dose of naloxone, allowing for further history regarding substance use. He required additional doses to maintain alertness and ultimately left the ED against medical advice. Based on urine and drug screening results, we suspect ingestion of fentanyl, brorphine, and amphetamines. Confirmatory testing was not performed because it was not available at our institution. Patient self-report of ingested substances is uncommon; thus diagnosis is typically based on clinical presentation rather than history alone.

Awareness of brorphine and other NPO compounds can help clinicians manage these cases effectively. Recent DEA statistics indicate that more than 107 000 Americans died from drug poisoning or overdose in 2023, with nearly 70% involving opioids.[14] Approximately 2 mg of fentanyl is considered potentially lethal, whereas the lethal dose of brorphine remains unknown. Alone or when in combination with other substances, even small amounts can be fatal. Rainbow-colored pills and powders are becoming increasingly prevalent and may contribute to rising overdose rates, particularly among younger populations.

CONCLUSIONS

Awareness of NPOs is critical for ED clinicians. Brorphine is one of many substances currently being manufactured and distributed. Prompt recognition of opioid toxicity and consideration of co-ingestants not detected on routine screening are essential for appropriate and timely treatment. Improved knowledge will help clinicians remain vigilant and prepared for emerging drug threats.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. frhdev. What is purple fentanyl? *Futures Recovery Healthcare* blog. February 1, 2024. Accessed March 1, 2025. https://futuresrecoveryhealthcare.com/blog/purple-fentanyl/

2. DEA warns of brightly colored fentanyl used to target young Americans. News release. United States Drug Enforcement Administration; August 30, 2022. Accessed March 10, 2025. https://www.dea.gov/press-releases/2022/08/30/dea-warns-brightly-colored-fentanyl-used-target-young-americans

3. Rahman B. Border agents seize 50 pounds of purple fentanyl designed for kids. *Newsweek*. July 26, 2024. Accessed March 12, 2025. https://www.newsweek.com/border-seize-purple-fentanyl-kids-1930570

4. Critical review report: brorphine. Expert Committee on Drug Dependence, World Health Organization. October 2021. Accessed March 15, 2025. https://cdn.who.int/media/docs/default-source/essential-medicines/unedited--advance-copy-44th-ecdd-review-report-brorphine.pdf?sfvrsn=d2f0cc18_3

5. Amaducci A, Aldy K, Campleman SL, et al. Naloxone use in novel potent opioid and fentanyl overdoses in emergency department patients. *JAMA Netw Open.* 2023;6(8):e2331264. doi:10.1001/jamanetworkopen.2023.31264

6. Brorphine. Drug and Chemical Evaluation Section, Diversion Control Division, United States Drug Enforcement Administration. December 2025. Accessed March 5, 2025. https://www.deadiversion.usdoj.gov/drug_chem_info/brorphine.pdf

7. Albores-García D, Cruz SL. Fentanyl and other new psychoactive synthetic opioids. challenges to prevention and treatment. *Rev Invest Clin*. 2023;75(3):93-104. doi:10.24875/RIC.23000109

8. Verougstraete N, Vandeputte MM, Lyphout C, et al. First report on brorphine: the next opioid on the deadly new psychoactive substance horizon? *J Anal Toxicol.* 2021;44(9):937-946. doi:10.1093/jat/bkaa094

9. Krotulski AJ, Papsun DM, Noble C, et al. The rise of brorphine – a potent new synthetic opioid identified in the Midwestern United States. News release. Center for Forensic Science Research and Education; July 2020. Accessed March 6, 2025. https://www.cfsre.org/images/content/reports/public_alerts/2020.07.27.Public-Alert_Brorphine_NPS-Discovery_072720.pdf

10. Grafinger KE, Wilde M, Otte L, Auwärter V. Pharmacological and metabolic characterization of the novel synthetic opioid brorphine and its detection in routine casework. *Forensic Sci Int.* 2021;327:110989. doi:10.1016/j.forsciint.2021.110989

11. Spyres MB and Jang DH. Amphetamines. In: Nelson LS, Howland HA, Lewin NA, et al, eds. *Goldfrank's Toxicologic Emergencies*. 11th ed. McGraw-Hill; 2019.

12. Glidden E, Suen K, Mustaquim D, et al. Characterization of nonfatal opioid, cocaine, methamphetamine, and polydrug exposure and clinical presentations reported to the Toxicology Investigators Consortium Core Registry, January 2010-December 2021. *J Med Toxicol*. 2023;19(2):180-189. doi:10.1007/s13181-022-00924-0

13. Opioids (Lexi-Tox). In: *UpToDate Lexidrug*. UpToDate, Inc. Updated February 23, 2026. Accessed March 14, 2025. https://online-lexi-com/lco/action/doc/retrieve/docid/lexier/1116780

14. Saccone RA. This holiday season talk to your loved ones about fentanyl. News release. United States Drug Enforcement Administration; December 19, 2024. Accessed March 6, 2025. https://www.dea.gov/press-releases/2024/12/19/holiday-season-talk-your-loved-ones-about-fentanyl

Manifestation of Isolated Vertebral Osseous Sarcoidosis: A Case Report

Mujtaba Azhar Siddiqui, MD; Unsa Khan, MD; Noor ul Sabah, MD; Asadulla Mohammed, MD

ABSTRACT

Introduction: Isolated vertebral osseous sarcoidosis is a rare form of sarcoidosis that may mimic malignancy or infection and can be difficult to diagnose in the absence of systemic symptoms.

Case Presentation: A 70-year-old African American woman presented with lower back pain, 5 years after an initial evaluation of incidental vertebral lesions identified on positron emission tomography imaging. Repeat imaging showed a lesion in the T4 vertebra. Computed tomography-guided biopsy and thorough evaluation excluded infection and malignancy, confirming vertebral sarcoidosis.

Discussion: Few cases of vertebral sarcoidosis have been reported, usually presenting with localized pain and lytic or sclerotic vertebral lesions. Diagnosis requires histopathologic confirmation and exclusion of alternative etiologies. Early recognition is important, as corticosteroid treatment often improves outcomes.

Conclusions: Sarcoidosis should be considered in the differential diagnoses of vertebral lesions, even in the absence of systemic involvement.

INTRODUCTION

Sarcoidosis is a multisystem granulomatous disorder characterized by the formation of nonnecrotizing granulomas, most commonly affecting the lungs and lymphatic system. However, it may also involve other organs, including the skin, eyes, bones, liver, spleen, heart, upper respiratory tract, and nervous system.[1] The incidence of sarcoidosis is notably higher in African Americans, with a threefold greater age-adjusted annual incidence compared with that of White individuals.[2] Osseous involvement in sarcoidosis is relatively uncommon, occurring in approximately 1% to 13% of cases, with vertebral involvement being particularly rare.[3] Diagnosis requires clinical, radiologic, and histopathologic evidence of noncaseating granulomas, as well as exclusion of other granulomatous diseases and malignancies.[4]

This report contributes to the limited literature on vertebral sarcoidosis by presenting the case of a 70-year-old African American woman without systemic symptoms who was ultimately diagnosed with isolated vertebral sarcoidosis after a comprehensive diagnostic workup.

CASE PRESENTATION

A 70-year-old African American woman with a history of asthma initially underwent positron emission tomography (PET) because of concern for possible malignancy or infection based on her presenting symptoms. The PET scan revealed hypermetabolic nodules and subtle osseous lesions. Five months later, she was admitted for ovarian vein thrombosis. A repeat PET scan was performed to evaluate for potential metastatic disease or occult malignancy in light of the incidental osseous findings on the prior scan. Findings demonstrated moderate degenerative skeletal changes, with focal pathologic activity most pronounced in the T4 vertebral body (Figure 1). A computed tomography (CT)-guided core biopsy of the T4 vertebra revealed benign bone tissue with nonnecrotizing granulomatous inflammation, and chest radiography showed bilateral hilar adenopathy without additional abnormalities (Figure 2).

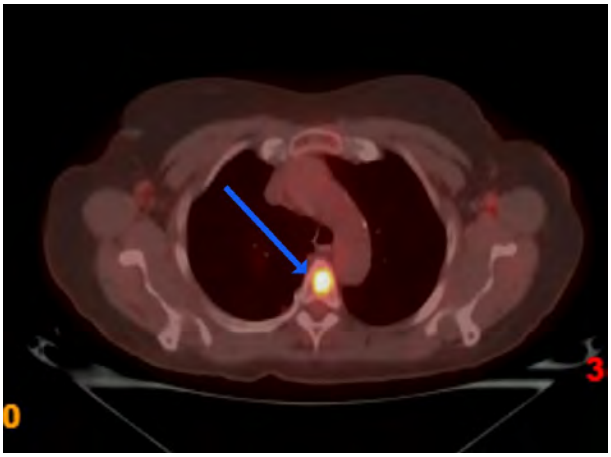
During the diagnostic evaluation, the differential diagnosis included malignancy, infectious etiologies, inflammatory disorders, and other metabolic or degenerative conditions. Malignant

• • •

Author affiliations: Dow University of Health Sciences, Karachi, Pakistan (Khan, Siddiqui); Quaid-e-Azam Medical College, Bahawalpur, Pakistan (Sabah); Lung Allergy and Sleep Medicine Center, Berkley, Michigan (Mohammed).

Corresponding author: Noor ul Sabah, MD, Bahawalpur Cantt, Bahawalpur, 63100, Pakistan; ORCID ID 0009-0008-9160-0111

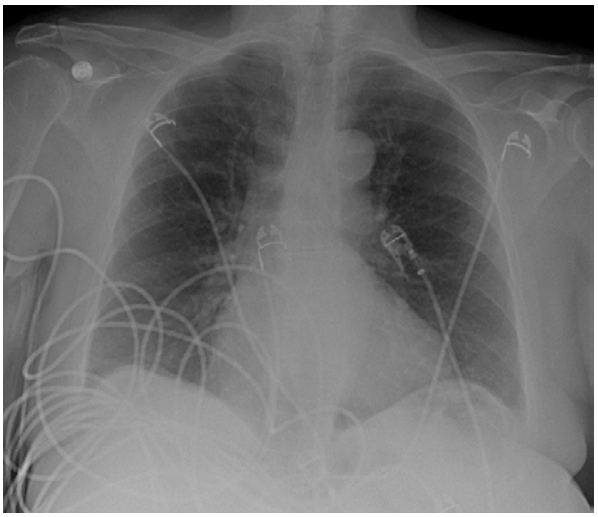
Figure 1. PET Scan Highlighting Increased Uptake in the T4 Vertebral Body



Axial PET image demonstrating a focal area of increased radiotracer uptake in the T4 vertebra (blue arrow), suggestive of active inflammatory or granulomatous pathology consistent with osseous sarcoidosis.

Abbreviation: PET, positron emission tomography.

Figure 2. Chest X-Ray Demonstrating Bilateral Hilar Lymphadenopathy



Frontal chest radiograph reveals prominence of the hilar regions bilaterally, consistent with bilateral hilar lymphadenopathy – a classic radiologic finding commonly associated with sarcoidosis.

causes considered included metastatic disease, such as breast or lung cancer and multiple myeloma, as well as primary bone tumors. Infectious etiologies included tuberculosis and fungal infections, including histoplasmosis. Inflammatory disorders considered included sarcoidosis and chronic granulomatous disease. Other potential causes included Paget disease of bone and degenerative skeletal changes.

Laboratory results revealed an elevated serum angiotensin-converting enzyme (ACE) level of 81 U/L, alkaline phosphatase level of 172 U/L, and alanine aminotransferase level of 51 U/L. Serum calcium, white blood cell count, and inflammatory markers were within normal limits.

The patient reported only lower back pain and denied systemic symptoms, including fever, weight loss, or respiratory complaints. Evaluations for malignancy, including serum protein electrophoresis and tumor marker testing, and for infection, including fungal cultures and acid-fast bacilli (AFB) testing were negative.

Based on biopsy findings and the exclusion of other diagnoses, a diagnosis of vertebral sarcoidosis was established. The patient was started on oral prednisone, 50 mg daily for 15 days, followed by a taper of 5 mg every 5 days until reaching a maintenance dose of 10 mg daily. A follow-up PET scan was scheduled 2 months later. The patient declined methotrexate therapy but remains on corticosteroid treatment.

DISCUSSION

Vertebral involvement in sarcoidosis is exceedingly rare, accounting for less than 1% of all cases.[5] Osseous sarcoidosis is typically detected incidentally during imaging for unrelated conditions, as most patients do not exhibit symptoms directly attributable to bone involvement.[6] This likely contributes to the underdiagnosis of isolated osseous sarcoidosis.[7]

In this case, the patient's elevated serum ACE level (81 U/L) and bilateral hilar adenopathy on imaging were suggestive, though nonspecific, findings of sarcoidosis.[4,8] The absence of systemic symptoms, including fever and weight loss, and negative evaluations for malignancy (including tumor marker testing and imaging) and infection (including fungal/AFB cultures) narrowed the differential diagnosis. Vertebral sarcoidosis was ultimately confirmed by biopsy of the T4 vertebral lesion, which demonstrated nonnecrotizing granulomas – the histopathologic hallmark of sarcoidosis.[9] While elevated alkaline phosphatase level (172 U/L) and alanine aminotransferase level (51 U/L) could suggest hepatic involvement, normal serum calcium and inflammatory markers argued against hypercalcemia or alternative inflammatory etiologies.[10] These diagnostic challenges underscore why vertebral sarcoidosis is frequently misdiagnosed initially.

A key diagnostic challenge is distinguishing sarcoid-related granulomatous lesions from bone metastases. Although imaging techniques are useful for identifying lesion location and extent, they often lack specificity. Therefore, histopathologic confirmation by biopsy remains the gold standard for diagnosis.[11,12] In this case, biopsy of the T4 vertebral lesion revealed nonnecrotizing granulomatous inflammation – findings that, while suggestive of sarcoidosis, are not pathognomonic in isolation.[8] Because granulomas may occur in other infectious or inflammatory conditions, it is essential to exclude alternative etiologies, including malignancies, tuberculosis, and fungal infections.[9] Accordingly, the patient underwent an extensive diagnostic evaluation, includ-

ing a comprehensive metabolic panel, complete blood cell count, ACE testing, inflammatory marker assessment, malignancy screening, and fungal and AFB cultures. Results were unremarkable except for an elevated ACE level. Together with imaging and biopsy findings, these results supported the diagnosis of isolated vertebral sarcoidosis.

While asymptomatic osseous sarcoidosis may resolve spontaneously and not require systemic treatment,[10] corticosteroids remain the first-line therapy because of their demonstrated clinical and radiologic efficacy.[13,14] Given the patient's persistent back pain and biopsy-confirmed diagnosis, treatment with oral prednisone was initiated.

CONCLUSIONS

This case highlights isolated vertebral sarcoidosis, a rare manifestation of sarcoidosis that can mimic malignancy or infection. The diagnostic evaluation, including histopathologic confirmation and exclusion of alternative etiologies, underscores the importance of considering sarcoidosis in the differential diagnosis of vertebral lesions. Although imaging findings may raise concern for metastatic disease, definitive diagnosis requires biopsy and careful clinicopathologic correlation. Corticosteroid therapy was initiated because of persistent symptoms; however, the clinical course of isolated osseous sarcoidosis remains variable and warrants follow-up.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Bargagli E, Prasse A. Sarcoidosis: a review for the internist. *Intern Emerg Med.* 2018;13(3):325-331. doi:10.1007/s11739-017-1778-6

2. Rybicki BA, Major M, Popovich J Jr, Maliarik MJ, Iannuzzi MC. Racial differences in sarcoidosis incidence: a 5-year study in a health maintenance organization. *Am J Epidemiol.* 1997;145(3):234-241. doi:10.1093/oxfordjournals.aje.a009096

3. Valencia MP, Deaver PM, Mammarappallil MC. Sarcoidosis of the thoracic and lumbar vertebrae, mimicking metastasis or multifocal osteomyelitis by MRI: case report. *Clin Imaging.* 2009;33(6):478-481. doi:10.1016/j.clinimag.2009.02.002

4. Wessendorf TE, Bonella F, Costabel U. Diagnosis of sarcoidosis. *Clin Rev Allergy Immunol.* 2015;49(1):54-62. doi:10.1007/s12016-015-8475-x

5. Varron L, Broussolle C, Candessanche JP, et al. Spinal cord sarcoidosis: report of seven cases. *Eur J Neurol*. 2009;16(3):289-296. doi:10.1111/j.1468-1331.2008.02409.x

6. Kucharz EJ. Osseous manifestations of sarcoidosis. *Reumatologia*. 2020;58(2):93-100. doi:10.5114/reum.2020.95363

7. Neville E, Carstairs LS, James DG. Sarcoidosis of bone. *Q J Med.* 1977;46(182):215-227. doi:10.1093/oxfordjournals.qjmed.a067502

8. Shah KK, Pritt BS, Alexander MP. Histopathologic review of granulomatous inflammation. *J Clin Tuberc Other Mycobact Dis*. 2017;7:1-12. doi:10.1016/j.jctube.2017.02.001

9. Rosen Y. Pathology of sarcoidosis. *Semin Respir Crit Care Me*d. 2007;28(1):36-52. doi:10.1055/s-2007-970332

10. Nel H, Gabbay E. Skeletal sarcoidosis. In: Ghosh S, editor. *Sarcoidosis - New Perspectives.* IntechOpen; 2022:chap 4. doi:10.5772/intechopen.998111.

11. Miller ER, Fanta CH, McSparron JI, Pan B, Coblyn JS, Sparks JA. Musculoskeletal and pulmonary outcomes of sarcoidosis after initial presentation of osseous involvement. *Sarcoidosis Vasc Diffuse Lung Dis.* 2019;36(1):60-73. doi:10.36141/svdld.v36i1.7326

12. Aptel S, Lecocq-Teixeira S, Olivier P, Regent D, Teixeira PG, Blum A. Multimodality evaluation of musculoskeletal sarcoidosis: imaging findings and literature review. *Diagn Interv Imaging.* 2016;97(1):5-18. doi:10.1016/j.diii.2014.11.038

13. Ben Hassine I, Rein C, Comarmond C, et al. Osseous sarcoidosis: a multicenter retrospective case-control study of 48 patients. *Joint Bone Spine*. 2019;86(6):789-793. doi:10.1016/j.jbspin.2019.07.009

14. Gowani ZS, Sathiyakumar V, Holt GE. Osseous sarcoidosis. *JBJS Rev*. 2015;3(4):e3. doi:10.2106/JBJS.RVW.N.00082

DEATHS FROM PRESCRIPTION PAINKILLERS HAVE INCREASED BY 38% IN WISCONSIN.

It's a myth that prescription painkillers are completely safe because a doctor prescribes them. The Dose of Reality is that in Wisconsin, prescription painkillers are involved in more overdose deaths than heroin and cocaine combined. In fact, 63% of opioid-related deaths in 2015 involved prescription drugs. And everyone is at risk, especially young people ages 12-25.

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.

DOSE OF REALITY
PREVENT PRESCRIPTION PAINKILLER ABUSE IN WISCONSIN.

Learn more at:
DoseOfRealityWI.gov
A message from Wisconsin Department of Justice, and the Wisconsin Department of Health Services

Wisconsin Department of Health Services

SMALL DONATIONS
MAKE A BIG DIFFERENCE

help where it's needed most.

SupportDisasterRelief.org

ad

Thank You!
to our Reviewers

The *WMJ* would like to thank everyone who served as a manuscript reviewer in 2025. Manuscript review is essential to the integrity of *WMJ*. We are grateful for the assistance of these individuals in ensuring authors receive objective and insightful feedback on their work.

Himanshu Agrawal, MD*
Olushola Akinshemoyin Vaughn, MD
Ronald Anguzu, MD, MPH, PhD
Erica Arrington, MD
Jessica C. Babal, MD
Zachary J. Baeseman, MD, MPH
Juan S. Barajas-Gamboa, MD
Bruce Barrett, MD, PhD
Sudhakar Basetty, MD*
Adam S. Bauer, MD*
Jason Beckerman, MD*
Sheryl Bedno, MD, DrPH
Tomer Begaz, MD*
Daniel D. Bennett, MD
Paul A. Bergl, MD
David Berkoff, MD
Joanne Bernstein, MD, MS*
Gary Bhagat, MD
Sanjay Bhandari, MD*
Keshani Bhushan, MD, MPH
Laura Birkeland, CGC*
Joseph Blustein, MD*
Rohan Bodapati, MD*
Nicole Bonk, MD
Stephanie M. Borchardt, MPH, PhD*
Edward Luke Bradbury, MD
Amber Brandolino, MS, CCRC
Meghan Beth Brennan, MD
Bonnie Brown, MD
Brian P. Buggy, MD
Kristen Bunnell, PharmD
Kristin Busse, PharmD
Andrew D. Calvin, MD, MPH*
Thomas Carver, MD
Leslie Christensen, MA-LIS*
Jacqueline Christianson, PhD*
Michael P. Cinquegrani MD, FACC, FSCAI
James H, Conway, MD, FAAP
Trevor Lynn Cooper, MD, MPP*
Alison T. Coren, MD*
Juan Felipe Coronado, MD
Andrew Coyle, MD*
Kenneth W. Crabb, MD, FACOG*
Richard A. Dart, MD*
Matthew Dellinger, PhD*
Ronda Dennis-Smithart, MD, FAAP
Jill D, Denson, PhD, MSW, APSW
Sara M. Deprey, PhD
Bri Deyo, MPH*
Subarna M. Dhital, MD
Sean Duffy, MD
Edmund H. Duthie, MD*
Kayla Duvall, MD
Mary L. Ehlenbach, MD
Christina Eldredge, MD, PhD
Ann E. Evensen, MD
Leonard Ezenagu, MD*
M. Leila Famouri, MD, MPH*
Ryan Feldman, PharmD
Laura E. Felley, MD, PhD
John Scott Ferguson, MD
Carlos E. Figueroa Castro, MD, MS
Joseph E. Fojtik, MD, MPH, FACP*
Norman Fost, MD, MPH
Michael O. Frank, MD
John J. Frey, III, MD
Anna Gaddy, MD*
David Galbis-Reig, MD, DFASAM*
Melanie Gartz, PhD, MS, MHS
Manish J. Gharia, MD
Victoria Gillet, MD*
Patrick H. Ginn, MD
Rebecca Green, MPH
Nathan Gundacker, MD
Stephen J. Halliday, MD, MSCI
Kellia Jane Hansmann, MD, MPH*
Daniel Hassumani, MD, MS
Buddhi Hatharaliyadda, MD
Alisa Hayes, MD, MSAM*
Robin Helm, MD*
Brian Hilgeman*
John Hokanson, MD
Sam Hooshmand, DO
Michael Houghan, MD*
Paul Hunter, MD
Damilola Idowu, MD
Tess Jewell, MD, MPH*
Corlin Jewell, MD*
Pinky Jha, MD
Bryan Johnston, MD*
Kristina Kaljo, PhD
Crystal Karas, MS
Balpreet Kaur, MBBS
Khadieja Khalid, MBBCh, BAO
Abdul Khan, MBBS, MD
Timothy E. Klatt, MD*
Kjersti Knox, MD
Patricia K. Kokotailo, MD
Sarah E. Koske, DVM, MPH
Jahanvi Patel Kothari, DO*
Karol Kremens, MD
Kesavan Kutty, MD, MACP, FACP, FCCP*
Leah Lalor, MD
Matthew Lambert, MD
German Larrain, MD, FACC*
Magnolia Larson, DO
Jennifer Larson, MD*
Charlotte LaSenna, MD
Kathryn Lauer, MD
Sangeun Lee, PhD, RN
Tyler Lennon, MD, MPH
Joseph L'Huillier
Amy E. Liepert, MD*
Jennifer E. Lochner, MD*
Noelle K. LoConte, MD
Leigh S. LoPresti, MD
Sharon Luu, MGCS*
George E. MacKinnon III, PhD, MS, RPh, FASHP
Jennifer Makrides, MD
David Mallinson, PhD
Venkata Manchala, MD*
Chetna Mangat, MBBS, MD
Lucille Marchand, MD, BSN
Andrea Ildiko Martonffy, MD
Tina C. Mason, MD, MPH, FACOG
Benson T. Massey, MD*
Eduard Matkovic, MD*
Joseph A. McBride, MD*
Katie McDermott, PhD, MEHP, RN, CPNP-AC*
Andrew J. McLean, MD, MPH*
Alex Means, MD*
Jill R. Meilahn, DO*
Cezarina Mindru, MD*
Mansoor Mirza, MD, FACP
Maria C. Mora Pinzon, MD, MS
George Lee Morris III, MD, MPH*
Michael Muriello, MD*
Marine Nalbandyan, MD, PhD, MPH
Paul W. Nannis, MSW
Shanthi Narla, MD*
Emmanuel Ngui, DrPH*
Shinoj Pattali, MD*
Barry J. Pelz, MD*
Erika L. Peterson, MD
Andrew E. Petroll, MD, MS
Mary Beth Phelan, MD
Seema M. Policepatil, MD*
Apurva Popat, MD*
David Quimby, MD
Lisa Quinn-Lee, PhD, MSSW, LICSW*
Peter S. Rahko, MD
Saurabh Rajguru, MD
Erik A. Ranheim, MD, PhD
David Rebedew, MD*
Caitlin J. Regner, MD*
Patrick L. Remington, MD, MPH*
Jean Marie Riquelme, MD*
Raul Rodriguez, MD*
Brenda Rooney, PhD*
Nathan J. Rudin, MD
Ani Saryan Kopf, MD
Justin A. Sattin, MD
Charles Schauberger, MD
Sarina B. Schrager, MD*
William R. Schwan, PhD
Michael Scolarici, MD
Robert Sedlacek, MD, FAAFP*
Christine S. Seibert, MD*
Umar A. Sheikh, PhD
Marianna Shershneva, MD, PhD
Tripti Singh, MD
Harmit Singh, MD
Tripti Singh, MD*
Siddhartha Singh, MD, MS, MBA
Paula Soung, MD
Geoffrey R. Swain, MD, MPH*
Kurtis J. Swanson, MD*
Erick Tarula, MD
Bradley W. Taylor, CRIO
Anu Taylor, MD*
Jonathan L. Temte, MD, PhD
Bipin Thapa, MD, MS*
Danny G., Thomas, MD, MPH
Rachna Tiwari, MBBS
Suzanne W. van Landingham, MD*
Ayanna Vasquez, MD, MS
Manasa Velagapudi, MD
Robert Vickrey, MD
Njeri Wainaina, MD, FACP*
Jennifer Walters, PA-C
Alexis Waters, PA-C*
Benjamin Weber, MD, MA*
Cara Westmark, PhD*
Harvey Woehlck, MD
Justin Yamanuha, MD*
Jiajie Yan, PhD
David T. Yang, MD
Megan Yanny, MD*
Narmella Yasoubim, MPhil, MSc
Craig C. Young, MD
Amy Zelenski, PhD*

• • •

The *WMJ* continually seeks to expand our list of highly qualified reviewers. To learn more or to sign up, visit wmjonline.org and click on "Reviewers."

**Completed review of 2 or more manuscripts.*