

advancing the art & science of medicine in the midwest

WMIJ

2025 • volume 124 • issue 1



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Wisconsin Medical Journal:
Building on a Year
of Excellence

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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.

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WMJ

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COVER ART

Person or Patient: A Clinical View Divided

Charu Jain

*Ink and watercolor on mixed media
paper, 11”x13”*

Artist Statement:

This anatomical illustration presents a meticulously detailed and realistic rendering of the human face, highlighting the intricate interplay of musculature, vascular structures, and skeletal landmarks. Balancing scientific accuracy with artistic precision, the drawing invites viewers to explore the complexity beneath facial expression and identity—bridging art and anatomy in a striking visual narrative that honors both the human form and the medical sciences.

See page 4 for information about the artist.

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

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THANK YOU TO OUR REVIEWERS Back Cover

The Importance of Body Donation to Wisconsin Health Science Programs and the Role a Health Care Team Can Play

To the Editor:

Wisconsin has two nonprofit academic, whole-body donation programs: the University of Wisconsin School of Medicine and Public Health (SMPH) Body Donor Program and the Medical College of Wisconsin (MCW) Anatomical Gift Registry. Donation to these programs supports the education of undergraduate and graduate-level health science students in gross anatomy and research laboratories and postgraduate medical training. Anatomical education is a cornerstone of foundational science curricula in health science programs. Learning from anatomical donors provides students with hands-on application of anatomical knowledge, appreciation of human anatomical variation, and comprehension of 3D anatomical relationships. Whole-body donation also strengthens the training of postgraduate medical professionals as they practice and perfect clinical skills and surgical techniques.

Beyond scientific concepts, students also learn about donors as their first patients: people who lived full lives with varied experiences, health, disease, and access to health care. In the anatomy lab, students develop and reflect upon the skills needed to treat their future patients respectfully and holistically.¹ Whole-body donors have lasting impacts on the students they help to teach. At both SMPH and MCW, students organize an annual memorial ceremony to honor and express immense gratitude to body donors and their families.

Whole-body donation to an academic program is different than organ donation or donation to a private body donation program, and the many options can be difficult for an individual who wants to “donate their body to science” to parse. The health care team, and especially those who help guide patients through end-of-life decisions, play an important role in education about all available options. For those individuals who seek to be part of health science education, whole-body donation to academic programs provides direct influence on hundreds of health science trainees each year in Wisconsin.

In 2020, due to COVID-19 restrictions, whole-body donation decreased significantly, and some

programs have not yet recovered.^{2,3} The numerous positive impacts whole-body donation has on undergraduate and postgraduate health professional training should encourage health care providers to be open to discussing whole-body donation with patients interested in exploring this option during end-of-life planning. Planning and registering with donation programs ensures that a donor’s family can carry out their loved one’s last wishes, and individuals can have a memorial service for their families while also donating their body to science. The health care team should familiarize themselves with the legal requirements and program policies of donation programs to best assist patients through end-of-life decisions.

—Meghan M. Cotter, PhD; Ryan Hillmer, PhD

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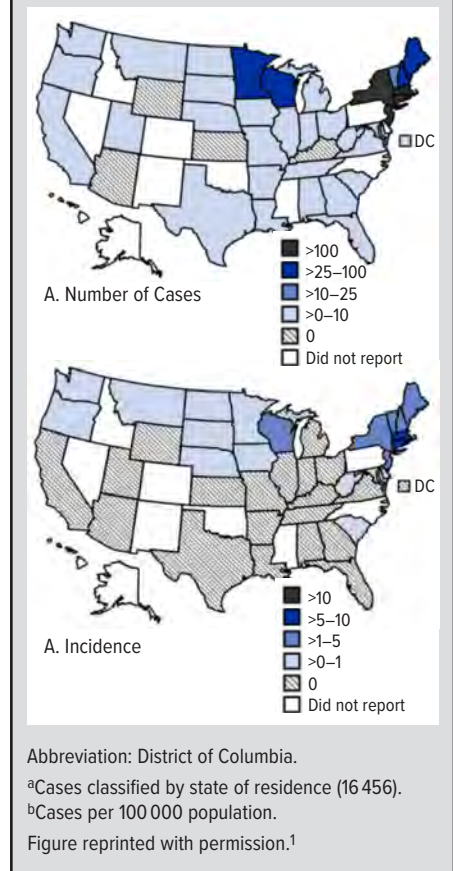
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Babesiosis—An Unseen Epidemic

To the Editor:

Babesiosis, a tick-borne zoonotic disease, is an emerging health issue in the United States, including in Wisconsin. A parasite, *Babesia microti*, is primarily transmitted by deer ticks (*Ixodes scapularis*), the same vector responsible for Lyme disease. Uncommon modes of transmission include blood transfusions, organ trans-

Figure. Average Number of Reported Babesiosis Cases (A)^a and Average Babesiosis Incidence (B),^b by State — United States, 2011–2019



plants, and transplacental spread. Clinical manifestations range from fever, chills, headache, and myalgia—potentially fatal outcomes in immunocompromised people.

Babesiosis is most common in northeastern and some Midwestern regions of the United States (See Figure). Its incidence has risen significantly—especially in the last decade—with a 25% increase reported between 2011 and 2019.¹ This trend coincides with environmental deviations, including warmer climates and land development, which amplify human exposure to ticks. Data suggest that each 1°C temperature increase correlates with an 18% rise in incidence, underscoring the impact of climate change on disease spread.²

The clinical history/patient presentation often indicates the diagnosis potential. Laboratory evidence includes anemia, thrombocytopenia, hypnatremia, elevated hepatic enzymes, and might include renal dysfunction. Confirmation comes through blood smear or polymerase chain reaction testing. Pharmacotherapy is a combination

of atovaquone and azithromycin or clindamycin and quinine. Supportive care is provided. Severe cases may require exchange transfusions. Co-infections with other tick-borne diseases, such as Lyme disease or anaplasmosis, are common and may necessitate additional treatment with doxycycline.³

Prevention is important and comes through public awareness and tick avoidance. As the disease burden grows, there is need for advancements at clinical and laboratory diagnostic recognition, therapeutic options, and vaccine development. This multifaceted approach should mitigate the impact of disease in this part of the country.

—Noor Fatima, MD; Steven Lippmann, MD

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Comment on ‘Enhancing Diagnosis of Obstructive Lung Diseases: Insights From Clinical Characteristics in a Prospective Cohort Study’

To the Editor,

We read the interesting study, “Classification of Obstructive Pulmonary Diseases Through Clinical Characteristics in a Prospective Cohort Study,¹ with great appreciation for its thoughtful approach to a complex diagnostic challenge. The study addresses the critical need for accurate and accessible methods to differentiate between chronic obstructive pulmonary disease (COPD),

asthma, and asthma-COPD overlap syndrome (ACOS)—particularly in resource-constrained settings where advanced diagnostic tools such as spirometry may not always be available.

The researchers’ use of structured clinical questionnaires, validated against spirometric results, is a pragmatic and innovative approach. By examining 1443 patients over 3 years, the study demonstrates that age, smoking history, environmental exposures such as wood smoke, and respiratory symptoms like wheezing and dyspnea are significant predictors of obstructive lung diseases. The diagnostic accuracy of the questionnaires, with area under the curve (AUC) values of 0.75 for COPD, 0.68 for asthma, and 0.78 for ACOS, underscores their potential utility in primary care.

The study’s methodology is also commendable. The prospective design ensures systematic and unbiased data collection, while adherence to standardized spirometry guidelines strengthens the reliability of the findings. Moreover, the inclusion of a large, diverse cohort enhances the generalizability of the results, making the study relevant to various clinical settings.

While the findings are promising, it is worth noting that the performance of these questionnaires may be influenced by the context in which they are used. Differences in health care infrastructure, patient populations, and training of clinicians could impact their effectiveness. The study also stops short of developing a new or integrated diagnostic tool, which could have built on the strengths of the existing questionnaires to further improve accuracy.

Nonetheless, the implications of this research are significant. It highlights the potential for non-specialist clinicians to use structured tools

for initial assessments, bridging diagnostic gaps and enabling earlier intervention for obstructive pulmonary diseases. This approach is particularly valuable in low-resource environments, where reliance on clinical acumen and simple tools can make a substantial difference in patient outcomes.

This study is an important contribution to respiratory medicine, blending clinical practicality with scientific rigor. It opens doors to improving diagnostic processes globally, emphasizing that even simple, well-structured tools can have a profound impact when thoughtfully applied.

—Rachana Mehta, PhD; Ranjana Sah, MD; Shubham Kumar, MS

REFERENCE

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“Person or Patient: A Clinical View Divided”

About the Artist

Charu Jain is a first-year medical student at the Icahn School of Medicine at Mount Sinai with a background in studio art from Stanford University. With a deep-rooted passion for the intersection of humanities and medicine, Charu explores how art can serve as a powerful tool in both patient care and medical education. Her work centers on the belief that creative expression fosters empathy, reflection, and human connection – qualities essential to cultivating compassionate, well-rounded physicians.

Shifting From ‘Patient-Centered’ to ‘Patient-Wanted’ Approach

Gagandeep Singh, MD

The relationship between physicians and patients in medical decision-making and ensuring positive clinical outcomes and patient satisfaction. With the growing influence of the internet and social media on health topics, this relationship is evolving—and sometimes not in a way that benefits our patients. While there's a lot of research on the physician-patient relationship, there hasn't been much focus on the gaps in care that arise when patients turn to online medical information.

Many patients today rely on the internet as their primary source of medical information, rather than consulting their health care providers. Some patients and their families seek out trustworthy sources like the Centers for Disease Control and Prevention, patient education pamphlets, and reputable health websites. Access to this evidence-based information empowers them to make informed decisions about their health, and these patients are often more knowledgeable about their medical conditions and more actively involved in their treatment choices.

However, many individuals unknowingly place their trust in unreliable medical information found online. In their search for quick

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answers, patients often resort to random Google searches, which may lead them to misleading or inaccurate information. This reliance can foster confusion and mistrust in treatment plans, especially considering the generally low

Ultimately, delivering the best possible care hinges on empathetic listening and collaborative treatment planning.

health literacy across the US. Unfortunately, there is minimal oversight over the quality of medical content available on the internet.

It is increasingly common for patients to arrive at doctor's appointments with self-diagnoses based on their own online research or advice from social media. This undermines a doctor's ability to perform a thorough evaluation, as patients may become less transparent about their medical histories or reluctant to consider other potential diagnoses. Instead, they may focus on demanding specific tests or medications, which ultimately delays the path to accurate diagnoses and appropriate treatment. This growing trend is particularly concerning for patients with complex conditions, as appointment time may be spent clarifying misunderstandings rather than addressing the comprehensive care they need.

Moreover, some patients seek specialist referrals for conditions that may not require such evaluations, driven by unreliable online sources. This not only complicates the work of primary care providers but also diverts cru-

cial resources away from those patients who truly need specialized care and are waiting for essential services.

A patient-centered approach, which fosters better communication, can help patients more

effectively express their concerns and enhance the clinician-patient relationship. When patients arrive with preconceived notions, it is vital for clinicians to take the time to thoroughly explain care plans that prioritize the patient's best interests. Sharing the latest evidence-based research empowers patients to make informed decisions about their treatment options.

Clinicians should encourage patients to seek credible information and provide educational materials to enhance their understanding of their health conditions. It is equally important for patients and their families to engage by asking questions and participating in care planning. During these discussions, clinicians should inquire about the sources of the patient's information and ensure that it is evidence-based, which can reduce conflicts in decision-making. Ultimately, delivering the best possible care hinges on empathetic listening and collaborative treatment planning.

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Fahad Aziz, MD, FASN

Wisconsin Medical Journal: Building on a Year of Excellence

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

Since its inception in 1903, the *Wisconsin Medical Journal (WMJ)* has played a pivotal role in serving the Midwest's medical community. As a peer-reviewed, indexed journal, *WMJ* has consistently published impactful scientific work, with a strong focus on educating health care professionals and promoting research. Originally published by the Wisconsin Medical Society (Society), *WMJ*'s ownership transitioned in 2019 to the Medical College of Wisconsin (MCW) and the University of Wisconsin School of Medicine and Public Health (SMPH). Today, a dedicated Publishing Board, comprising members from both institutions and a Society representative, guides *WMJ*'s mission and direction.

Nearly three years ago, I began my journey as editor-in-chief, supported by the invaluable guidance of esteemed board members — Robyn Perrin, PhD, ELS, Elizabeth Petty, MD, Jonathan Temte, MD, PhD, MS, from SMPH, and Asriani M. Chiu, MD, Amalia Lyons, MD, FACP, and Sara L. Wilkins, MA, MPA, from MCW. Their collec-

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tive wisdom ensured a smooth and successful transition into my role. I am also deeply grateful for the unwavering support of the Deans from both Institutions: Joseph Kerschner, MD, now dean emeritus of the School of Medicine at MCW, and Robert Golden, MD, SMPH dean

and vice chancellor for medical affairs at UW–Madison. Their encouragement and leadership have been instrumental in sustaining *WMJ*'s excellence. Additionally, working closely with Kendi Neff-Parvin, our outstanding managing editor, and Robert Treat, PhD, our insightful deputy editor, has been both a privilege and a profound learning experience.

We remain dedicated to advancing *WMJ*'s legacy of scientific excellence while continuing to support the medical community across Wisconsin and beyond. This editorial highlights the journal's achievements in 2024 and outlines our ambitious goals for 2025. Our mission is to inspire progress in the medical field by fostering a collaborative community that values knowledge-sharing and promotes professional growth.

Reflecting on 2024: Achievements and Milestones Publications

The year 2024 marked a period of remarkable growth for the journal, with an unprecedented rise in manuscript submissions. We received a

Through shared knowledge and rigorous peer review, together, we have created a platform that continues to make a meaningful difference in the medical community.

record-breaking 178 submissions, an increase of approximately 11% compared to the previous year. These submissions covered diverse categories, including original research, comprehensive reviews, detailed case reports, and insightful commentaries.

Our publication efforts kept pace with this momentum, resulting in 137 published manuscripts, a 37% increase from the previous year. To accommodate this surge in high-quality work, we expanded our publication schedule to six issues per year. This has proven highly effective in ensuring we provide ample space for valuable contributions from the medical community.

Publication of Special Issue

In the final month of 2024, *WMJ* made a sig-

nificant contribution to the understanding of maternal and child health by publishing a special double issue. This landmark edition featured 43 manuscripts as well as original artwork, showcasing the expertise and experiences of over 175 health professionals, researchers, students, and artists.

This issue aimed to illuminate the complexities surrounding maternal and child health through comprehensive studies, expert insights, and impactful case reports designed to improve care. Key themes explored include social determinants of health, obstetric health care delivery, health behaviors and practices, and pediatric health. By focusing on these critical areas, this issue underscores *WMJ*'s commitment to advancing knowledge and improving health care outcomes for mothers and children.

Editorial Fellowships

In 2023, the *WMJ* took a significant step forward with the launch of its Editorial Fellowship Program — a visionary initiative designed to prepare the next generation of medical professionals to advance medical knowledge and uphold the journal's esteemed legacy. This program focuses on developing skills essential for managing and disseminating medical literature, cultivating future leaders aligned with *WMJ*'s mission.

We proudly celebrate the completion of the fellowship by our inaugural cohort of editorial fellows, which included Corlin Jewell, MD, David Mallinson, PhD, and Eduard Matkovic, MD. Building on their success, we welcomed our second cohort: Raul Rodriguez, MD, an assistant professor of infectious diseases, and Victoria Ronan, MD, an assistant professor of pediatrics and critical care, both from the Medical College of Wisconsin. The contributions of these fellows have already made a meaningful impact on advancing *WMJ*'s goals.

Looking ahead, we are excited to recruit a third cohort of editorial fellows in the fall of 2025. This ongoing cycle of mentorship and leadership development is vital to our commitment to editorial excellence, ensuring *WMJ* continues to be a valuable resource in medical scholarship and communication.

Limited Series

In 2024, the Publishing Board and editorial leadership introduced a new journal feature—the limited series. This series of columns is meant to provide in-depth information on topics deemed relevant to the practice of medicine. The first series, authored by Robert Calder, MD, MS, and Jayshil Patel, MD, aims to equip medical students and practicing clinicians with essential biostatistics knowledge — a crucial skill set for interpreting medical literature and improving clinical decision-making. Both experts bring valuable insights to this initiative, aiming to strengthen biostatistical understanding among health care professionals. Through this initiative, *WMJ* aims to foster lifelong learning and empower medical professionals.

2025 Outlook

As we look ahead to 2025, we remain committed to maintaining our publication schedule of six issues annually and plan to end the year with a special issue dedicated to the theme of Medical Education. We anticipate this issue will showcase groundbreaking insights in medical education and inspire continued dialogue within the medical community.

This issue will feature topics that address crucial aspects of medical education and training. Potential areas of focus include the impact of health policy on education; the application of research methodologies in curriculum analysis; and the integration of technology such as artificial intelligence, virtual reality, simulation, telemedicine, and e-learning in education. In addition, we hope to explore themes such as community engagement to advance health equity, innovations promoting culturally responsive care, and quality improvement initiatives. It will also highlight topics like educational psychology, systems-based approaches, and the role of mentorship, advising, and coaching in medical education.

The deadline for submissions is July 15, 2025. Visit our website (www.wmjonline.org) to learn more.

Seeking Editorial Talent

To manage the growing volume of submissions and enhance our publication process, *WMJ* is

looking to expand its editorial team. We are actively seeking two to three deputy editors to improve operational efficiency and expedite manuscript processing. This expansion also provides new professionals with valuable editorial experience, fostering the next generation of medical editors.

In addition, we are looking to broaden our editorial board, which currently includes a diverse group of physicians, nurse practitioners, nurses, and pharmacists. As some board members complete their tenure, we aim to recruit new members from various medical specialties to support *WMJ*'s mission and vision.

Recognizing the essential role of peer reviewers, we are also seeking to expand our reviewer pool. Increasing reviewer engagement will improve manuscript turnaround times and ensure our commitment to publishing high-quality medical research.

We invite dedicated professionals eager to contribute to their expertise to join us in these roles. Please contact us at wmj@med.wisc.edu for more information.

Finally, we extend our heartfelt appreciation to all those who contribute to the journal's success—those mentioned above, as well as our colleagues at Ebling Library, whose expertise and assistance is invaluable; the authors; and, of course, our valued readers. The collective efforts of this committed community have shaped the journal's impact, producing publications that are both informative and influential. Through shared knowledge and rigorous peer review, together, we have created a platform that continues to make a meaningful difference in the medical community.

Inpatient Care at Home: The Physician Perspective

Joshua Shapiro, MD; Nicole Bonk, MD; Melissa Dattalo, MD, MPH; Mandy McGowan, RN

Mr Johnson opened the front door with a warm, “Good morning, Doc!” His attending physician, Dr Shapiro, entered his home, took off his shoes, and casually asked, “How are things going?” He replied, “I’m down 2 pounds again this morning...had a pretty good night, slept well with one pillow, and didn’t wake up short of breath this morning. We cooked chicken and veggies last night and used spices from the cabinet without much salt. My edema seems a bit better today. When I went out for the paper this morning, I still struggled a bit, but my breathing definitely seems improved.”

A few days prior, our team had admitted Mr Johnson to our home-based hospital care service from the emergency department (ED).

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He was signed out to the team from the ED clinician as a 75-year-old man with chronic obstructive pulmonary disease (COPD) and a recent admission for acute heart failure who presented to the ED with a recurrent heart failure exacerbation. The day he came to the

it challenging to build and scale, and there was no reimbursement for acute care in the home outside of individual payer contracts. The public health emergency helped with the second obstacle by presenting a payment option through a Centers for Medicare and Medicaid

On paper, Mr Johnson’s hospitalization in HBHC looked quite similar to his recent stay in the brick-and-mortar hospital...But the patient and the clinical team were able to partner in a different way than in the brick-and-mortar hospital.

ED, he described how he had gone to the curb to get his newspaper in the morning and was so short of breath he exclaimed, “I thought I was going to die out there.” Now, he had been enrolled in home-based hospital care for a few days.

Acute hospital care in patient homes is not a new care model. Led by Dr Bruce Leff of Johns Hopkins in the 1990s, a series of landmark studies was completed over the course of over 20 years with researchers at Johns Hopkins, Mount Sinai, and Brigham and Women’s Hospital.¹⁻³ The results of the work had clear outcomes: lower rates of delirium, lower costs of care, lower readmission rates, reductions in mortality, and high patient experience ratings. Despite the significantly positive outcomes, programs were slow to grow due to two major factors: the complexity of the care model made

(CMS) waiver introduced in November 2020. The Acute Hospital Care at Home (AHCAH) waiver provides fee-for-service reimbursement for approved hospitals to provide inpatient-level care in patient homes by waiving the hospital condition of participation that requires nursing services to be provided on premises 24 hours a day. Since the waiver became available, 378 hospitals have interviewed with CMS and have been granted this waiver, including the University of Wisconsin Health system.

Through a collaborative planning effort between UW Health and its home care affiliate, UW Health Care Direct, the UW Health Home-Based Hospital Care (HBHC) program launched on July 11, 2023. This program joined UW Health’s existing Home-Based Primary Care (HBPC) Department and UW Health Care Direct’s foundational home care business

lines to expand the suite of services available to patients in their homes in the Madison, Wisconsin, area. HBHC provides acute, inpatient care through daily physician home visits, twice daily registered nurse home visits, and a complement of other care, including medical social worker visits, medication delivery, mobile medical imaging, home meal delivery, and access to an array of specialty consult services. The addition of HBHC to UW Health has allowed UW Hospital to save hundreds of brick-and-mortar bed days since program launch, opening beds for those who require the acute services only available in the hospital facility and assisting with the capacity issues that plague most health systems.

In November 2023, CMS published the initial findings from the first 16 months of the AHCAH waiver initiative, and the results were outstanding.⁴ The UW Health HBHC results mirror those found in the CMS journal article: reduced readmissions, lower complications, and extraordinary patient satisfaction.

The encounter described between Dr Shapiro and Mr Johnson is very different than a typical patient visit in the brick-and-mortar hospital. How did Mr Johnson spontaneously provide so much information, while patients in the hospital often require much more prompting? In the brick-and-mortar hospital, we often encounter patients looking at us through sleepy eyes as we round early in the morning, acknowledging they often do not sleep well, and we are waking them up to a litany of questions. It is inherently more challenging for patients to be as engaged in their care in the brick-and-mortar hospital. Now, in his own home, Mr Johnson and the questions had more meaning.

Since being admitted to our HBHC program, our care team members have had ample opportunity for education in the patient's familiar environment. Throughout this episode of HBHC, Mr Johnson slept well in his own bed and tried our advice in modifying how he and his family cook low-sodium meals. Our care team worked together to see if he had clinically improved enough to take the journey to the curb that was so treacherous just a few days prior. His familiarity with his routines and gauging his symptoms in his own environment gave

our team a solid benchmark to understand his progress. He was able to sleep in his own bed, away from hospital nighttime awakenings, stay more active, and clinical plans could be created around his real-life activities.

While our care team worked together to optimize his heart failure, Dr Shapiro also dug a little deeper into Mr Johnson's COPD. He had a prescription for home oxygen to use at night and with activity, but while in his home, he was able to demonstrate how none of his oxygen delivery devices are easy to take to the curb and back. He also talked about his fishing boat that sat in the driveway all summer because he worried about carrying his oxygen onto the boat and the possibility of running out of oxygen on the lake. He spoke of the joys of fishing with his son and how this remains one of the most meaningful activities in his life. Although Dr Shapiro did not significantly change his oxygen prescription, he was able to use what she had learned about him to supply a variety of oxygen delivery devices to use to walk to the curb, go out on the boat, and while moving around his home.

On paper, Mr Johnson's hospitalization in HBHC looked quite similar to his recent stay in the brick-and-mortar hospital. Our care team used the same diuretics, did the same daily lab checks, followed his weights and his urine output, and did the same clinical assessments. But the patient and the clinical team were able to partner in a different way than in the brick-and-mortar hospital. Mr Johnson was able to incorporate the education on weights and dietary changes into his daily life while still hospitalized. Our care team was able to better understand his needs and make a number of subtle modifications that have the power to change the trajectory of a chronic illness. He gained a mastery of his disease process and symptoms. Meanwhile, we found ways to tailor his care to support the activities that bring him the most joy. And at the same time, we were able to gauge his improvement against real daily tasks rather than the typical walk down an inpatient unit.

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A Qualitative Assessment of Interprofessional Knowledge Gaps in the Setting of Child Physical Abuse

Elizabeth A. Cleek, PhD, RN; Lynn K. Sheets, MD; Joshua P. Mersky, PhD; Joan P. Totka, PhD, RN; Kristin A. Haglund, PhD, RN

ABSTRACT

Introduction: Health care professionals can protect children by identifying and reporting injuries concerning for child physical abuse, such as sentinel injuries (bruising and intra-oral injuries in precruising infants). Citing knowledge and collaboration barriers, health care professionals sometimes fail to recognize sentinel injuries as concerning for abuse. Interprofessional education may be an ideal format to improve health care professionals' responses to sentinel injuries. However, it is traditionally limited to health care professions, while responding to suspected child physical abuse requires collaboration between health care professionals and non-health care professionals. This study's purpose was to understand if an interprofessional education framework could support the need and development of interprofessional education for child physical abuse beyond health care professions.

Methods: Data were collected through semistructured interviews and analyzed using a qualitative descriptive methodology. Participants included 27 professionals who had engaged in child physical abuse responses in a US midwestern urban county. Participant professions included health care, child protective services, law enforcement, courts, victim advocates, and child advocacy center employees.

Results: Six themes were identified: 4 themes aligned with competencies of the interprofessional education framework, 1 described engaging with families, and 1 described features unique to sentinel injury investigations.

Conclusions: This study supports the need for child physical abuse interprofessional education beyond health care professions. Legal thresholds for responding to suspected abuse differ by profession, and there is no shared interprofessional language around child physical abuse. This contributes to a steep learning curve for new professionals. This study also supports that an existing interprofessional education framework can provide the foundational framework for development of such education.

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INTRODUCTION

Child physical abuse (CPA) is a United States public health problem victimizing approximately 100000 children annually,¹ posing profound health risks for children,²⁻⁴ and significant societal costs.⁵ To address this problem, health care professionals (HCPs) are tasked as mandated reporters legally required to report reasonable suspicions of CPA to child protective service (CPS) agencies.¹ Yet, protecting children from physical abuse requires that HCPs act beyond mandated reporting. They also partner with CPS, law enforcement, court systems, and other community agencies in responding to suspected abuse – often while maintaining a professional relationship with the reported child and family.⁶

Protecting children from physical abuse requires early, interprofessional responses.^{7,8} As CPA disproportionately affects infants and children under 3 years of age,¹ early interventions may mitigate its lifelong associated health risks.⁴

Interprofessional responses are required as no one profession can end this public health problem.^{7,8} The HCP role in CPA responses may be particularly important in cases of sentinel injuries, which are early and readily identifiable CPA red flags.²

Sentinel Injuries of CPA

Sentinel injuries of CPA include minor injuries, such as bruising and intra-oral injuries in precruising infants.² Cruising, the developmental milestone of walking while holding onto furniture,

is achieved in 75% of infants by 12 months.⁹ Prior to cruising, these minor injuries are highly associated with abuse^{2,3} and should prompt consideration of a mandated report.¹ However, HCPs sometimes minimize the significance of sentinel injuries, failing to consider abuse.²

Multiple barriers contribute to HCPs' sometimes limited responses to sentinel injuries and other injuries concerning for CPA. Response barriers include HCP knowledge deficits,¹⁰ biases,^{11,12} ambiguity about reasonable suspicion as the legal reporting threshold,¹³ fear of negative consequences for the child and HCP,¹⁰ and past negative experiences with CPS.¹⁰ Collaboration barriers include HCP confusion about reporting processes, law enforcement frustration with others encroaching on their role, CPS perceived disrespect by other professions, and role confusion by all professions.⁶ Given identifying, reporting, and collaborating barriers, interprofessional education (IPE) may be an ideal pedagogical format for improving HCP responses to suspected CPA and child safety.

Interprofessional Education

IPE occurs when different professions come together to learn from, about, and with each other.¹⁴ It improves interprofessional teamwork by impacting learner collaborative skills, attitudes, and knowledge, which is posited to improve patient outcomes.¹⁵ IPE is rooted in health care and health sciences curricula;^{14,15} however, HCPs collaborate with professions beyond health care (eg, CPS, law enforcement, court systems) when responding to suspected CPA.⁶ Therefore, IPE for CPA may need to expand beyond health care and health sciences.

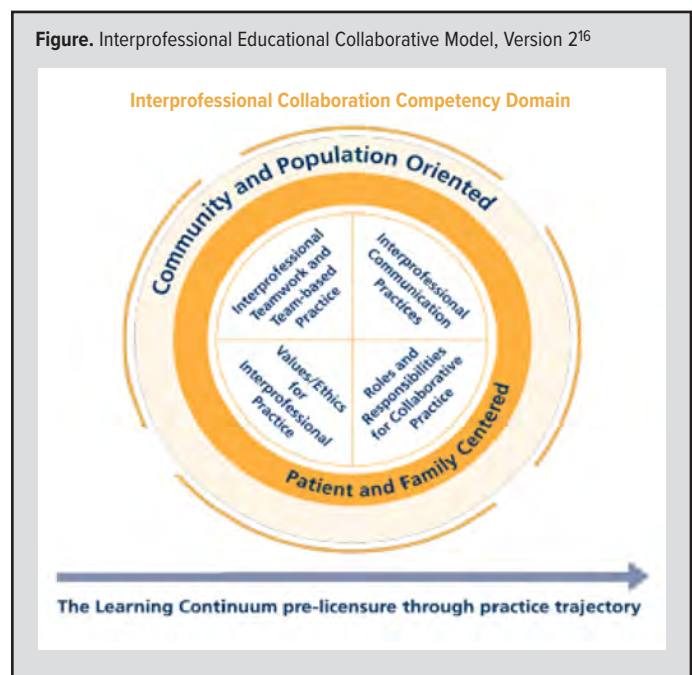
Interprofessional Educational Collaborative Framework

The Interprofessional Education Collaborative (IPEC)¹⁶ provides a well-recognized framework for IPE curricula and is the primary framework supporting this study. This framework is grounded in 4 core competencies supporting interprofessional collaboration: values/ethics, roles and responsibilities, interprofessional communication, and teams and teamwork (see Figure).¹⁶

At the time of our study, version 2 was the current IPEC framework.¹⁶ IPEC version 3¹⁷ was published in 2023. While both versions support the same 4 core competencies, population health, health equity, and diversity within health care teams are newly emphasized in version 3. Yet, IPEC version 3 still does not describe the potential need for IPE to extend beyond health care professions in addressing public health problems such as CPA.

Purpose

IPE training and approaches for including non-health care professions may improve the interprofessional responses needed to protect children from physical abuse. The purpose of this study was to understand if the IPEC framework is helpful in describing interprofessional knowledge gaps and collaboration barriers in non-health care professions in the setting of CPA. This a priori



knowledge is necessary for IPE curricula development. Sentinel injuries were utilized as a CPA focus as they require multidisciplinary responses, provide a mental construct to facilitate participant responses, and are often-misunderstood CPA symptoms, potentially leading to varied responses. Thus, a secondary purpose was to determine if IPE specific to sentinel injuries might require addressing additional knowledge gaps and collaboration barriers beyond those for other injuries concerning for CPA.

METHODS

Setting and Population

Study participants were recruited from an urban US Midwestern county. A purposive—or selective—sample was utilized. Initial participants were recruited through professional, academic, and community partners of the research team. Snowball technique ensued through participant referrals. Inclusion criteria required engagement in at least 1 CPA case (not limited to sentinel injuries) in the study county during the previous 5 years. Engagement in a CPA case referred to reporting to CPS, CPS investigation, law enforcement investigation, and/or court proceedings. Sample size adequacy was determined through thematic saturation.

Study Ethics

Human subjects research approval was obtained from the Marquette University Institutional Review Board. All participants provided written informed consent prior to study participation. Participants were offered \$10 gift card incentives, but several declined, as accepting gifts violated professional rules.

Confidentiality was prioritized as all participants practiced within 1 county. The research team was concerned that published participant comments might upset participants from other professions and that study participants might recognize each other

through detailed demographic identification. Demographics were collected by anonymous written survey. Professional roles were described generally or specifically in free text, at participant discretion. Race/ethnicity were not collected, with concerns some participants might be identifiable by these descriptors. Finally, group interview participants were reminded to not disclose statements made by others.

Study Design and Data Collection

This study utilized a qualitative descriptive design.¹⁸ Data were collected through 8 individual and 3 group interviews, occurring during January through March 2020. Group interviews were profession-specific, organization-specific, and interprofessional-interorganizational. The first 8 interviews occurred in person; the last 3 occurred by telephone due to public health social distancing requirements. In-person interviews occurred in private offices or closed conference rooms at participant workplaces. Researcher EC conducted all interviews, utilizing an interview guide (see Appendix) developed by the study team through literature review, study team expertise, and discussion. The interview guide included open-ended questions about IPEC competencies¹⁶ in CPA, engaging with families in CPA responses, differences between responses to sentinel injuries versus other CPA injuries, and additional needed IPE competencies not found in the IPEC framework. Interviews were audio recorded, transcribed verbatim by a professional transcriptionist, validated and deidentified by researcher EC, and uploaded into Nvivo software (NVivo, Version 1.0, QSR International; 2020) for analysis.

Data Analysis

Thematic analysis was completed through 6 phases described by Braun and Clarke: familiarizing oneself with the data, generating initial codes, searching for themes, reviewing themes, naming and defining themes, and producing the report.¹⁹ Initial analyses were completed separately by EC and KH, then compared and discussed for investigator triangulation.

Rigor and Credibility

Rigor was operationalized through the criteria of credibility, dependability, confirmability, and transferability.²⁰ Credibility was addressed through investigator triangulation (EC and KH) and theory triangulation with interprofessional participants and research team. Dependability was addressed through the principal investigator's field notes.²⁰ Confirmability was addressed 2 ways: the profession of victim advocate was added to the study at study participant recommendations, and member checks were completed during interviews to allow for participant clarification and

Table 1. Participant Demographics

	CAC (n=6)	CPS (n=2)	Attorneys (n=5)	HCPs (n=3)	LE (n=6)	VAs (n=5)	Total (N=27)
Age, mean (SD)	42 (12.6)	36 (3)	42 (7.2)	44.3 (9)	50 (5.5)	37.8 (8.3)	42.5 (9.6)
Sex							
Female	6	2	4	3	4	5	24 (88.9%)
Male	0	0	1	0	2	0	3 (11.9%)
Years in role, mean (SD)	12.7 (7.2)	7.5 (4.5)	14.6 (5.9)	15.7 (7.8)	20.8 (3.7)	9.2 (4.2)	14.1 (7.2)
Aware of term sentinel injury							
Yes	6	2	4	3	5	5	25 (92.6%)
No	0	0	1	0	1	0	2 (7.4%)
Involved in sentinel injury cases							
Yes	6	2	5	1	5	3	22 (81.4%)
No	0	0	0	2	1	0	3 (11.1%)
Missing	0	0	0	0	0	2	2 (7.4%)

Abbreviations: CAC, child advocacy center; CPS, child protective services; HCPs, health care professionals; LE, law enforcement; VAs, victim advocates.

further explanation. Finally, transferability was addressed through purposive (selective) sampling and detailed description.

RESULTS

Participants

Twenty-seven individuals participated in this study (see Table 1), including HCPs, attorneys, law enforcement, victim advocates, CPS workers, and child advocacy center (CAC) staff. The CAC is a regional multidisciplinary outpatient evaluation center for child maltreatment concerns. CAC participants were unique as they included social work and HCPs who routinely worked together. This was not true for community HCP, attorney, law enforcement, victim advocate, or CPS participants. Most participants were female (24 of 27), and years of experience ranged from 3 to 26. Participants estimated their engagement in CPA cases. Community HCPs had the lowest range (3-20), while at least 1 participant in each other group reported 100 or more cases during the previous 5 years. Most participants (25 of 27) were aware of the term sentinel injuries prior to this study, and 81.4% (22 of 27) had participated in a sentinel injury case investigation.

Themes

Six themes were identified. Four themes aligned with IPEC framework competencies,¹⁶ 1 described interactions with families, and another described differences between responses to sentinel injuries and other CPA injuries. (Table 2 includes themes and illustrative participant quotations.)

Valuing Interprofessional Colleagues Is Shown Through Disagreeing Respectfully

Participants noted treating each other with value means you "sometimes agree to disagree." Participants reported that all professionals involved in CPA investigations want to protect children. However, they did not always agree on the best outcome after an investigation. When professionals value each other, disagree-

Table 2. IPEC Domains as Described for Child Physical Abuse and Sentinel Injury Curricula

Theme	Source	Quote
Values/Ethics: Valuing interprofessional colleagues is shown through disagreeing respectfully	Attorney CPS	"We might agree to disagree. So really just clarifying so that I at least understand your position. It doesn't mean I am going to agree with it, but I want to make sure that I understand it and how you got to that position. It's explaining your point of view, asking them for any additional information, saying 'thank you' and then doing what you need to do."
Roles and Responsibilities: Professionals in different child welfare roles work under different laws	CPS	"We have a very specific framework. If it [suspected child abuse] doesn't fit, we can't intervene, even if they [HCPs and CAC] don't like it, even if they don't think it [staying in the family home] is in the child's best interest or for their well-being. We're not saying we're not concerned. But if it doesn't rise to the level of intervention, it doesn't rise to the level of intervention."
Interprofessional Communication: Interprofessional communication is intentional and potentially time-intensive	LE CAC Attorney	"I've been out at the hospital for child abuse cases, where me and my partner [sic] sat down with the advocacy [hospital's child protection team] doctor, the social worker, the ER doc, and we're all at the table just like this and we'll go through the case. And that's very helpful, to have everyone there at the same table, literally the same table... So when we have that and everyone's on board and together, it's great." "I have found more success with bringing the worker [CPS] into the room to show them the injuries right away versus just looking at the photos...they'll see the extent of it firsthand versus just looking at photos. I think that that really gives them an 'aha' moment." "I don't think it helps relationships when they [HCPs] are clearly resistant or annoyed by the fact that I'm asking these questions. And I'm like, 'I'm trying to understand and learn, and you should want to teach me because you called this in and you obviously want to keep this kid safe, and I'm the person trying to do that.'"
Teams and Teamwork: Assumptions lead to failures in teamwork	LE	"[HCPs will ask] 'And so are you going to arrest somebody?' And well, slow down...We don't violate civil rights here. We have standards to fulfill before we can make those arrests. I understand they're not lawyers or LE professionals so therefore they don't understand that we have our process."
Experiences With Families: Treating families ethically	CPS HCP CAC	"I'm a white woman from a middle-class family. If I go out and I work with a middle-class family, it might be easier for me to give them the benefit of the doubt because they look like me. They live like me. It's easier to make a connection. It's a natural thing. However, that's also a very dangerous route to take." "I oftentimes tell them [families] that I'm reporting, that I'm the advocate for the child and that's why they bring their child to me, is because they want me to do the best job I can in taking care of their child. So, part of that responsibility involves asking for help from outside organizations or from child welfare when I feel that their child is either at risk for a health issue due to neglect, where the parent can't meet their health needs in a significant way, or when I'm concerned about maltreatment." "We [HCPs] are taught to be very transparent with patients and families and there are times that we aren't able to be."
Potential Barriers to Reporting Sentinel Injuries	Attorney CAC	"I look at almost all of my really serious child abuse cases and in most, if not all of them, there's a previous sentinel injury that went undetected...All of these cases to me highlight that if something had been done at an earlier date (and it doesn't have to be an arrest or a prosecution, it can be merely just having the authorities alerted or an investigation done in some way...) that the outcome for this particular child could have been very different than what I'm seeing on my desk." When it's not as clear-cut, I think that's when we see the drop off in buy-in where everyone's kind of like 'eh-this isn't of high priority,' versus, and I think for babies, too. Babies can't talk. They can't tell us what happened. There's only so many people that engage with a baby, you know."

Abbreviations: IPEC, Interprofessional Educational Collaborative; CAC, child advocacy center; CPS, child protective services; HCP, health care professional; LE, law enforcement; ER, emergency room.

ments are addressed without damaging relationships. In contrast, permanent harm might occur when respect is not shown. One CPS participant described disrespectful disagreements as “people sort of accusing each other of either not caring about families or not caring about children...” Participants added that disrespectful experiences are hard to forget and result in less future collaboration with a negative effect on future investigations as professionals may hesitate to work together again.

In contrast, professional disagreements mean a willingness to hear others' views. Difficult conversations, if done well, can lead to broader views. A law enforcement participant said, “... I might be

thinking one track here, and then you talk to a doctor or you get the history of the family through CPS...and it makes you think differently.” Even so, the idea that you still “need to do what you need to do” describes participant beliefs that collaboration does not override one's own responsibilities.

Professionals in Different Child Welfare Roles Work Under Different Laws

Participants discussed frustrations resulting from professions in CPA investigations practicing under state laws that do not align. For example, HCPs may report any concern of CPA.²¹ However, CPS cannot intervene unless a child's physical injury rises to the

severity as described by state law: "...lacerations, fractured bones, burns, internal injuries, severe or frequent bruising or great bodily harm."²¹ One CPS participant said, "We're not saying we're not concerned – but if it doesn't rise to the level of intervention, it doesn't rise to the level of intervention." Nonetheless, this perceived lack of action left some HCPs feeling unheard. In contrast, the CPS participants reported frustration in needing to assess concerns of abuse that (to them) clearly did not rise to a level of intervention. The disparity between HCP reporting laws²⁰ and laws guiding CPS responses²² can leave both professions frustrated by others' actions and inactions.

Interprofessional Communication Is Intentional and Potentially Time Intensive

Participants used multiple descriptors to explain that effective interprofessional communication is an intentional process, including "face-to-face," "direct," "timely," "reciprocal," and "avoids profession specific jargon," and indicated that interprofessional communication often requires a lot of back-and-forth communication.

Despite being time-intensive, multiple participants reported that face-to-face communication is most effective. Direct communication improves professionalism, timeliness, and the quality of shared information. To these points, law enforcement participants voiced frustration about being consulted "weeks" after a CPS referral, as the time lapse meant potential loss of evidence. Similarly, attorneys expressed frustration about receiving information late when preparing for trial as it potentially weakened court cases. One CAC participant said she collaborated with CPS more effectively when discussing CPA findings immediately: "I have found more success with bringing the [CPS] worker into the room to show them the injuries right away versus just looking at the photos... I think that really gives them an 'aha' moment."

In contrast, the 3 HCPs said they rarely, if ever, received follow-up communication after reporting suspected abuse to CPS. Without feedback, 1 HCP wondered if reporting served any purpose as she did not know if the child became safer.

Participants said that reciprocal communication—eg, dialogue—is critical to professional communication. As professions involved in CPA investigations have different educational backgrounds and professional languages, dialogue can ensure mutual understanding. Participants reported that communication broke down when professionals resented others questioning their conclusions. However, they indicated that follow-up questions reflected a desire to collaborate better and were not intended as disrespectful or doubting another's competence.

Participants also said that avoiding profession-specific technical language decreases the need for extended back and forth communication. HCPs frequently use medical terminology not understood by other professions (eg, "subconjunctival hemorrhage" and "failure to thrive"). HCP reports of suspected abuse

can lack gravity with CPS or law enforcement, who may not know medical terminology. One attorney suggested that HCPs keep information "as simple as you can" to increase the effectiveness of suspected CPA reports.

Assumptions Lead to Failures in Teamwork

Participants did not always understand how other professions arrived at conclusions in CPA investigations. These knowledge gaps can lead to negative assumptions. For example, one of the CPS participants said, "you will have an attorney who is emailing one of our staff wanting information and nobody is responding. And the conclusion they [the attorneys] reach is, 'this person isn't doing their job'." While many participants were aware of disparaging assumptions made about them or their colleagues, all were quick to explain the assumptions were incorrect.

Individuals may incorrectly assume others have similar expertise in CPA cases. One of the attorneys provided an example of when a novice CPS worker did not understand the medical and child welfare importance of failure to thrive, the reason for their shared court case. The experienced attorney described her frustration but then reminded herself that she had not always known about this diagnosis and learned "on the job" and then provided education for the novice CPS worker.

Treating Families Ethically

Treating families and children well requires being transparent, nonjudgmental, and empathetic. Participants noted that treating families well is ethical but also pragmatic, as it assists investigations. Families are more apt to provide information when they are treated respectfully. HCP participants reported that they usually tell parents when reporting to CPS.

Participants also recommended treating families objectively. HCPs said they assured parents they were not judging them but responding to clinical findings and seeking assistance for the family. Several participants discussed the need to recognize and acknowledge implicit biases. Law enforcement participants said that many families they work with are part of marginalized communities, and families were surprised when treated respectfully. Participants shared that unrecognized and unacknowledged implicit biases may lead to unfair treatment of families through either too harsh or too lenient assessments, leading to process errors in CPA cases.

Many participants empathized with parents, describing the need to be thoughtful and kind. One law enforcement participant said, "I treat them how I'd want to be treated in that situation." Objectivity and empathy were balanced, recognizing that families may not be truthful in CPA evaluations. For HCPs, this tension contradicts most interactions with families. Thus, CAC participants recommended remaining cautious—along with empathetic and objective—with families. Finally, participants from all groups said that the needs of the child's safety are always prioritized over the needs of parents and of the family.

Barriers to Identifying and Reporting Sentinel Injuries

Most participants expressed little or no discomfort about reporting or investigating sentinel injuries as red flags of CPA. Law enforcement and attorneys noted sentinel injuries may be more difficult to investigate and prosecute as these cases can be circumstantial. Several participants said this made collaboration more critical, as sentinel injury cases are not always easy to investigate.

Participants from all professions said that sentinel injuries are valuable red flags of CPA. HCPs, CAC participants, and attorneys emphasized this most strongly, sharing that they had seen the consequences of missed sentinel injuries. However, 1 CPS participant wondered if CPS referrals for all sentinel injuries might be “heavy-handed” and unnecessarily traumatizing for families because she perceived that most sentinel injuries were not diagnostic for CPA.

Most participants had received formal sentinel injury education and were familiar with the term. However, some participants misunderstood sentinel injuries to represent any injury suggesting CPA, including some fractures or some head injuries. Additionally, some participants understood “any unexpected bruising or intracranial injuries” to mean bruising needed to be near the mouth to be a sentinel injury. (When these misunderstandings were identified, researcher EC clarified the definition of sentinel injuries before continuing interviews.) Most participants agreed that ongoing, readily accessible sentinel injury education was needed due to frequent staff turnover in multiple professions.

DISCUSSION

We applied the IPEC framework to assess interprofessional collaboration in CPA responses, and we identified gaps in collaboration and knowledge. Participants have different professional languages, often work under different CPA legal mandates, and may have various levels of expertise and knowledge regarding CPA. Our results indicated that even when HCPs and other professionals recognize collaboration barriers, they do not always know how to address them. Thus, IPE could help bridge collaboration challenges to improve child safety when physical abuse is suspected.

IPE may be particularly beneficial for HCPs, who are uniquely qualified and well-positioned to protect victimized infants and young children since they may interact routinely with them during multiple well-child visits.^{9,23} It was recognized by our HCP participants that reporting and participating in responses to suspected CPA may be a rare event. Even so, participants recognized the importance for all HCPs who care for children to have this knowledge. IPE may assist HCPs in developing collaborative skills needed for responding to suspected CPA.

Next steps for developing an IPE curriculum for CPA may begin in this same study county. Participants identified the need to develop ongoing, readily accessible education within their own county—potentially among new employees in each profession.

Limitations

As is common in qualitative studies, generalizability of this study is limited. It was completed with a small sample in a US Midwestern urban county with an accessible CAC. Most participants had had education regarding sentinel injuries. It is unknown if study findings would be replicated within other contexts, such as rural counties or counties in other US regions. Importantly collaboration barriers in communities without a CAC may have greater barriers to CPA knowledge and collaboration.

CONCLUSIONS

Interprofessional education may reduce barriers to collaboration between the interdisciplinary professionals charged with protecting children through suspected CPA responses. Significant barriers include not understanding the different legal thresholds among disciplines for responding to suspected physical abuse and no shared interprofessional language around CPA. IPE might improve and shorten the learning curve for new professionals involved with CPA cases. Finally, it could increase professionals’ understanding of the work of other disciplines and improve interprofessional communication. The IPEC framework would provide a solid foundation for IPE curricula for CPA.

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Exploring Health Care Barriers for the Unhoused: Insights from a Rural Midwestern Community

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ABSTRACT

Introduction: People experiencing homelessness are more likely than the general population to have chronic health conditions and often encounter significant barriers to health care access. Many of these barriers can be affected by community-based factors, such as availability of reliable transportation, past experiences with health care systems, and community attitudes toward the unhoused population. This project aims to assess the needs and barriers to health care identified by people experiencing homelessness in a rural Midwestern city.

Methods: The survey used was adapted from a survey previously conducted to assess the needs of the homeless population in Milwaukee, Wisconsin. Surveys were distributed during outreach around the city of Wausau, Wisconsin. Data were transcribed and reviewed, and descriptive statistics were calculated.

Results: A total of 45 surveys were completed. Most participants identified as White, non-Hispanic males ($n=24$, 53%) and were 46 to 55 years old ($n=14$, 31%). Barriers to health care included lack of housing, cost, transportation, lack of a mailing address, inadequate hours, and disrespectful care. Eighty-six percent of participants ($n=38$) reported having a mental health diagnosis, yet only 26% ($n=12$) stated that they see a mental health professional.

Conclusions: Individuals experiencing homelessness in a rural community have broad and complex barriers to accessing health care. Given limited resources in smaller communities, innovative and holistic solutions should be considered when aiming to make care more equitable.

INTRODUCTION

The experience of homelessness is complex and multifaceted, often stemming from a combination of factors, such as unaffordable housing, unemployment, mental health challenges, the loss of a family member, eviction, or substance use. These diverse challenges highlight the need for a comprehensive array of services to address the unique circumstances of each individual facing homelessness.

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In 2023, homelessness in the United States continued to rise, totaling over 653 100 individuals on a single night; and 18% of individuals were noted to be people experiencing homelessness in rural areas.¹ Each January, the US Department of Housing and Urban Development (HUD) completes its annual Point-in-Time Count of all those experiencing homelessness on a given night. In January of 2023, there were an estimated 4775 individuals experiencing homelessness in the state of Wisconsin.² Sixty-four percent of unhoused individuals in this Point-in-Time Count were located outside of Milwaukee, Racine, and Dane counties.² Milwaukee, Racine, and Dane counties are significant urban centers in Wisconsin, carrying a higher population density and also boasting diverse populations in terms of ethnicity, culture, and socioeconomic backgrounds versus other Wisconsin counties.

Furthermore, 64% of unhoused individuals experiencing homelessness in Wisconsin reside in smaller communities. Literature on rural homelessness is sparse; however, we know that when compared to urban areas, rural areas have more significant health disparities, less community resources, more suicide and drug-related deaths, and less access to mental health care.³⁻⁷

Moreover, individuals experiencing homelessness often face the challenging dilemma of prioritizing essential needs, such as securing food and shelter, over accessing health care services.⁸ Unfortunately, this predicament leads to underutilization of health care resources, ultimately culminating in late-stage disease presentations and, consequently, poorer prognoses when these individuals do seek medical attention.⁹ Recent studies examining health insurance coverage within unhoused populations reveal

that despite improvements in resources over the last decade, a substantial portion of individuals experiencing homelessness (42%-72%) are insured.^{10,11} Still, persistent barriers hinder their access to essential medical care, highlighting a pressing issue that necessitates attention and intervention.¹²

Mental health is a significant concern for many Americans today. The National Institute of Mental Health reports that as of 2021, 22.8% of the population has received a mental health diagnosis.¹³ In contrast, HUD reports a higher prevalence among individuals experiencing homelessness, with 31.4% having a serious mental illness and 24% reporting substance abuse.¹⁴ This is particularly worrisome in unhoused populations in rural communities, where mental health resources are scarce. The reasons for these disparities are well documented and the result of a lack of trained mental health providers in rural communities, underutilization of services, and limited care coordination in medical care.¹⁵⁻¹⁷ Addressing these systemic issues is crucial for ensuring equitable mental health support for all individuals, irrespective of their housing status or geographical location.

The overarching goal of this study is to shed light on the health needs and barriers to care faced by unhoused populations in central Wisconsin. By identifying these challenges, we hope to pave the way for the development and implementation of effective solutions to enhance access to health care services and ultimately improve health outcomes within this vulnerable population. The information provided in this study can be utilized by various stakeholders, including policymakers, health care providers, social service agencies, and community organizations to address the identified needs and barriers to care among this population. Overall, we hope the insights from this survey serve as a catalyst for positive change both within and beyond our community by providing valuable information about the health needs and concerns of our unhoused population and offer actionable recommendations for improving access to care and addressing health disparities.

METHODS

A survey tool was developed to assess the health needs and barriers to care of individuals in central Wisconsin by adapting a previous Medical College of Wisconsin questionnaire.⁸ This survey was created in collaboration with those who work closely in the space, including case managers, local organization leaders who focus on serving our unhoused population, and the Marathon County Health Department. All members had the capacity to suggest additional questions or veto questions. These individuals were asked to review the survey on a voluntary basis given their experience in the field. The final survey was reviewed by the Medical College of Wisconsin Institutional Review Board and ultimately focused on assessing health status, health resource utilization, and barriers to care. It received approval by the Medical College of Wisconsin Institutional Review Board on March 15, 2023.

Participants were eligible to participate in the survey if they

met the criteria of being a “person or family in Marathon County lacking stable or regular residence,” were 18 years or older, and were able to comprehend English.

A medical student interviewed participants through community outreach during the nightly intake process at local shelters in Wausau, Wisconsin. Given the length of the survey and the desire to establish rapport with study participants, it was determined that it may be best to administer the survey in an interview format. Participants were asked if they wanted to participate in the study, were read the informational letter, and asked if they met the study inclusion criteria. Participation was voluntary, and participants did not receive incentives.

The interviews were carried out predominantly at local organizations (eg, shelters) in a private area by a medical student. The student used a mobile Qualtrics survey (either on a phone or laptop) to record participant responses. The interviews were not recorded; rather the student conducting the interviews scribed participant responses. Topics included participants’ backgrounds and demographics, reasons for homelessness, barriers to care, health resource utilization, mental health care and diagnoses, substance use, and access to harm reduction. The survey included close-ended and open-ended questions to assess needs and barriers to health care in this population. Close-ended questions ranged from simple yes or no responses to some utilizing a Likert scale to assess opinions. Descriptive statistics were calculated from these responses. The data from open-ended questions were compiled in Excel and thematically encoded by a 2-person medical student team.

RESULTS

A total of 45 surveys were completed. The response rate was 82%. Questions from the survey and results are shown in Table 1. Participant demographics included the following: 31 identified as White (69%); 4 Asian (9%), 4 Black/African American (9%), 3 American Indian/Alaskan Native (7%), and 3 “other” (7%). Only 5 participants (11%) identified as Hispanic. Three participants (7%) were veterans. The most common age group was 46 to 55 (n = 14, 31%), and 33 (73%) participants identified as male. Twenty-four participants (53%) rated their health as “poor” or “fair,” including 7 female participants (58%) and 5 minority participants (36%).

Respondents were asked to indicate how often they utilized the health services listed in Table 2 in the last 12 months. Nineteen (43%) had used the emergency department, and 12 (27%) had an overnight hospital stay. Only 8 participants (18%) had seen a dentist in the last year, and 20 (44%) saw a mental health provider in the last year. Twenty participants (45%) said they have a primary care provider, yet 38 (84%) have active health insurance.

Participants were asked to rate potential barriers to health care on a scale from 1 to 5 (1 = not a barrier to care and 5 = a significant barrier to care). Significant barriers included lack of housing, cost of care, lack of transportation, and not having a mailing address (Table 3). Sixty percent (n = 27) of participants did not have an income.

Table 1. Responses to Health Needs Assessment Among Wausau's Unhoused Population

Variable	n (%)	Variable	n (%)
Race (n=45)		Do you have access to harm reduction (clean needles, Narcan, etc)? (n=45)	
White	31 (69)	Yes	24 (53)
Asian	4 (9)	No	21 (47)
African American/Black	4 (9)	In the past year, have you had unprotected sex? (n=45)	
Alaskan Native/American Indian	3 (7)	Yes	14 (31)
Other	3 (7)	No	31 (69)
Ethnicity (n=45)		(For females) In the past year, have you been pregnant or worried about becoming pregnant? (n=12)	
Hispanic	5 (11)	Yes	3 (25)
Non-Hispanic	40 (89)	No	9 (75)
Age (n=45)		(For females) Are you currently using birth control? (n=11)	
18–25	3 (7)	Yes	2 (18)
26–35	5 (11)	No	9 (82)
36–45	13 (29)	Do you have any chronic illnesses you are prescribed medications for (diabetes, high blood pressure, heart disease, asthma, etc)? (n=44)	
46–55	14 (31)	Yes	21 (48)
56–65	9 (20)	No	23 (52)
66+	1 (2)	Do you have a mental health diagnosis? (n=44)	
Sex (n=45)		Yes	38 (86)
Male	33 (73)	No	6 (14)
Female	12 (27)	Within the past 12 months, did you worry your food would run out before you got money to buy more? (n=45)	
Overall, how do you feel your health is? (n=45)		Never	9 (20)
Poor	8 (18)	Rarely	3 (7)
Fair	16 (36)	Sometimes	16 (36)
Good	16 (36)	Fairly often	7 (16)
Very Good	3 (7)	Frequently	10 (22)
Excellent	2 (4)	How often does anyone, including family, threaten you with harm? (n=44)	
Do you have a primary care physician or clinic you regularly visit? (n=44)		Never	16 (36)
Yes	20 (44)	Rarely	9 (20)
No	24 (55)	Sometimes	6 (13)
Do you have a dentist you regularly visit? (n=45)		Fairly often	4 (9)
Yes	5 (11)	Frequently	9 (20)
No	40 (89)	Where do you usually sleep? (n=45)	
Do you currently have a mental health counseling service, including substance use counseling? (n=45)		Shelter	31 (69)
Yes	12 (27)	Outside	9 (20)
No	33 (73)	Car	1 (2)
Do you have health insurance? (n=45)		Couch or friends	3 (7)
Yes	38 (84)	Own place	0
No	7 (16)	Hotel	1 (2)
Who is your insurance provider? (n=38)			
BadgerCare or Medicaid	31 (67)		
Private	2 (4)		
Medicare	5 (11)		

Thirty-eight participants (84%) had health insurance, with state insurance being the most common (n=31, 67%). Thirty-seven participants (82%) reported substance use. The most used substances reported were tobacco/nicotine products (n=34, 92%), alcohol (n=17, 46%), cannabis (n=17, 46%), methamphetamine (n=8, 22%), hallucinogens (n=4, 11%), and cocaine (n=4, 11%). Eleven female participants (92%) and 10 minority participants (71%) stated that they use substances. Twenty-one (47%) participants indicated that they do not have access to harm reduction methods (eg, clean needles, fentanyl testing strips, naloxone). Thirty-eight participants (86%) stated that they have a mental health diagnosis, yet only 12 (27%) indicated they currently see a mental health professional. Nine female participants (75%) stated

they have a mental health diagnosis, but only 4 (33%) currently see a mental health professional. Twelve (86%) minority participants said that they have a mental health diagnosis, but only 2 (14%) currently see a mental health professional.

Participants were asked what they believed was causing their homelessness. Responses are listed in Box 1. Responses to why they were not using mental health or substance use counseling are listed in Box 2.

DISCUSSION

The findings from this survey reveal a notable disparity in the utilization of health resources among unhoused individuals within the Wausau community. Noteworthy aspects include the utilization of

Table 2. Health Services Utilized in Last 12 Months, N=45

Health Resource	Utilized Service n (%)
Emergency department	19 (42)
Mental health provider	20 (44)
Dental	8 (18)
Urgent care	15 (33)
Primary care provider	18 (40)
Free clinic	3 (7)
Overnight hospital stay	12 (27)

Table 3. Likert Scale of Perceived Barriers to Accessing Health Resources (N=43)

Barrier	1	2	3	4	5
	n (%)	n (%)	n (%)	n (%)	n (%)
Inadequate hours	14 (33)	3 (7)	14 (33)	8 (19)	4 (9)
Money	4 (9)	1 (2)	5 (12)	8 (19)	25 (58)
Transportation	3 (7)	2 (5)	11 (26)	4 (9)	23 (53)
Substance Use	23 (53)	3 (7)	7 (16)	5 (12)	5 (12)
Safety	23 (53)	3 (7)	8 (19)	3 (7)	6 (14)
Language barrier	36 (84)	1 (2)	4 (9)	0 (0)	2 (5)
Ability to read or write	37 (86)	2 (5)	1 (2)	0 (0)	3 (7)
Housing	1 (2)	2 (5)	4 (9)	8 (19)	28 (65)
Childcare	41 (95)	1 (2)	1 (2)	0 (0)	0 (0)
No mailing address	7 (16)	2 (5)	14 (33)	7 (16)	13 (30)
Disrespectful care	21 (49)	2 (5)	5 (12)	4 (9)	11 (26)

1=not a barrier, 2=not usually a barrier, 3=neutral, 4=somewhat of a barrier, 5=significant barrier.

the emergency department (ED) (42%), dental care (18%), and overnight hospital stays (27%) in the last 12 months. In comparison to the general adult US population, unhoused individuals in Wausau, Wisconsin, exhibit heightened utilization of the ED (recent data found that 21.3% of US adults in 2018 had 1 or more ED visits in the past year vs 42% in this cohort), more overnight hospital stays (5.2% of individuals aged 1 to 64 had an overnight hospital stay in 2018 vs 27% in this cohort), and lower utilization of dental care (in 2020, the general adult population utilization of dental care was 62.7% vs 18% utilization in this cohort).¹⁸⁻²¹ Furthermore, this population not only demonstrates elevated rates of ED utilization but also experiences higher frequency of hospital admission and overnight hospital stays. Importantly, our unhoused population faces significant health risks related to dentition.²²

A significant number of respondents (86%) acknowledged being diagnosed with a mental health disorder; however, a substantial number stated they were not accessing mental health care. Most commonly, individuals reported not accessing care due to wanting to independently address their concerns, substance use, and a lack of trust in clinicians. Furthermore, 82% of respondents reported substance use. The accessibility of mental health care is a widespread challenge across the United States, with rural communities facing even greater limitations.¹⁵ Specifically, rural individuals are less likely to see a mental health professional and

Box 1. Participant Responses When Asked What They Believe Caused Their Homelessness

"My wife and I lost my apartment because I lost my job in December. We fell behind in rent; the landlord used to work with us but is now not willing to work with us."

"Addiction."

"Not able to have an adequate credit score for rentals and not having enough money for double deposits."

"A lot of different things. Physically I've had a lot of surgeries, lots of health problems, lots of medical bills, divorced, and I have a mental disability."

"Developed blood clots and got behind on rent from being in hospital and not able to work."

"Started using drugs 8 years ago and going through psychosis."

"I had a job, but I got hit by a car in and had to stay in hotels to heal."

"Me and myself and I. I hate life."

"I have epilepsy and just got out of the hospital. I was staying with my brother, and I am a recovering addict. It was a bad situation for me to be around all the drinking and everything."

"Suffer from alcoholism badly."

"Background checks; landlords don't give second chances."

"Got kicked out because of religious reasons."

"Parents died, kids left, and was left alone. No one to take care of and freaked out."

"Myself."

Box 2. Participant Responses When Asked Why They Were not Using Mental Health or Substance Use Counseling

"Missed appointments and now can't go back."

"Lost job and started doing drugs. Didn't need it."

"Big trust issues."

"Been through treatment as a kid. Now I'm old enough to decide if I want to go."

"Tried it and didn't work."

"Don't like being on medications."

"I'm old and have been going through this for a long time. I want to stop drinking though."

"I don't like doctors. It's hard to find good decent doctors and people I can trust."

"Sometimes you just have to cope with it yourself and give yourself time from people."

"Don't feel comfortable speaking with them. Don't know if I can trust them."

"No reason for not, just haven't."

"Don't feel like I need one."

see clinicians with less specialization.¹⁵ The shortage of health care professionals poses a significant challenge for all patients.^{16,17} This challenge is further intensified by the constrained resources available to people experiencing homelessness, encompassing difficulties with transportation and the financial burden associated with seeking care.

The unhoused individuals in this community reside in a small town in central Wisconsin. Wausau is home to 39,968 people. People experiencing homelessness in Wausau have articulated facing mul-

multiple obstacles to accessing health care. Predominantly, individuals cite the cost of care, lack of transportation, and lack of housing as significant barriers. Similarly, unhoused individuals in an urban Wisconsin city also faced difficulty accessing care for these reasons.⁸ However, it is important to note that homelessness in smaller rural towns in the United States differs significantly from homelessness in urban cities. In comparison to their urban counterparts, rural areas often have fewer shelters, lack of or limited public transportation, lack of privacy, fewer job opportunities, and rising rent. Furthermore, these factors contribute to the compromised health outcomes of rural unhoused populations, even when individuals do seek medical attention at clinics. Finding solutions for these systemic barriers in rural settings is essential for fostering equitable health care access. Some solutions may be to include individuals with lived experience in policy decision-making, antistigma education, improved transportation, increasing access to mental health resources, and improving coordinated care in these communities.^{23,24}

Limitations of this study include the exclusion of participants below the age of 18 and those unable to read or complete the survey in English. Given the nature of the interview format and limited interviewers, the survey could be conducted only in English. Another constraint was the predominant inclusion of participants from shelters in the Wausau area, thus not providing a comprehensive representation of the entire population. Notably, a significant portion of the unhoused community in Wausau abstains from utilizing shelters, opting instead to sleep outdoors or “couch surf” (often “couch surfers” are not accounted for in surveys and are an example of hidden homelessness). Additionally, it is important to acknowledge that the willingness to utilize services may be more pronounced among the shelter-utilizing population, potentially creating a bias compared to their unhoused counterparts who do not frequent shelters.

CONCLUSIONS

Individuals experiencing homelessness in central Wisconsin have numerous complex health needs and face considerable barriers to care. These findings underscore the intricate interplay between homelessness, substance use, and mental health. A significant portion of the population reports chronic illnesses, mental health diagnoses, and substance use without adequate access to care. These multifaceted challenges necessitate comprehensive, compassionate care, emphasizing holistic and inclusive health care solutions and providing direction for future interventions. Strategies to improve access to health care may include improving public transportation, improving access to mental health care, antistigma education, and including individuals with lived experience in policymaking.

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Health Care Workers' Views of Health Care's Contribution to Greenhouse Gas Emissions and Reducing Health Care Emissions

Claire Gervais, MD

ABSTRACT

Introduction: Climate change is the greatest global public health threat of this century, increasing respiratory, cardiovascular, and vector-borne diseases; mental health effects; and premature deaths. The US health care sector is responsible for 8% to 10% of the nation's greenhouse gas emissions; therefore, engaging health care systems in emissions reduction could improve health for all communities.

Methods: A 10-question survey was emailed to a convenience sample consisting of 211 faculty physicians, nurse practitioners, and physician assistants and an unknown number of other staff employed at 21 UW Health family medicine clinics. The survey measured knowledge of health care greenhouse gas emissions and included 2 open-ended questions to solicit opinions on sustainability priorities and barriers to waste reduction. Each clinic also received a 15-minute presentation on health care climate impact during one of their regularly scheduled meetings.

Results: Of the 130 survey respondents, 34% knew the health care sector is responsible for 8% to 10% of the US carbon emissions and 9% of non-greenhouse air pollutants. Only 26% knew that most of these emissions come from purchasing and transportation. However, 92% thought environmental sustainability should be incorporated into all clinical operations, and 74% wanted to know how to affect purchasing to reduce emissions. Top priorities were identified as investing in renewable energy, increasing recycling, and reducing waste (eg, single-use instruments). Top barriers to waste reduction were thought to be cost, complacency, and time.

Conclusions: Despite lack of knowledge of the health care sector's contribution to US greenhouse gas emissions, most surveyed health care workers wanted their health care system to incorporate environmental sustainability into all clinic operations. Additional research identifying knowledge gaps and soliciting opinions of other medical specialties and health care systems on health care greenhouse gas emissions may increase awareness of health care emissions, inform health care leaders, and lead to emissions reduction.

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INTRODUCTION

Climate change is depicted by the *Lancet* Countdown on Health and Climate Change as the greatest global health threat of the 21st century, with recent alarming increases in the rate of global warming directly threatening public health.¹ Similar to other public health issues, health impacts from climate change affect all of us but disproportionately threaten vulnerable communities due to exposure to poor air quality and extreme temperature, more work-related weather exposure, and flooding threats.² Extreme heat kills more Wisconsinites than any other weather disasters and is expected to become more frequent and last longer in the future.³ Likewise, flooding is anticipated to become more frequent and intense, increasing drinking water contamination, waterborne illnesses, and mold growth, affecting those with asthma and allergies.

Despite health care's mission to do no harm, the US health care sector is responsible for 8% to 10% of the nation's greenhouse gas emissions and 9% of harmful non-greenhouse air pollutants.⁴ Health care emissions are understandably a large

part of US greenhouse gas emissions. In fact, hospitals are the second most energy-intensive commercial buildings in the country since they are large buildings open 24 hours, 7 days a week while running energy-intensive heating, cooling, and ventilation systems.⁵ Additionally, medical waste, unsustainable materials, production of pharmaceuticals, and anesthesia gas—specifically sevoflurane and desflurane—are large contributors to health care

emissions.⁶ Therefore, while providing up-to-date care, health care systems are major contributors to the health impacts of climate change.

Studies show that health care workers care about how climate change is affecting their patients' health.⁷ One survey showed motivated health care professionals engage in health care sustainability, driven by concerns about these health implications and excessive health care waste, while recognizing their influence as health care professionals.⁸ However, upon review of sustainability survey literature, most surveys target surgery personnel about environmentally sustainable operating room practices and waste reduction.⁹⁻¹² Another survey estimated the ecological footprint¹³ of physicians and medical students and how they can reduce that footprint. A survey of family medicine physicians and their patients¹⁴ focused on climate change and dysphoria, but there were no family medicine surveys specific to health care greenhouse gas emissions or health care emissions reduction. This survey fills that gap by focusing on health care greenhouse gas emissions while engaging clinicians and other staff on specific ways to reduce these emissions.

METHODS

A survey of health care workers sought to measure knowledge of health care greenhouse gas emissions and query survey recipients about specific actions to decrease emissions and identify barriers to waste reduction. It was prepared as part of an educational initiative to engage health care workers—particularly physicians, nurse practitioners, and physician assistants—regarding health care environmental sustainability and to inform health care leaders of health care worker concerns and priorities. UW Health sustainability leaders were involved in developing the survey questions.

A 10-question online convenience survey (Box) was distributed using Qualtrics from February through June 2023 to 211 UW family medicine service line clinicians, which include faculty physicians, nurse practitioners, and physician assistants, and an unknown number of other staff. The survey inquired about their knowledge of health care greenhouse gas emissions and opinion on sustainability priorities at UW Health. There were 2 open-ended questions on sustainability priorities and barriers to waste reduction.

To increase uptake and engagement, the survey was distributed by the author to each of the 211 clinic faculty physicians, nurse practitioners, and physician assistants several days prior to a short presentation given to each clinic on health care greenhouse gas emissions and climate impact. The survey remained open, so a few respondents completed the survey after the presentation. Clinic office managers were asked to distribute the survey to nurses, medical assistants, patient service representatives, and other staff, but since this group of health care workers was not the primary group to engage, there was less focus on capturing this population of health care workers, nor is it known how many of them received the survey.

Box. Environmental Sustainability Survey Questions

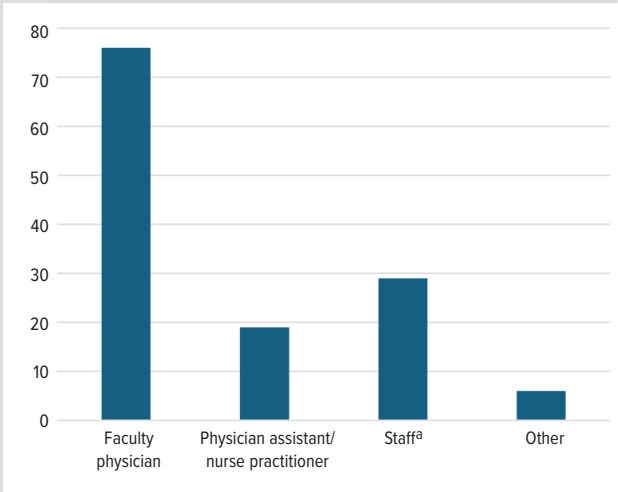
1. Tell us who you are:
 - Faculty physician
 - Physician assistant/nurse practitioner
 - Staff (includes nursing, patient services representative, other employees)
 - Other
2. What specific environmental sustainability issues should be addressed either in your clinic or within UW Health? (Consider specific waste issues, energy efficiency, chemical exposure, healthy food and give details) Please include what your clinic has worked on.
3. Of the following, choose 5 sustainability items that UW Health should prioritize:
 - ENERGY
 - Turn off electronics between use
 - Investing in renewable energy
 - UW Health vehicle emissions
 - WASTE
 - Printing patient instructions/after visit summaries/other purposes
 - Glove, mask, gown waste
 - Single use plastic/metal instrument waste
 - Food waste
 - Packaging waste
 - Recycling
 - TOXINS
 - Health risk of weed killers, insecticides
 - Health risk of cleaning chemicals for rooms and instruments
4. Please list other items that may not be listed in the previous question that you are concerned about in regard to sustainability.
5. Are you aware that it has been estimated that the US health care system is responsible for 8% to 10% of the nation's carbon emissions and 9% of harmful non-greenhouse air pollutants?
6. Are you aware that the majority of the health care greenhouse gas emissions come from purchasing, transportation, and other goods and services?
7. Are you interested in how you may affect purchasing to reduce greenhouse gas emissions?
8. Do you think UW Health should incorporate environmental sustainability into all clinical operations including infectious disease and safety?
9. Are you aware of the work on sustainability at UW Health including sustainability updates in the UW Health Weekly Wrap-Up email and/or the sustainability page on U-Connect?
10. What barriers do you see that may interfere with waste reduction at UW Health and how may UW Health overcome those barriers?

A separate, slightly different survey was distributed to all 47 family medicine residents by a family medicine resident. The survey differed by leaving off one of the open-ended questions, and a question was added asking if they wanted to become more involved in working on sustainability during their residency.

RESULTS

A total of 130 health care workers responded, though 5 individuals did not complete every question. For the target audience of 211 physicians, nurse practitioners, and physician assistants, 95 (45%) responded. There were an additional 35 respondents from other staff (Figure 1). Only 43 of 128 respondents (34%) knew that the health care sector is responsible for 8% to 10% of the US carbon emissions and 9% of harmful non-greenhouse air pollutants (Figure 2). Similarly, only 33 of 127 (26%) knew that the majority of greenhouse gas emissions come from purchasing,

Figure 1. Survey Participants, N=130



^aStaff includes nursing, patient service representative, other employees.

Figure 2. Responses to Survey Question 5, N=128

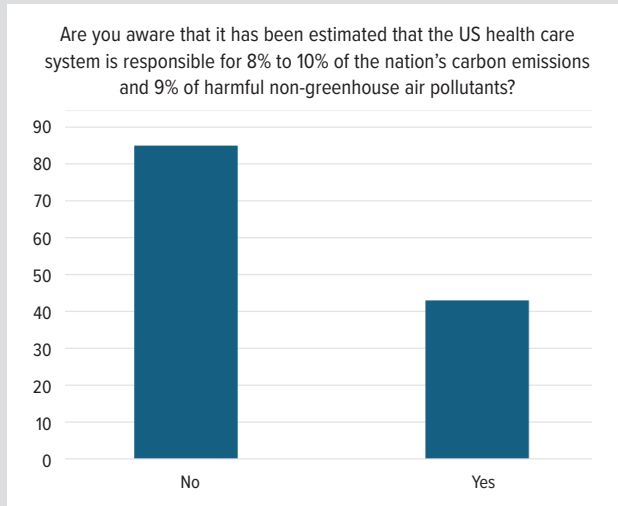
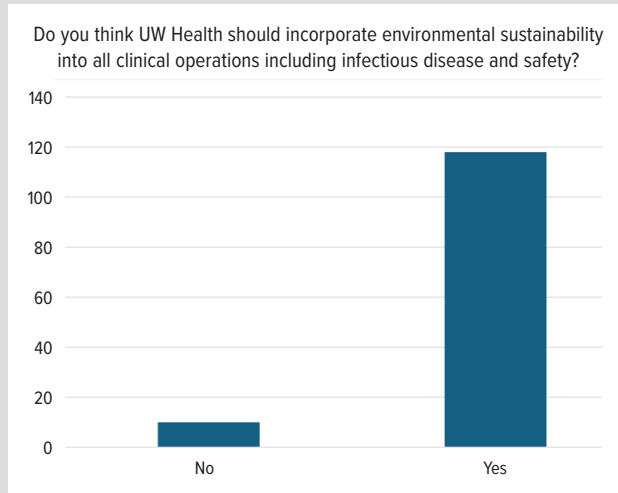


Figure 3. Responses to Survey Question 8, N=128



transportation, and other goods and services. One hundred eighteen of 128 respondents (92%) thought sustainability should be incorporated into all clinical operations, including infectious disease and safety (Figure 3). Ninety-five of 128 respondents (74%) wanted to know how they could affect purchasing to reduce emissions.

When asked to choose 5 top sustainability priorities (Figure 4), the highest-ranking choice was investing in renewable energy (n=88). Other high-ranking choices were glove/mask/gown waste (n=68), recycling (n=61), single use plastic/metal instruments (n=61), packaging waste (n=57), printing patient instructions/after visit summary/other printing (n=55), and health risk of cleaning chemicals for rooms and instruments (n=47).

An open-ended question asked recipients to list other items not listed as a priority. More specific comments about waste (n=24) emerged including “too much glove use,” “stop double bagging,” and “one-time use products.” Nineteen comments were made about recycling such as “proper sorting of waste/recycling,” “getting recycling back after COVID,” and “labeling recycling bins.” Specific comments (n=17) about energy efficiency mentioned “heat and AC [air conditioning] too high,” “lights, computers, radio left on,” and “switch to renewables.” Sixteen respondents commented about paper waste from faxes, forms, and paper on exam tables. Six commented on personal protective equipment (PPE), overuse of gowns and gloves, or switching to reusable gowns. Eight mentioned plastic speculums, including “replace with reusable lighted speculum.” There were 8 food-related comments, including “healthy food options onsite” and “compost at each clinic.” Driving/commuting was mentioned 4 times with suggestions for offering incentives to reduce individuals driving to work and reducing flying for business trips or CME events. Three mentioned adding electric vehicle charging stations to existing clinics. Two mentioned chemical use by a landscaping company.

Forty-two of 129 (33%) respondents were aware of UW Health’s sustainability work and where to find this information on UW Health’s website.

Barriers to waste reduction were identified on an open-ended question. Top barriers mentioned were cost (n=45), complacency (n=31), and time (n=28). Many other barriers were identified, including concern for compromising patient care or safety (n=19), education about sustainability measures (distribution of knowledge/culture to new staff) (n=15), leadership support (higher level not listening to physician concerns) (n=16), other priorities (n=15), culture/convenience (n=14), The Joint Commission “favoring of disposables” (12), demands of protection from infectious disease through PPE (n=9), resources (n=9), and lack of incentives (n=4).

Of the 47 family medicine residents, 22 (47%) responded to a separate survey. Fifty-nine percent knew that the health care sector is responsible for 8% to 10% of the US carbon emissions, and 31% knew that where the majority of the emissions came

from. Eighty-two percent were interested in how they could affect purchasing to reduce emissions, and 100% thought sustainability should be incorporated into all clinical operations. Similar to the other survey, cost (3) was thought to be a top barrier to waste reduction on an open-ended question. Other barriers identified by residents included demands of protection from infectious disease through PPE (2), convenience of disposables (1), and communication/education (1). Thirty-two percent were interested in becoming more involved in working on sustainability during their residency. None of the residents knew about UW Health's sustainability work and where to find it on the website.

DISCUSSION

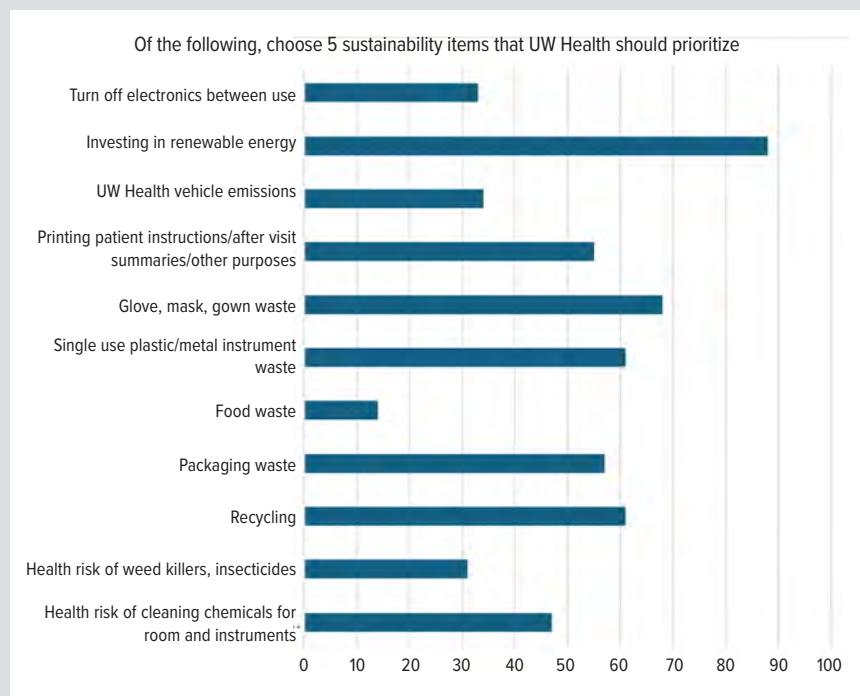
The survey showed that only a third of health care workers knew that the health care sector is a major contributor to US greenhouse gas emissions and air pollutants despite alarmingly high health care greenhouse gas emissions,⁴ defeating health care's mission to do no harm. Significantly more family medicine residents were aware, implying that younger physicians may be better educated on climate change and the health care sector impact.

Despite lack of knowledge of the health care sector greenhouse gas emissions, the vast majority of health care workers agreed that environmental sustainability should be incorporated into all clinical operations, including infectious disease and safety. More specifically, health care workers wanted their health care system to invest in renewable energy, decrease waste, and reduce the use of disposable instruments.

Barriers to waste reduction identified by the survey were many, but cost, complacency, and time were most frequently mentioned. A scoping review of barriers and enablers to implementing environmental sustainability practices identified similar barriers.¹⁵ This survey and the scoping review both identified a focus on leadership and a clear operational vision as keys to successful implementation. Survey respondents identified both leadership and The Joint Commission as barriers to waste reduction. Recognizing climate change as an important public health threat, The Joint Commission recently transformed its priorities, offering a voluntary sustainability certification,¹⁶ which all health care leaders could implement in their health care systems.

One intention of the survey was to inform health care leaders of the strong interest health care workers have to reduce health care greenhouse gas emissions in an effort to catalyze more widespread systemic change. A 2023 *Wisconsin Medical Journal* article¹⁷

Figure 4. Responses to Survey Question 3, N=125^a



^aSome respondents did not choose 5 sustainability items.

encouraged health care providers to use their trusted voices to have conversations about climate change to create public pressure to reduce greenhouse gas emissions. The survey sought to create a collective voice as an even more impactful influence on decision-makers. In this way, surveying other health care systems or medical specialties could illicit additional opinions about health care emissions reduction to collectively influence their health care leaders to execute ambitious environmental sustainability strategies.

Survey Limitations

The survey had several limitations. It was a convenience sampling of the UW Health Department of Family Medicine and Community Health and may not generalize to other medical specialties or health care systems. Knowledge and values around environmental stewardship and health care impacts likely vary in other medical groups. Those who chose not to complete the survey may be less informed about the intersection between climate health and health care's contribution to greenhouse gas emissions. The survey remained open, so a few respondents completed the survey after the clinic presentation. The presentation revealed how health care systems contribute to emissions, so this would favor respondents stating they knew how health care contributes to US carbon emissions. Despite this, results showed the majority of faculty physicians, nurse practitioners, physician assistants, and staff did not know these facts. Another limitation is that we did not use a validated survey instrument, since the survey originally was designed to gauge health care worker's knowledge and opinions

for internal use. Additionally, the project was focused on health care professionals, but since the presentations varied and at times were given to a mix of health care workers, the “other” category was used to capture health care workers who were not otherwise specified.

CONCLUSIONS

In this survey, most health care workers were not aware of the extent that health care contributes to US greenhouse gas emissions but had strong and specific opinions about prioritizing emissions reduction. The vast majority agreed that sustainability should be incorporated into all clinical operations. Surveying other medical specialties or health care systems could identify knowledge gaps and illicit unique opinions to inform health care leaders of their concerns.

Ironically, the health care sector contributes significantly to climate change, jeopardizing public health for all of us, but especially for the most vulnerable populations. Amplifying health care workers’ concerns collectively may inspire their leaders to develop a clearer vision for emissions reduction. It is imperative that UW Health and all health care systems increase education about health care greenhouse gas emissions and implement systemic actions at all levels to most effectively reduce emissions. More research is needed to identify strategies to engage health care leaders to overcome barriers and systemically reduce health care emissions to improve public health.

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Association of Rare Variants in Kidney Developmental Genes With Chronic Kidney Disease and Blood Pressure: A UK Biobank Study

Benjamin L. Spector, MD; Byunggil Yoo, MS; Neil Miller, PhD; Monica Gaddis, PhD; Isabelle Thiffault, PhD; Laurel Willig, MD

ABSTRACT

Introduction: Chronic kidney disease (CKD) and hypertension are heritable traits. The source of this heritability remains largely unknown, and exploration has been limited principally to common genetic variants, with few studies having examined rare variants.

Methods: In this cross-sectional observational study, we evaluate whole exome sequencing data using the UK Biobank to identify the ability of rare variants in 58 kidney developmental genes to predict CKD or elevated blood pressure using logistic regression models with subgroup analysis performed by ancestry.

Results: Significant predictors of CKD included rare variants in *CLCN5* (OR 1.59; 99% CI, 1.02–2.47; $P=0.007$). Predictors of blood pressure included rare variants in *SIX1* (OR 0.57; 99% CI, 0.35–0.94; $P=0.004$) and *NPHS1* (OR 0.84; 99% CI, 0.72–0.99; $P=0.005$), which were protective against blood pressure elevation, and *WT1* (OR 1.58; 99% CI, 1.02–2.45; $P=0.007$), which was associated with elevated blood pressure. In individuals of White British ancestry, rare variants in *SIX1* protected against elevated blood pressure (OR 0.58; 99% CI, 0.34–0.99; $P=0.009$). Among individuals of non-White British ancestry, predictors of CKD included rare variants in *SLC12A3* (OR 2.02; 99% CI, 1.08–3.78; $P=0.004$) and *CALB1* (OR 3.12; 99% CI, 1.15–8.47; $P=0.003$). Presence of rare variants in *WT1* significantly predicted elevated blood pressure (OR 2.49; 99% CI, 1.08–5.78; $P=0.005$).

Conclusions: From this study, we conclude that rare variants in kidney developmental genes contribute to the risk of developing CKD and elevated blood pressure. These associations vary by ancestry.

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INTRODUCTION

Nearly 15% of the United States population suffers from chronic kidney disease (CKD), with approximately 10% having CKD stage 3 or above, generating Medicare costs exceeding \$75 billion annually.¹⁻³ Despite this high prevalence and economic burden, development of novel CKD treatments has largely stagnated.

CKD and elevated blood pressure are complexly interrelated. Hypertension is among the sequelae of kidney dysfunction due to several pathophysiologic mechanisms, including hyperactivity of the renin-angiotensin-aldosterone axis, sodium retention causing fluid overload, and increased sympathetic nervous system activity. Conversely, hypertension is an independent predictor of reduced kidney function. Evidence indicates that an individual's total nephron number, termed "nephron endowment," is inversely correlated to the risk of hypertension and

CKD.^{4,5}

Genetic studies of congenital renal hypoplasia and hypodysplasia, an extreme form of low nephron endowment, suggest that nephron endowment is genetically predetermined.⁶ Similarly, studies have found CKD and estimated glomerular filtration rate (eGFR) have 30% to 70% heritability,⁷⁻¹⁰ and blood pressure is 20% to 50% heritable.¹¹ Genome-wide association studies—the primary method employed to identify the heritability of these traits—have identified a few common variants in kidney developmental genes associated with CKD, supporting the theory that lower nephron endowment may contribute to the general population's CKD risk.^{8,12-14} However, much of the heritability of CKD

Table 1. Demographic Features of Individuals With and Without Elevated Blood Pressure

	All (n=49989)			White British (n=41275)			Non-White British (n=8714)		
	Present	Absent	P value	Present	Absent	P value	Present	Absent	P value
Elevated blood pressure	42 167 (84.4%)	7822 (15.6%)		35 111 (85.1%)	6164 (14.9%)		7056 (81.0%)	1658 (19.0%)	
Vascular heart disease	5165 (12.2%)	267 (3.4%)	<0.001	4293 (12.2%)	222 (3.6%)	<0.001	872 (12.4%)	45 (2.7%)	<0.001
Diabetes	3732 (8.9%)	191 (2.4%)	<0.001	2905 (8.3%)	142 (2.3%)	<0.001	827 (11.7%)	49 (3.0%)	<0.001
Hyperlipidemia	11 625 (27.6%)	587 (7.5%)	<0.001	9730 (27.7%)	466 (7.6%)	<0.001	1895 (26.9%)	121 (7.3%)	<0.001
Overweight	30 997 (73.5%)	3560 (45.5%)	<0.001	25 797 (73.5%)	2825 (45.8%)	<0.001	5200 (73.7%)	735 (44.3%)	<0.001
Smoker	4223 (10.0%)	903 (11.5%)	<0.001	3385 (9.6%)	667 (10.8%)	0.004	838 (11.9%)	236 (14.2%)	0.009

Values are displayed as n (%) unless otherwise indicated.

Table 2. Demographic Features of Individuals With and Without Chronic Kidney Disease

	All (n=49989)			White British (n=41275)			Non-White British (n=8714)		
	Present	Absent	P value	Present	Absent	P value	Present	Absent	P value
Chronic kidney disease	1060 (2.1%)	48 929 (97.9%)		870 (2.1%)	40 405 (97.9%)		190 (2.2%)	8524 (97.8%)	
Vascular heart disease	363 (34.2%)	5069 (10.4%)	<0.001	295 (33.9%)	4220 (10.4%)	<0.001	68 (35.8%)	849 (10.0%)	<0.001
Diabetes	242 (22.8%)	3681 (7.5%)	<0.001	187 (21.5%)	2860 (7.1%)	<0.001	55 (28.9%)	821 (9.6%)	<0.001
Hyperlipidemia	607 (57.3%)	11 605 (23.7%)	<0.001	511 (58.7%)	9685 (24.0%)	<0.001	96 (50.5%)	1920 (22.5%)	<0.001
Overweight	869 (82.0%)	33 688 (68.9%)	<0.001	710 (81.6%)	27 912 (69.1%)	<0.001	159 (83.7%)	5776 (67.8%)	<0.001
Smoker	115 (10.8%)	5011 (10.2%)	0.52	93 (10.7%)	3959 (9.8%)	0.38	22 (11.6%)	1052 (12.3%)	0.75
Elevated blood pressure	998 (94.2%)	41 169 (84.1%)	<0.001	822 (94.5%)	34 289 (84.9%)	<0.001	176 (92.6%)	6880 (80.7%)	<0.001

Values are displayed as n (%) unless otherwise indicated.

and elevated blood pressure remains elusive. Few studies have examined the role of rare variants in explaining this missing heritability.

We aimed to identify genes of kidney development in which rare variants are predictive of blood pressure outcomes or CKD. We accomplished this by using the UK Biobank, a biorepository containing genetic information linked to the electronic health records of approximately 500 000 volunteer participants, to examine the relationship between rare variants in kidney developmental genes and kidney dysfunction, including blood pressure elevation and CKD. We hypothesized that very rare variants in genes implicated in nephrogenesis result in abnormal nephron development and decreased nephron endowment, thereby leading to increased risk of elevated blood pressure and CKD.

METHODS

Study Population

This research was conducted using the UK Biobank Resource, a biorepository of volunteer participants aged 40 to 69 years that links genomic data with deidentified electronic medical record information under application 65332. Analysis was limited to those 49 989 individuals for whom whole exome sequencing data were available at the time of access to the biorepository. Subgroup analyses by ancestry were carried out for those identified as having White British ancestry and those with non-White British ancestry. Individuals were stratified as White British based on principal component analysis carried out by the UK Biobank indicating

similar genetic ancestry in addition to self-identifying as “White British.” This study was determined to be nonhuman subject research by the Children’s Mercy Hospital Institutional Review Board under application STUDY00001390.

Study Variables

Phenotypes of Interest

The primary outcomes of interest included the categorical variables of elevated blood pressure and CKD. Presence of elevated blood pressure was determined through use of *International Classification of Diseases 9th Revision* and *10th Revision* (ICD-9 and ICD-10, respectively) codes, reported high blood pressure, reported use of antihypertensive agents, presence of a numeric value in the field “age high blood pressure diagnosed,” systolic blood pressure ≥ 130 mmHg, or diastolic blood pressure ≥ 80 mmHg. Individuals were considered to have CKD through use of ICD-9 and ICD-10 codes indicating CKD stages 3-5 or end stage kidney disease, calculated eGFR < 60 mL/min/1.73 m² using the CKD-EPI 2021 equation,¹⁵ or presence of an end stage kidney disease report (Appendix 1).

Other clinical covariates included the categorical variables of current smokers, diabetes, vascular heart disease (stroke, angina, myocardial infarction), hyperlipidemia, and overweight defined as body mass index (BMI) ≥ 25 kg/m² or by applicable ICD-9 and ICD-10 codes (Appendix 1). Criteria used to identify the presence of these covariates, including ICD-9 and ICD-10 codes and other available parameters, are summarized in Appendix 1.

Selection of Genes

Eighty-three candidate genes were selected for analysis based on prior studies demonstrating their associations with renal development and kidney function.¹² Genes were categorized according to their contributions to 5 structural compartments in kidney development: (1) early nephron development, (2) podocytes, (3) tubulointerstitial cells, (4) collecting duct, or (5) endothelium (Appendix 2). As there are an estimated 11% of variants missing from the reported UK Biobank whole exome sequencing data,¹⁶ only those genes with reported variants in $\geq 70\%$ of the study population or subgroup of interest were included in final analysis to ensure adequate representation of the cohort.

Definition of Qualifying Variants

Qualifying rare variants were defined as those with minor allele frequency $< 0.1\%$ and classified as nonbenign. Variants were annotated using the multistage variant characterization pipeline, Rapid Understanding of Nucleotide variant Effect Software (RUNES),¹⁷ which incorporates Variant Effect Predictor,¹⁸ comparisons to the National Center for Biotechnology Information dbSNP,¹⁹ known disease-causing variants from the Human Gene Mutation Database (HGMD),²⁰ and in silico prediction of variant consequences with RefSeq²¹ and Ensembl²² annotations. Using this RUNES pipeline, variants were categorized as nonbenign if they were reported previously in HGMD and/or ClinVar (category 1), previously unreported but expected to be pathogenic (category 2), or were a variant of uncertain significance (category 3). Variants were designated as nonqualifying if minor allele frequency was $\geq 0.1\%$ or if the variant was predicted not to cause disease (category 4) or was known to be neutral and/or benign (category 5). Further detail regarding RUNES categorization is summarized in Appendix 3.

Statistical Analysis

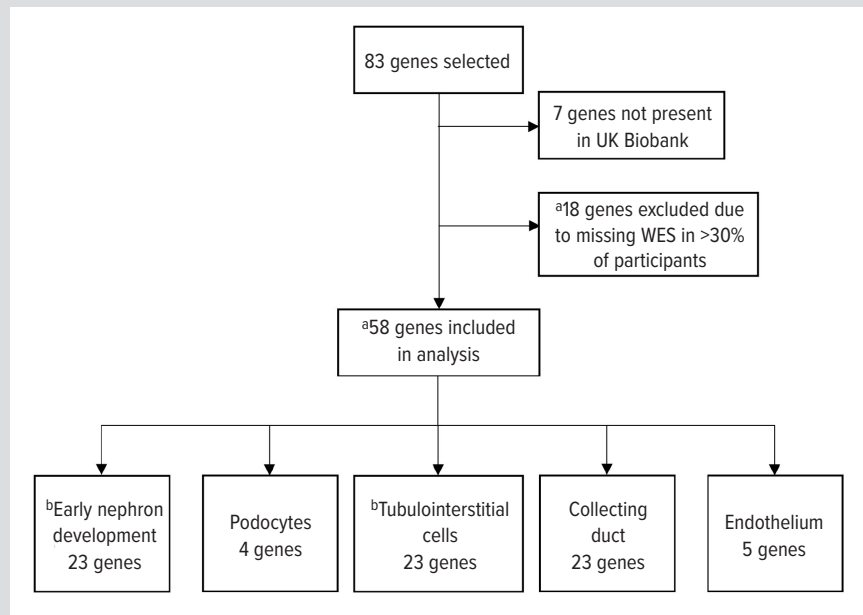
Clinical Covariate Distribution

Chi-square analysis was used to compare the proportions of individuals with clinical covariates outside of the primary outcomes of interest in presence versus absence of disease (Tables 1 and 2).

Association of Qualifying Variants with Outcomes of Interest

To determine association between presence of qualifying variants in different kidney developmental compartments and the primary phenotypes of interest—elevated blood pressure and CKD—binary logistic regression models were created with separate models for each compartment: early nephron development, podocytes,

Figure 1. Flowchart of Gene Selection for Analysis



Abbreviation: WES, whole exome sequencing.

^aIn non-White British individuals, 19 genes were excluded due to missing WES in $>30\%$ of participants, resulting in 57 unique genes in the non-White British subgroup analysis.

^b*LEF1* and *GDNF* were included in the analysis of the early nephron development and tubulointerstitial cells developmental compartments.

tubulointerstitial cells, collecting duct, and endothelium. Genes included in regression models were those with $P < 0.25$ in chi-square univariate analysis assessing association of qualifying variants and the primary outcome of interest. This process was performed separately for each ancestral subgroup analysis (White British and non-White British subgroups). Logistic regression was not carried out for compartments if no genes met the predetermined threshold for inclusion during univariate analysis.

For each outcome of interest, logistic regression analyses included known modifiable risk factors for the disease process. In the case of elevated blood pressure, modifiable risk factors accounted for in the logistic regression models included presence of vascular heart disease, diabetes, overweight, hyperlipidemia, and current smoking status. Given the known associations of vascular heart disease, diabetes, and elevated blood pressure with CKD, these modifiable risk factors were accounted for in the logistic regression models examining CKD. Principal component analysis was performed by the UK Biobank in assignment of ancestry, so accordingly did not require inclusion in our regression models. The degrees of variance of these traits explained by our logistic regression models were calculated by Cox and Snell's R^2 and Nagelkerke's R^2 .

Statistical significance was set at a Bonferroni-corrected critical α -level of 0.01 to account for multiple comparisons.

Qualifying Variant Distribution

We hypothesized that individuals with outcomes of interest pos-

Table 3. Logistic Regression Models Assessing the Association of Qualifying Variants With Presence of Elevated Blood Pressure by Developmental Compartment

Compartment	All			White British			Non-White British		
	Gene	OR (99% CI)	P value	Gene	OR (99% CI)	P value	Gene	OR (99% CI)	P value
Early nephron development	<i>ANPEP</i>	0.87 (0.70–1.08)	0.10	<i>CITED1</i>	0.66 (0.35–1.23)	0.085	<i>CRABP2</i>	0.73 (0.32–1.68)	0.33
	<i>CITED1</i>	0.74 (0.42–1.30)	0.16	<i>COL2A1</i>	0.92 (0.74–1.15)	0.34	<i>EYA1</i>	1.29 (0.78–2.12)	0.19
	<i>COL2A1</i>	0.86 (0.71–1.04)	0.043	<i>CRABP2</i>	1.67 (0.77–3.62)	0.086	<i>PAX2</i>	1.97 (0.90–4.34)	0.026
	<i>ETV4</i>	1.55 (0.73–3.29)	0.13	<i>ETV4</i>	2.21 (0.84–5.82)	0.036	<i>WT1</i>	2.49 (1.08–5.78)	0.005
	<i>JAG1</i>	0.98 (0.77–1.25)	0.82	<i>LEF1</i>	0.84 (0.61–1.15)	0.14			
	<i>LEF1</i>	0.89 (0.68–1.18)	0.29	<i>SIX1</i>	0.58 (0.34–0.99)	0.009			
	<i>SIX1</i>	0.57 (0.35–0.94)	0.004						
	<i>WT1</i>	1.58 (1.02–2.45)	0.007						
Podocytes	<i>NPHS1</i>	0.84 (0.72–0.99)	0.005	<i>NPHS1</i>	0.823 (0.675–1.004)	0.011			
	<i>PODXL</i>	0.86 (0.66–1.11)	0.12						
Tubulointerstitial cells	<i>CD248</i>	1.22 (0.87–1.71)	0.13	<i>CLCN5</i>	0.846 (0.670–1.070)	0.066	<i>CLCN5</i>	0.67 (0.44–1.02)	0.013
	<i>CLCN5</i>	0.87 (0.70–1.07)	0.079	<i>COL1A1</i>	0.861 (0.693–1.069)	0.075	<i>COL3A1</i>	1.10 (0.75–1.61)	0.53
	<i>COL1A1</i>	0.95 (0.79–1.15)	0.49	<i>CSPG4</i>	0.933 (0.778–1.119)	0.32	<i>CUBN</i>	1.21 (0.89–1.66)	0.11
	<i>CSPG4</i>	0.91 (0.78–1.07)	0.15	<i>DES</i>	1.233 (0.742–2.050)	0.29	<i>DES</i>	1.39 (0.81–2.39)	0.11
	<i>DES</i>	1.27 (0.84–1.90)	0.14	<i>FOXD1</i>	0.896 (0.676–1.188)	0.32	<i>FOXD1</i>	1.20 (0.76–1.88)	0.30
	<i>LEF1</i>	0.80 (0.61–1.05)	0.035	<i>LEF1</i>	0.823 (0.598–1.133)	0.12	<i>LRP2</i>	0.94 (0.76–1.16)	0.43
	<i>PAPPA2</i>	1.07 (0.90–1.30)	0.33	<i>PAPPA2</i>	1.106 (0.892–1.372)	0.23	<i>MCAM</i>	1.13 (0.69–1.83)	0.53
	<i>SERPINE2</i>	0.82 (0.58–1.15)	0.13	<i>SLC12A1</i>	1.180 (0.937–1.487)	0.064	<i>PDGFRB</i>	0.96 (0.69–1.35)	0.77
	<i>SLC12A1</i>	1.16 (0.94–1.42)	0.067	<i>TPM2</i>	1.730 (0.991–3.018)	0.011	<i>TPM2</i>	1.43 (0.77–2.65)	0.13
	<i>SLC12A3</i>	0.93 (0.79–1.10)	0.25						
	<i>TPM2</i>	1.38 (0.89–2.15)	0.061						
	Collecting duct	<i>KRT8</i>	1.11 (0.88–1.40)	0.27	<i>CALB1</i>	1.133 (0.787–1.631)	0.38	<i>KRT8</i>	1.18 (0.78–1.78)
				<i>KRT8</i>	1.104 (0.819–1.486)	0.39			
Endothelium	<i>FLT1</i>	0.91 (0.78–1.07)	0.14				<i>KDR</i>	1.13 (0.83–1.56)	0.31
							<i>TEK</i>	1.10 (0.72–1.68)	0.58

Table 4. Logistic Regression Models Assessing the Association of Qualifying Variants with Presence of Chronic Kidney Disease by Developmental Compartment

Compartment	All			White British			Non-White British		
	Gene	OR (99% CI)	P value	Gene	OR (99% CI)	P value	Gene	OR (99% CI)	P value
Early nephron development	<i>CITED1</i>	1.46 (0.45–4.78)	0.41	<i>ALDH1A1</i>	1.143 (0.574–2.277)	0.019	<i>CCND1</i>	2.50 (0.64–9.82)	0.085
	<i>HNF1A</i>	0.34 (0.11–1.08)	0.016	<i>CITED1</i>	1.429 (0.380–5.378)	0.23	<i>COL2A1</i>	0.37 (0.10–1.39)	0.054
	<i>ITGA8</i>	0.79 (0.53–1.20)	0.15	<i>HNF1A</i>	0.182 (0.029–1.137)	0.19	<i>CRABP2</i>	3.23 (0.63–16.63)	0.065
	<i>PAX8</i>	0.48 (0.13–1.78)	0.15	<i>SIM2</i>	0.581 (0.242–1.394)	0.037	<i>EYA1</i>	1.47 (0.49–4.47)	0.37
	<i>SOX9</i>	0.59 (0.22–1.59)	0.17	<i>SOX9</i>	0.414 (0.112–1.525)	0.058	<i>LEF1</i>	1.29 (0.42–3.89)	0.56
	<i>WT1</i>	0.70 (0.26–1.89)	0.35				<i>PAX2</i>	0.00	1.00
Podocytes	<i>PODXL</i>	1.47 (0.86–2.51)	0.065	<i>NPHS2</i>	0.49 (0.11–2.22)	0.23	<i>PDGFRB</i>	1.42 (0.66–3.06)	0.25
							<i>SALL1</i>	1.95 (0.80–4.73)	0.054
Tubulointerstitial cells	<i>CDH1</i>	1.39 (0.78–2.46)	0.14	<i>CLCN5</i>	1.49 (0.96–2.31)	0.019	<i>CDH1</i>	2.15 (0.80–5.76)	0.045
	<i>CLCN5</i>	1.59 (1.02–2.47)	0.007	<i>COL3A1</i>	1.25 (0.78–2.01)	0.23	<i>CLCN5</i>	2.11 (0.87–5.09)	0.03
	<i>CLDN1</i>	0.57 (0.090–3.57)	0.43	<i>CSPG4</i>	0.80 (0.52–1.24)	0.19	<i>CLDN1</i>	0.00	1.00
	<i>COL3A1</i>	1.15 (0.71–1.86)	0.46	<i>LRP2</i>	0.77 (0.55–1.06)	0.037	<i>COL1A1</i>	1.46 (0.75–2.82)	0.15
	<i>CSPG4</i>	0.82 (0.54–1.24)	0.21	<i>SLC12A3</i>	0.71 (0.45–1.13)	0.058	<i>DES</i>	1.20 (0.42–3.40)	0.66
	<i>FOXD1</i>	1.27 (0.74–2.17)	0.26	<i>TPM2</i>	0.30 (0.048–1.88)	0.091	<i>FOXD1</i>	2.03 (0.90–4.57)	0.025
	<i>UMOD</i>	1.18 (0.67–2.06)	0.45				<i>LEF1</i>	1.80 (0.67–4.82)	0.13
							<i>LRP2</i>	1.21 (0.73–2.00)	0.33
Collecting duct	<i>CALB1</i>	1.48 (0.79–2.78)	0.11				<i>CALB1</i>	3.12 (1.15–8.47)	0.003
	<i>GATA2</i>	0.53 (0.17–1.71)	0.16				<i>GATA2</i>	0.00	1.00
	<i>RET</i>	1.47 (0.93–2.35)	0.031				<i>RET</i>	1.99 (0.98–4.06)	0.013
Endothelium	<i>FLT1</i>	1.31 (0.92–1.87)	0.047	<i>KDR</i>	1.27 (0.86–1.86)	0.11			
	<i>KDR</i>	1.19 (0.84–1.67)	0.20						

sessed more qualifying variants relative to the overall study population. To assess this hypothesis, the number of qualifying variants within each individual was categorized into 1 of 5 groups: no qualifying variants, 1 variant, 2 variants, 3 to 5 variants, and 6 or more variants. Chi-square analysis was performed comparing individuals with and without disease for each phenotype of interest to determine if the distribution within each cohort matched the distribution of the larger study population. Subgroup analyses by ancestry were performed using identical methods. Statistical significance was set at a critical α -level of 0.05.

Statistical Software

Statistical analysis was performed using SPSS version 28.0.0.0 (Statistical Package for the Social Sciences; SPSS Inc, Chicago, Illinois).

RESULTS

Genes Included in Analysis

Of the 83 genes initially identified, 58 were included in final analysis (57 in the non-White British subgroup) (Figure 1, Tables 3 and 4). A full listing of identified genes and rationale for exclusion is provided in Appendix 2. A numeric count of unique qualifying rare variants per gene, median number of individuals possessing each variant by gene, RUNES category, and functional impact is summarized in Appendix 4.

Association of Qualifying Variants and Phenotypes of Interest

Elevated Blood Pressure

When examining the cohort in its entirety, we found that qualifying variants in *SIX1* (OR 0.57; 99% CI, 0.35–0.94; $P=0.004$) and *NPHS1* (OR 0.84; 99% CI, 0.72–0.99; $P=0.005$) were protective against elevated blood pressure, whereas qualifying variants in *WT1* (OR 1.58; 99% CI, 1.02–2.45; $P=0.007$) were predictive of elevated blood pressure. Among White British individuals, qualifying variants in *SIX1* were protective against blood pressure elevation (OR 0.58; 99% CI, 0.34–0.99; $P=0.009$). In subgroup analysis of non-White British individuals, presence of qualifying variants in *WT1* in the early nephron development compartment was the only statistically significant predictor of elevated blood pressure (OR 2.49; 99% CI, 2.49–5.78; $P=0.005$). Though statistical significance was not reached, qualifying variants in *CLCN5* in tubulointerstitial cell regression model approached significance in protection against elevated blood pressure (OR 0.67; 99% CI, 0.49–0.92; $P=0.013$). Among genes significantly associated with elevated blood pressure, there was no difference in distribution of functional impact of variants between individuals with versus those without elevated blood pressure (Appendix 5A).

Odds ratios of all genes included in the regression models of the primary and subgroup analyses are summarized in Table 3.

Chronic Kidney Disease

In the analysis of the cohort in its entirety, presence of a qualifying

variant in *CLCN5* as part of the logistic regression model for the tubulointerstitial cell compartment was the only significant predictor of CKD (OR 1.59; 99% CI, 1.02–2.47; $P=0.007$).

There were no genes in which qualifying variants were significant predictors of CKD in White British subgroup analysis. In non-White British individuals, genes in which qualifying variants were significant predictors of CKD included *SLC12A3* (OR 2.02; 99% CI, 1.08–3.78; $P=0.004$) for tubulointerstitial cells and *CALBI* in the collecting duct compartment (OR 3.12; 99% CI, 1.15–8.47; $P=0.003$). Among genes significantly associated with CKD, there was no difference in distribution of functional impact of variants between individuals with versus those without CKD (Appendix 5B).

Odds ratios of all genes included in regression models of primary and subgroup analyses are summarized in Table 4.

Qualifying Variant Distribution

Elevated Blood Pressure

There were no significant differences in the proportion of qualifying variant counts among individuals with elevated blood pressure versus the full study population. This was true in the primary analysis, as well as in subgroup analyses (Figure 2A-C).

Chronic Kidney Disease

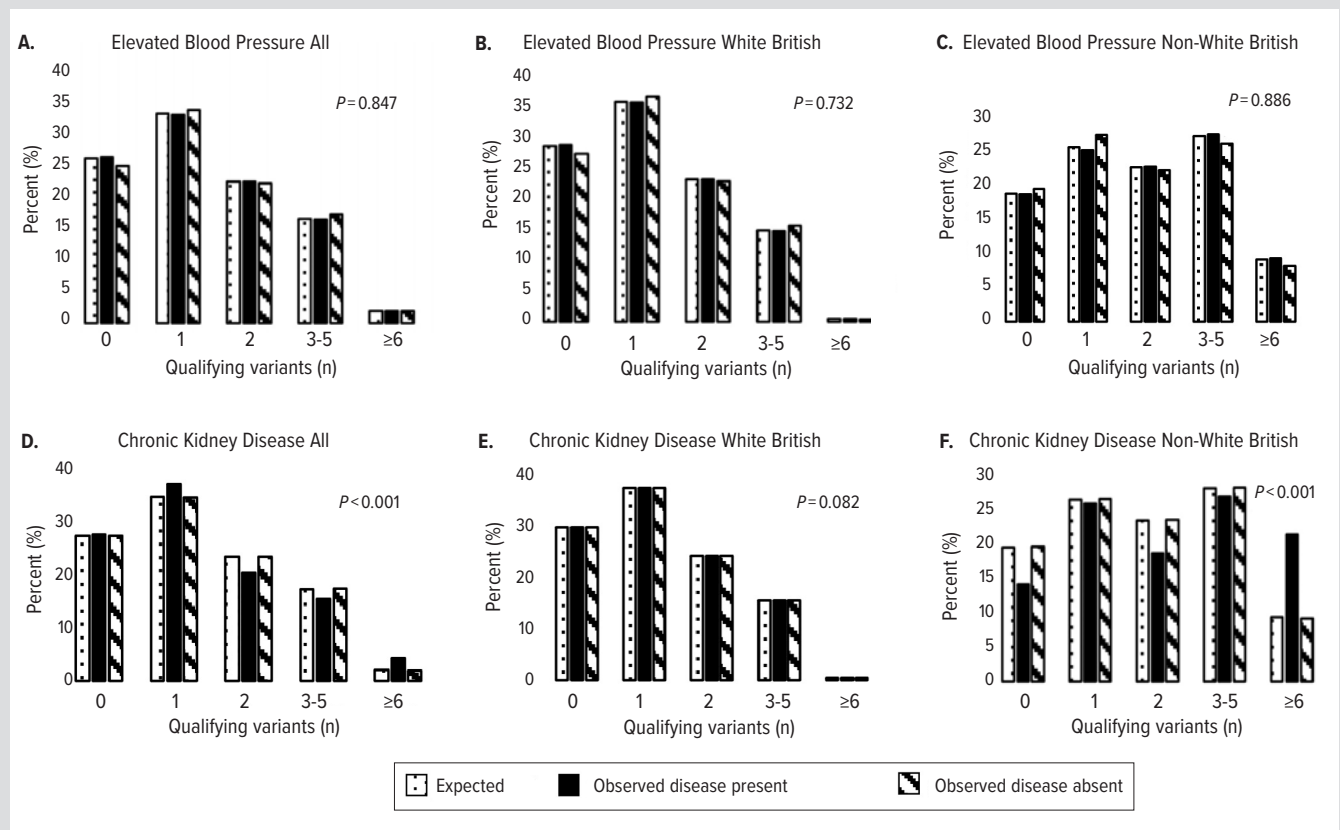
The proportion of variant counts within individuals with CKD differed significantly from proportions found in the overall study population ($P<0.001$), with overall higher proportions of individuals with no qualifying variants or 6 or more qualifying variants among individuals with CKD. When examining participants of White British ancestry, we found that the distribution of variant counts within individuals with CKD did not significantly differ from proportions found in the overall White British subpopulation ($P=0.082$). In individuals of non-White British ancestry, we found that a higher proportion of individuals with 6 or more qualifying variants was present in individuals with CKD versus the larger non-White British subpopulation ($P<0.001$) (Figure 2D-F).

DISCUSSION

Our study highlights several important findings. We demonstrated that rare variants in kidney developmental genes are associated with hypertension and CKD, and that the implicated genes vary by ancestry. Further, while rare variants in some genes predict deleterious consequences, their presence in others confers a protective effect. Finally, individuals with CKD possess higher numbers of qualifying rare variants in kidney developmental genes than is expected relative to the larger population.

We found that rare variants in some genes implicated in structural kidney development are associated with development of elevated blood pressure and CKD later in life. This finding is in keeping with our hypothesis that rare variants in these genes contribute to nephron endowment and supports the idea that rare

Figure 2. Expected Versus Observed Qualifying Variant Counts in the Overall Cohort (A, D), Individuals Genetically Identified as White British (B,E), and Genetically Identified as Non-White British (C,F)



genetic variants—rather than exclusively common variants—contribute to the missing heritability in kidney function and disease. However, large proportions of the variance in blood pressure and CKD are not accounted for by our logistic regression models, which individually explain 6.9% to 15.3% of the variance in the case of blood pressure, and 1.1% to 9.2% of the variance in CKD. This unexplained variance suggests other factors (eg, variants in other genes, gene-gene, or gene-environment interactions) are at play, and evaluation of rare variants should be expanded to a wider selection of genes.

Interestingly, the specific genes in which rare variants predicted elevated blood pressure or CKD differed by ancestry. It is possible we are capturing the rare variants that predispose some populations to hypertension and CKD (eg, individuals of South Asian, sub-Saharan African, Aborigine, and Hispanic descent) when compared to White British individuals. Alternatively, such variation may arise from the heterogeneity of the non-White British subgroup, as this subgroup represents an admixture of many ancestral backgrounds. The characterization of certain variants as “rare” may be inaccurate, as they may be common variants within a more specific ancestral subgroup that is underrepresented in the UK Biobank. In this way, the number of qualifying variants within the non-White British subgroup may be overestimated.

Surprisingly, our analyses demonstrated that in some instances, rare qualifying variants have a protective rather than deleterious effect on blood pressure. This finding potentially stems from our definition of a qualifying variant. Because variants of uncertain significance (RUNES category 3) were included in our definition and can convey deleterious, neutral, or protective effects, some qualifying variants may be protective but have yet to be classified. To examine this effect further, we performed separate binary logistic regression analyses examining the ability of qualifying RUNES category 3 variants to predict elevated blood pressure and CKD, with results demonstrating associations in protective as well as deleterious directions (Appendix 6). Adding to this hypothesis is the large proportion of variants of uncertain significance that comprise qualifying variants in genes predictive of disease presence/absence, with those ranging from 64.1% to 100% of the qualifying variants in each predictive gene depending on disease state and ancestry (Appendix 7). An additional consideration is that qualifying variants in some kidney developmental genes may lead to impaired handling of sodium and water, as is seen in many tubulopathies, which could lead to hypotension. This consideration is supported by a prior study by Ji et al demonstrating that rare variants in the salt handling genes *SLC12A3*, *SLC12A1*, and *KCNJ1(ROMK)* are associated with reduced blood pressure.²³ Of note, rare variants in

SLC12A3 and *SLC12A1* were evaluated in our study but were not significantly associated with blood pressure.

Finally, we found that individuals with CKD possess higher numbers of rare variants in kidney developmental genes than would be expected in our entire cohort and in the non-White British subgroup. The fact that this association did not reach significance in the White British subgroup once again calls into question our characterizations of variants as “rare” among the non-White British subgroup. We attempted to account for this potential discrepancy by calculating expected qualifying variant counts for the whole study cohort and for each of the ancestral subgroups separately. Our finding that, among those with CKD, the proportion of individuals with high carriage of qualifying variants (ie, 6 or more variants) was ≥ 2 times the proportion found in the overall populations in the primary analysis and in non-White British subgroup analysis suggests there could be an additive effect relating the number of rare variants in kidney developmental genes possessed by an individual to CKD risk (Figure 2).

Limitations

Our study does have limitations. Relative to the general population of the United Kingdom, the UK Biobank tends toward a healthy subject bias with lower rates of all-cause mortality, cancer, smoking, alcohol use, and obesity, in addition to fewer self-reported health conditions.²⁴ This bias is seen in our analysis, with only 2.1% of the study population having CKD stage 3 and above compared to the estimated 10% of the general population.¹ Despite this bias, a large-scale meta-analysis by Batty et al comparing risk associations in the UK Biobank relative to risk associations in pooled data from 18 English and Scottish studies representative of the general population found that the associations in the UK Biobank were generalizable.²⁵ This finding supports our assertion that the significant associations in rare genetic variants and elevated blood pressure and CKD in the present study can be applied more generally.

However, caution is still needed when generalizing findings to the non-White British subgroup. As discussed previously, the admixed nature of the non-White British group and low representation of this group within the UK Biobank could lead to mischaracterization of genetic variants as rare due to ethnic disparities within the UK Biobank, thereby increasing risk of type 1 error. Alternatively, because the low number of non-White British individuals decreases the power of this subgroup analysis, the potential for a type 2 error rate is elevated as it pertains to associations in non-White British individuals. These possibilities highlight the need to enhance diversity and decrease disparities that exist within genomic research. The limitation of these relatively low sample sizes may be overcome to some extent with larger replicative studies, as the number of individuals possessing whole exome sequencing data within the UK Biobank has rapidly expanded to more than 450 000 participants since we accessed the biorepository.

A final limitation of our study is the use of whole exome sequencing and the restriction to genes implicated in kidney development. As we are increasingly appreciating, much genetic regulation takes place in intronic regions, which is missed through use of whole exome sequencing. The limited number of genes we examined limits our ability to examine gene-gene and gene-environment interactions. However, by limiting our analysis to those genes involved in nephrogenesis, we were able to support the hypothesis that rare variants in genes that could impact nephron endowment are predictive of elevated blood pressure and CKD, an inference that could not be made as easily in a broader genome-wide association study.

CONCLUSIONS

This study demonstrates that rare variants in kidney developmental genes can help predict the presence or absence of elevated blood pressure and chronic kidney disease; however, the implicated genes vary based on ancestry. These findings indicate that rare variants explain a portion of the risk of developing hypertension and CKD and serve as putative targets for disease risk screening in the future as the field of precision medicine continues to expand.

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Data Availability: The data generated from this study can be found within the published article and its appendices. Raw data of the UK Biobank are available from <https://www.ukbiobank.ac.uk>.

Appendices: Available at wmjonline.org.

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Evaluation of LGBTQ+ Health Education in the Preclinical Curriculum at a Public Midwest Medical School

Tess I. Jewell, BA; Elizabeth M. Petty, MD

ABSTRACT

Introduction: People who identify as lesbian, gay, bisexual, transgender, and queer/questioning (LGBTQ+) face health disparities and negative health care experiences. Medical student education may be leveraged as a strategy to improve care for these patients; however, studies suggest gaps in current LGBTQ+ health education.

Objective: This project sought to evaluate how LGBTQ+ health is taught in the preclinical curriculum at a Midwest medical school.

Methods: The institution's curriculum repository was searched systematically for materials that included information on LGBTQ+ health used in preclinical courses in the 2021-2022 academic year. Information was compiled based on previously utilized evaluation tools and additional measurements developed by the authors to provide further clarity.

Results: Seventy items were identified in the curriculum repository; 38 (54%) were required for students to review. Commonly addressed topics include communication skills, terminology, and variations in sex characteristics. Topic gaps identified include mental health, cancer screening, and gender-affirming care. Among the 33 clinical skills sessions in the preclinical curriculum, 5 standardized patient cases included LGBTQ+ patient representation.

Conclusions: There was variability in coverage of LGBTQ+ health topics, with particularly more on language and variations in sex characteristics and less on mental health, cancer screening, and gender-affirming care. This study identifies opportunities to improve LGBTQ+ health education and demonstrates a framework that may be applied to evaluate curricula in other programs, to ideally enhance coverage of this material and, ultimately, improve care of LGBTQ+ patients.

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INTRODUCTION

People who identify as lesbian, gay, bisexual, transgender, and queer/questioning (LGBTQ+) tend to have worse health compared to their cisgender and heterosexual counterparts¹ and may have negative experiences when seeking health care.² LGBTQ+ communities also face myriad health disparities,³⁻⁵ which may be driven in part due to LGBTQ+ individuals not feeling comfortable seeking care^{3,6} or insufficient clinician knowledge about preventive care for these communities.⁴

Medical education may be one area of intervention to address LGBTQ+ health disparities and improve patient experiences by equipping students with knowledge and skills to serve LGBTQ+ individuals.^{2,7} In 2014, the Association of American Medical Colleges (AAMC) published a report detailing 8 domains with 30 total competencies for medical students to address the needs of LGBTQ+ patients in medical education.⁷ Of note, some people who are

born with variations in sex characteristics (also known as differences in sex development) or who identify as intersex also identify within the LGBTQ+ community and are considered within the "LGBTQ+" umbrella in this study, and these communities also were included in the AAMC report.⁷

Despite these guidelines, since 2018, detailed evaluations of preclinical curriculum have been reported at only 4 private medical schools, all of which have found gaps in LGBTQ+ health topic coverage.⁸⁻¹¹ Different strategies were used across schools to evaluate curriculum content. A team at the Medical of Wisconsin recently audited its preclinical curriculum compared to a textbook

on sex and gender.⁸ Two other studies utilized LGBTQ+ health learning objectives from Vanderbilt University to evaluate its curricula.^{9,10} A team at Boston University developed a sexual and gender minority curriculum assessment tool (SGM-CAT) based on the competencies in the AAMC report, which it used to evaluate the curriculum.¹¹ In addition to these comprehensive curriculum evaluations, a number of other studies utilized data from student or faculty perceptions about their curriculum, which have also identified gaps in the LGBTQ+ health-related education at medical schools.¹² This project sought to evaluate the degree to which LGBTQ+ health topics are taught in the preclinical curriculum at a public medical school in the Midwest, in a state with mixed political ideologies and diverse perspectives on gender-affirming care and LGBTQ+ issues.

METHODS

Setting

The University of Wisconsin School of Medicine and Public Health (UWSMPH) is 1 of 2 medical schools in Wisconsin and the only public medical school in the state. It is located in Madison, Wisconsin, and has 3 statewide academic campuses with hubs in La Crosse, Marshfield, and Milwaukee, and teaching sites throughout the state. The curriculum in the MD program is organized into 3 “phases.” Phase 1 is the preclinical part of the curriculum and consists of the first 18 months of medical school and focuses on basic sciences while integrating public health and clinical medicine. This phase is broken into 6 integrated preclinical blocks. Phase 2 consists of 12 months of integrated clinical rotations organized into 4 thematic blocks. Phase 3 involves the last 16 months of medical school and is dedicated to career exploration, acting internships, elective courses, and internship preparation.

Curricular Components

In the 2021-2022 academic year, the phase 1 curriculum included the following required learning experiences for preclinical students: 364 lectures, 18 classes with patients (eg, patient panel), 2 medium group learning sessions, 16 anatomy labs, 86 case-based learning sessions, 35 patient-centered education cases, 33 clinical skills sessions, 14 clinical learning experiences (eg, outpatient primary care preceptor clinic), 340 prework videos, 110 videos or assignments that were required to be completed after lecture or another course activity, 178 other required prework learning activities (eg, a peer-reviewed journal article), and 43 other required sessions. That same year, the curriculum included the following optional aspects: 9 team-based learning sessions, 241 “core resources,” and 438 “additional resources” or other optional materials. “Core resources” are written materials that are highly recommended for students to review alongside the corresponding lecture content. “Additional resources” may take the form of videos, websites, peer-reviewed articles, or other written materials

that are provided to supplement students’ learning, typically going in more depth or providing more context to the corresponding lecture content.

Identifying Curriculum Materials with LGBTQ+ Health Content

The institution’s curriculum repository, managed through iSEEK (iSeek.ai), was searched systematically between August 2022 and September 2023 using terms related to LGBTQ+ identities for materials that included information on LGBTQ+ health used in preclinical courses in the 2021-2022 academic year. Specific terms used were “LGBT,” “gay,” “lesbian,” “transgender,” “trans,” “intersex,” “queer,” “non-binary,” “nonbinary,” “homosexual,” “transsexual,” “sexual and gender minorities,” “gender dysphoria,” “gender fluid,” and “gender-incongruent.” All materials with any mention of LGBTQ+ health were included for review and analysis.

The standardized patient cases used to teach clinical skills sessions are not provided to students and, therefore, are not accessible through the curriculum repository. Members of the clinical skills team provided the cases that included LGBTQ+ identifying patients to the research team for review for this project. These cases are used in clinical skills sessions that involve groups with 4 students each, who work with a standardized patient actor who portrays the patient in the written case scenario. The written patient cases are provided to the standardized patient as a guide, and the precise details of what is discussed in the scenarios with students can be variable. The gender identity, pronouns, sexual orientation, and presenting concerns for each standardized patient case were recorded.

Curriculum Material Review

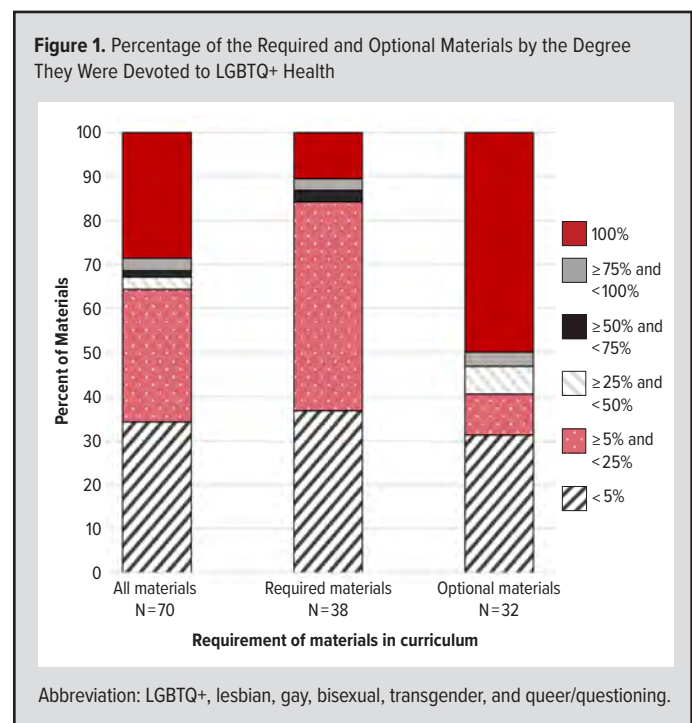
Information from all materials identified as having any material related to LGBTQ+ health was recorded, including the following: if it was a material that was required or optional for students to review, the block during which the material was provided, the type of material (eg, lecture, case-based learning session, team-based learning session, or anatomy session), and the amount of the material that was dedicated to LGBTQ+ health. This amount was determined based on the percentage of slides in presentations or sentences in written documents that were specific to LGBTQ+ health and were classified as <5%, ≥5 and <25%, ≥25 and <50%, ≥50% and <75%, ≥75 and <100%, or 100%. The percentages were determined for each material individually and designated by the amount of the material that addressed any aspect of LGBTQ+ health.

The parts of the material specific to LGBTQ+ health were compiled into a spreadsheet based on the criteria in the SGM-CAT¹¹ and Vanderbilt University learning objectives as described in other medical school curriculum evaluations.^{9,10} Both tools were used in an effort to support a more robust evaluation of the curriculum with opportunities for comparison of curricula across programs as these tools were used at different institutions. Given the vari-

able nature of what might be discussed specifically in standardized patient cases, these cases were included for the “standardized patient cases” learning objective but were not included as containing information about any other specific topics.

Materials also were given a rating on the depth of their coverage of each learning objective or tool criterion. The rating when material on the topic was present could be “+,” “++,” or “+++.” The criteria for this rating scale were developed by the authors, and then 1 author (TIJ) scored the materials accordingly, and all questions were discussed with the senior author (EMP) to come to consensus. This scale was developed as the authors found that the frequency of times a topic in the SGM-CAT or Vanderbilt University learning objectives was mentioned across curriculum items did not correlate consistently to the amount of material in total that students received on the topic, as one curriculum item may mention the topic peripherally while another devotes the majority of the material in the item to the topic. For each topic in the SGM-CAT and Vanderbilt University learning objectives, all corresponding content for the topic across all required and optional curriculum materials was compiled and the depth rating was made based off of the compilation on each topic across the preclinical curriculum. Of note, the standardized patient cases were excluded from the determination of amount and depth of the material dedicated to LGBTQ+ health given the high potential for variability between different actors and how scenarios unfold depending on student approaches and questions.

The depth rating “+” corresponds to limited coverage of the topic; for example, the topic is mentioned in a sentence or figure in 1 or more materials, but further context is not provided. The depth rating “++” corresponds to moderate coverage of topic, in which the topic is explained in some detail, however, there are essential gaps that are not covered. For example, for the SGM-CAT item “contraception, family planning, and fertility,” a rating of “++” was made for the required preclinical curriculum materials because across all required materials, fertility (including fertility preservation) and aspects of family planning were discussed related to LGBTQ+ health, but there was very limited discussion of contraception within LGBTQ+ health. Specifically, this included content from a lecture about fertility, conception, and family planning that described related considerations for LGBTQ+ communities in clinical care (eg, the importance of discussing fertility preservation before initiating gender-affirming hormonal medications or surgery that long-term estrogen exposure may damage testicles), as well as hypothetical cases to teach students learn about fertility options (eg, cryopreservation, gestational carrier) for different couples (specifically a transgender woman in a relationship with a cisgender woman and a transgender man in a relationship with a cisgender man). The only mention of contraception related to LGBTQ+ health was a note in a lecture about LGBTQ+ health equity that stated that medical provider discrimination may include chastising someone for not taking birth control despite



it being irrelevant to them in a same-sex relationship. There was no discussion around the fact that some providers may not offer contraceptives to female patients in a same-sex relationship due to an assumption that they don't need contraception, as well as no discussion about the fact that testosterone is not a form of contraception, which can be a common misconception.

The depth rating “+++” corresponds to thorough coverage of topic, in which the topic is explained to a level of detail that would provide sufficient coverage for a medical student to have at least a basic understanding of the full concept, but not necessarily including all details that an expert in this field would have. For example, the Vanderbilt University learning objective topic “gender dysphoria vs transgender” in required materials received a rating of “+++” because the 1 curriculum item that addressed this, which was a lecture about terminology, defined transgender and gender dysphoria and also explained how the terms were similar and different.

RESULTS

Seventy items in the preclinical curriculum were identified in the curriculum repository as having material related to LGBTQ+ health. This included 23 lectures, 8 core resources, 1 case-based learning session, 24 additional resources, 4 materials for clinical skills sessions, 1 prework video, and 9 other required preparation materials. Thirty-eight (54%) items were required for students to review and 32 (46%) were optional. Across the 33 required clinical skills sessions in the preclinical curriculum, 4 sessions included at least 1 case that portrayed an LGBTQ+ identifying patient, and 5 total patient cases were identified.

There was wide variability regarding how much of the

required and optional material was dedicated to LGBTQ+ health-related content. This is displayed graphically in Figure 1. Among required course materials, almost half (46%) of the materials consisted of between 5% and 25% LGBTQ+ health content, with 36% having less than 5%, 3% from 50% to 75%, 3% from 75% to 100%, and 10% were fully dedicated to LGBTQ+ health content. Among optional course materials, half (50%) were 100% focused on LGBTQ+ health content, with 31% having less than 5%, 9% having 5% to 25%, 6% having 25% to 50%, and 3% having 75% to 100% of their content devoted to LGBTQ+ health content.

The number of required and optional materials that addressed the Vanderbilt University learning objectives and SGM-CAT criteria, as well as the depth provided for each item, are displayed in Tables 1 and 2, respectively. The most frequently addressed of the Vanderbilt University learning objective topics were “communication/interview skills,” “embryology—variations in sex characteristics,” and “embryology—gender vs sex.” (Note that the language used in the tool for “embryology—variations in sex characteristics” was “disorders of sex development;” however, given the outdated and pathologizing nature of this terminology, we use “variations in sex characteristics”¹³ instead.) The depth of coverage for these 3 topics was comprehensive across both the required and optional materials (consistent rating of “+++”). Other topics that were not covered as frequently but had a high depth rating included “embryology – changing terminology” and “gender dysphoria vs transgender.”

The following topics were never mentioned in the required or optional curriculum materials: “availability/efficacy of rectal microbicides,” “eating disorders in MSM (men who have sex with men),” “gay couples and fertility options,” “increased heart disease rate in lesbians,” “puberty suppression in management of trans youth,” and “vaginitis spread in lesbians.”

The most frequently addressed SGM-CAT topics were “terminology and language use,” “development of gender and sexual identity across lifespan,” and “comprehensive sexual history.” There were many materials that mentioned information related to “development of gender and sexual identity across lifespan,” but

Table 1. Frequency of Vanderbilt University LGBTQ+ Health Learning Objectives, as Reported in Other Studies,^{9,10} in Required and Optional Preclinical Curriculum Materials

Topic	Both		Required Materials		Optional Materials	
	N		N	Depth	N	Depth
Communication/interview skills	24		15	+++	9	+++
Embryology – variations in sex characteristics ^a	20		8	+++	12	+++
Embryology – gender vs sex	13		6	+++	7	+++
Assumptions/biases	9		6	++	3	+
Transitioning options and associated risks	8		2	+	6	++
Standardized patient cases	6		6	++	0	N/A
Embryology – changing terminology	5		2	+++	3	+++
LGBTQ+ ^b patients and having children	5		3	++	2	++
Intake forms	4		2	++	2	++
Problem-based learning integration	4		4	++	0	N/A
Exclusive WSWs: Pap, breast exams, and HPV screening	3		0	N/A	3	++
HIV in MSM	3		1	+	2	+
LGBTQ+ ^b teen issues	3		1	+	2	+++
Sexually transmitted infection recommendations in MSM	3		1	+	2	+
Substance abuse screening	3		1	+	2	+++
Depression and suicide rates in LGBTQ+ ^b teens/adults	2		0	N/A	3	+++
Depression screening	2		0	N/A	2	++
Gender dysphoria vs transgender	2		1	+++	1	+++
Hormone therapy pharmacology	2		1	+	1	++
MSMs and need of hepatitis A/HPV shot	2		1	+	1	+++
Sexually transmitted infections in lesbians	2		1	+	1	+
Anal cancer risks, treatment, anal Pap in MSM	1		0	N/A	1	+
Anal Paps	1		0	N/A	1	++
Gay teen issues	1		0	N/A	1	+
Lesbian nulliparity and risk of breast/ovarian/cervical cancer	1		0	N/A	1	+
Lesbian obesity	1		0	N/A	1	+
Availability/efficacy of rectal microbicides	0		0	N/A	0	N/A
Eating disorders in MSM	0		0	N/A	0	N/A
Gay couples and fertility options	0		0	N/A	0	N/A
Increased heart disease rate in lesbians	0		0	N/A	0	N/A
Puberty suppression in management of trans youth	0		0	N/A	0	N/A
Vaginitis spread in lesbians	0		0	N/A	0	N/A

Abbreviations: HPV, human papillomavirus; LGBT, lesbian, gay, bisexual, and transgender; LGBTQI, lesbian, gay, bisexual, transgender, questioning/queer, and intersex; MSM, men who have sex with men; Pap, Papanicolaou test; WSW, women who have sex with women.

^aThe language used for this item was “disorders of sex development,” however given the outdated and pathologizing nature of this terminology, we use “variations in sex characteristics”¹³ instead.

^bThe acronym used for these items was either “LGBTQI” or “LGBT;” however, for clarity and consistency with the rest of the manuscript, this is instead listed as “LGBTQ+.”

the majority (12 of 15) were in optional course materials, and the depth of coverage of this topic in the required curriculum was minimal. The SGM-CAT topics with the most comprehensive coverage based on depth ratings were “terminology and language use,” “comprehensive sexual history,” “health and health care disparities and inequities,” and “health care trust and discrimination.” While all SGM-CAT topics were mentioned at least once across the required and optional materials, the topic “mental health” was addressed only in optional course materials. The number of materials that mentioned SGM-CAT topics are displayed in Figure 2.

Among the 33 required clinical skills sessions in the pre-clinical curriculum, 4 sessions included standardized patients

with LGBTQ+ identities, with 5 total LGBTQ+ patient cases. These sessions focused on inclusive sexual history, reproductive endocrinology, gastrointestinal conditions, and motivational interviewing. The patients represented include 3 men (all use he/him pronouns), 1 woman (she/her), and 1 nonbinary person (they/them). Further information is not provided in this manuscript given that these cases may continue to be used in the curriculum for student instruction.

DISCUSSION

This evaluation of the preclinical curriculum at a public institution in the Midwest determined that while several topics related to LGBTQ+ health are covered in the curriculum, there remain multiple gaps in how comprehensively some topics are addressed and whether some topics are addressed at all—particularly among materials that students are required to engage with. Topics with more comprehensive coverage included communication/interview skills, terminology/language use, a comprehensive sexual history, and variations in sex characteristics. Notable gaps identified in the curriculum based on the evaluation tools utilized included mental health, sexually transmitted infection screening and prevention, cancer screening, and gender-affirming care. Four of 33 clinical skills sessions were found to have standardized patients with LGBTQ+ identities. There was also variability of coverage of the topics across the required versus optional course materials, which is important to consider as students could miss key information if they solely utilize the required materials.

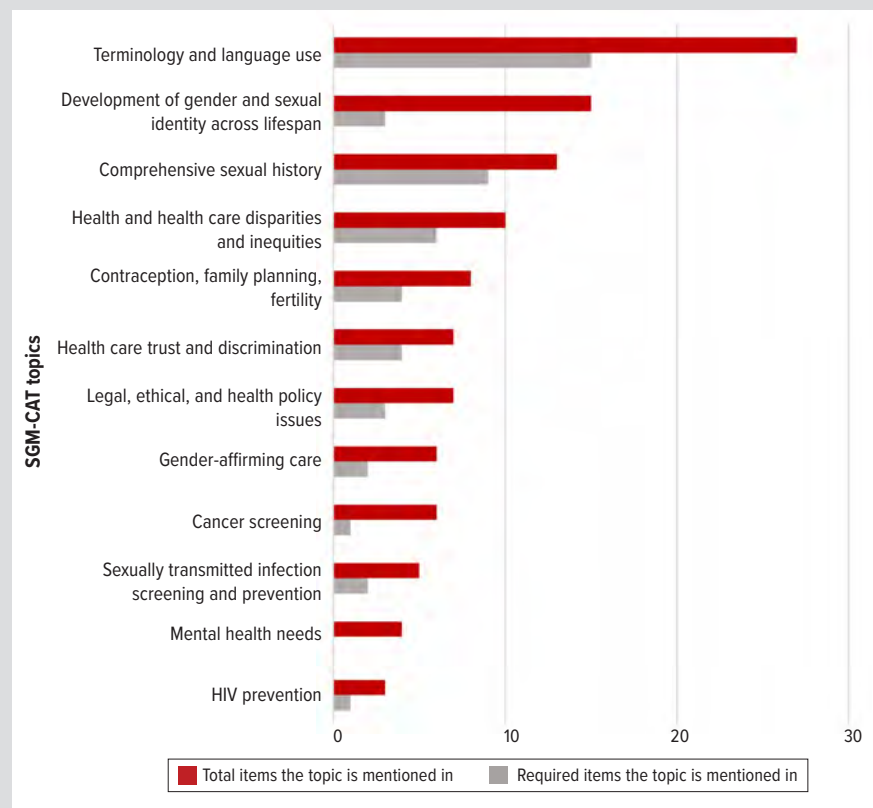
To our knowledge, 4 other medical schools in the United States have conducted comprehensive evaluations of how their curriculum covers LGBTQ+ health topics since 2018. Of note, all of these programs are at private medical schools and are located in Massachusetts,¹¹ Washington, DC,^{9,10} and Wisconsin.⁸ While the framework utilized at these schools varied from one another and the procedure used in this study, there were areas of strengths and weaknesses identified in the curriculum across all schools as it related to LGBTQ+ health content coverage. For example, compared to the findings, as reported by course direc-

Table 2. Frequency of SGM-CAT¹¹ LGBTQ+ Health Topics Across Required and Optional Preclinical Curriculum Materials

Topic	Both N	Required Materials		Optional Materials	
		N	Depth	N	Depth
Terminology and language use	27	15	+++	12	+++
Development of gender and sexual identity across lifespan	15	3	+	12	++
Comprehensive sexual history	13	9	+++	4	+++
Health and health care disparities and inequities	10	6	+++	4	+++
Contraception, family planning, and fertility	8	4	++	4	+
Legal, ethical, and health policy issues	7	3	++	4	++
Health care trust and discrimination	7	4	+++	3	++
Cancer screening	6	1	+	5	+++
Gender-affirming care	6	2	+	4	++
Sexually transmitted infection screening and prevention	5	2	+	3	++
Mental health	4	0	N/A	4	++
HIV prevention	3	1	+	2	+

Abbreviations: SGM-CAT, sexual and gender minority curriculum assessment tool; LGBTQ+, lesbian, gay, bisexual, transgender, and queer/questioning.

Figure 2. Frequency of Items That Mention Each of the 12 SGM-CAT Topics Across Preclinical Curriculum



Abbreviations: SGM-CAT, sexual and gender minority curriculum assessment tool.

tors from the institution that developed and utilized the SGM-CAT,¹¹ our curriculum similarly had multiple instances where the following topics were discussed: terminology and language, health disparities and inequities, and health care discrimination and trust. Differences between the 2 preclinical curricula included that our curriculum appears to have less information on gender-affirming care and mental health but more information on a comprehensive sexual history and contraception, fam-

ily planning, and fertility. Compared to the 2 studies that evaluated their curricula based on the Vanderbilt University learning objectives,^{9,10} the only topics that were not covered across all 3 curricula were vaginitis spread in lesbians and availability/efficacy of rectal microbicides. When comparing topics that were covered across the 3 curricula, it was variable which topics were covered to a more comprehensive extent. Communication and interviews skills were covered comprehensively across all 3 curricula. Compared to the 2 other institutions,^{9,10} our institution appeared to have more material devoted to embryology and variations of sex characteristics and less related to depression screening and aspects of gender-affirming care.

In 2011, it was reported that there was median of 5 hours of LGBTQ+ curriculum delivered in preclinical and clinical curriculum at medical schools across the United States and Canada.¹⁴ Given that the LGBTQ+ content in our curriculum is integrated into blocks with other content and different teaching formats and the curriculum evaluation methods we used, it is difficult to accurately determine the hours spent on LGBTQ+ preclinical curriculum in this study. More important than the number of hours, however, is the breadth and depth of relevant topics students learn that will enable them to optimize care and health outcomes for LGBTQ+ patients across a wide range of clinical specialties.

While there were a number of LGBTQ+ health topics in the preclinical curriculum identified with limited coverage, we will focus on areas we believe are particularly important given health disparities faced by LGBTQ+ communities. There was a major deficit in the preclinical curriculum of information about mental health—including depression and suicide—as it relates to LGBTQ+ health. Given that LGBTQ+ individuals face disproportionate rates of mental health conditions, substance use, self-harm, and suicide,³ it is essential to consider how physician education can be leveraged to address these health disparities. Similarly, our evaluation found a paucity of content on cancer screening for LGBTQ+ communities in the required preclinical curriculum, which also is essential to address given the higher rates of cancer but lower rates of screening in these populations, and it is thought that the lack of clinician knowledge contributes to this disparity.⁴ Lastly, our curriculum lacked information on many aspects of gender-affirming care. Transgender individuals experience numerous health inequities, and medical education has been identified as a mechanism to improve care and health for this population.⁵ While a variety of specific curriculum interventions have been studied related to LGBTQ+ health, including gender-affirming care,¹² we are not aware of interventions that focus specifically on mental health or cancer screening. However, these topics all are encompassed within competencies published in the 2014 AAMC report, which includes clinical scenarios and discussion points that address the topics that could be integrated in medical school curricula.⁷

There are a number of aspects that need to be considered to fully

unpack the landscape of LGBTQ+ health education and medical student learning. Due to the integrated nature of this curriculum, LGBTQ+ topics were spread longitudinally across the preclinical curriculum. In this longitudinal fashion, it is important to strive for consistency in inclusive language use across all coursework. As described in a recently published article, this should include using person-first language, avoiding stereotypes, and using gendered language accurately and only when necessary.¹⁵ The clinical curriculum also should be evaluated to confirm vertical integration of these topics from the preclinical curriculum. Of note, this may look different across individual institutions based on the organization of content in the preclinical curriculum. Beyond the core curriculum, educators also should consider how students are using optional resources or extracurricular activities in their learning about LGBTQ+ health.

It is also important to consider how the landscape of topic coverage in the curriculum may or may not align with student knowledge or preparedness to care for LGBTQ+ patients. Therefore, future study with student input is needed to solidify the key curricular components that will prepare medical students to care for LGBTQ+ patients in appropriate and affirming manners. Future studies that examine how students' skills and knowledge about LGBTQ+ health are assessed during medical school and how that translates to patient care outcomes would be important. This also would be an essential step in clarifying the optimal distribution and depth of coverage of LGBTQ+ health topics in medical school education, with the goal to best prepare all students to care for LGBTQ+ individuals.

Strengths and Limitations

A key strength of this study is that it includes a comprehensive search and review of all materials provided in the preclinical curriculum, such as required lectures, required prework materials, and optional materials for additional information, among other curricular materials. Another strength is that we quantified the amount of LGBTQ+ health-related content in each material, which provides additional context into how much of this content students were provided.

Limitations of this study are that only the preclinical curriculum for 1st and 2nd year phase 1 medical students in 1 time period was evaluated, and materials were identified from a database search using selected key terms. It is important to note that some relevant material might not have explicitly included the search terms we used, and, therefore, some material could have been missed. There is also variability in the language and terminology used between different instructors. Furthermore, we did not assess the degree to which students used the optional materials. Lastly, while we made an effort to quantify the amount of the material that focused on LGBTQ+ health, we do not know the precise time that faculty members spent teaching this content or the time that students spent learning the content.

CONCLUSIONS

Existing frameworks for curriculum evaluation were leveraged and adapted to evaluate and quantify the coverage of LGBTQ+ health topics in the UWSMPH preclinical curriculum. This study identifies areas of strength and opportunities for improvement in the delivery of LGBTQ+ content in this preclinical curriculum. It further demonstrates a framework that may be applied to evaluate curricula in other programs and ideally promote enhanced coverage of this material and improve health, health care, and experiences of LGBTQ+ patients.

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Use of Flags in the Electronic Medical Record: A Retrospective Analysis

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ABSTRACT

Introduction: Implicit bias in patient care and outcomes is well documented. However, the presence of bias in hospital security interactions is a relatively new area of research. Flags placed on the electronic medical record identify patients considered high risk for negative outcomes, including those with security interactions.

Objective: We sought to explore the types of flags and their frequency, differences among patients with flags, and their pattern over time.

Methods: We conducted a retrospective chart review of flags placed on electronic medical records over 13 years of adults 18 years or older who were patients at a Midwest, tertiary, academic medical center. Descriptive statistics were used to explore patient demographic data. Chi-square tests were executed to compare patients with different flag types.

Results: Three flag types were investigated: “communication alert,” “vulnerable/unsafe, behavior” and “risk management.” The communication alert flag was most common, although Black male patients were more likely to receive a vulnerable/unsafe behavior flag than a communication alert flag ($P=0.001$). Patients who were prescribed anti-anxiety medications, antidepressants, antipsychotics, and psychotherapeutics also were more likely to receive a vulnerable/unsafe behavior flag than a communication alert flag ($P=0.001$). The highest number of flags was placed during quarter 3—the months of July, August, and September.

Conclusions: Records of patients with certain demographics and on certain medications were more likely to be labeled with vulnerable/unsafe behavior flags. There is no clear protocol to determine what behaviors elicit which flag. Standardized procedures could help provide transparency to this issue.

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INTRODUCTION

Disparities in policing have long plagued the United States and have received significant public attention in recent years. Studies have shown that non-White suspects are more likely to get arrested, experience nonlethal police force, and die from excessive police force.¹⁻³ These findings and events have led many to question the integrity of policing systems. Investigations into officers and entire police departments have found discriminatory practices and even overt racism, which have prompted numerous attempts for police reform.

Hospitals have begun to follow suit, looking into their own policing or security systems in attempts to identify bias and to hold themselves accountable. Although the majority of hospitals employ non-sworn security personnel, some institutions employ sworn police officers or sheriffs to mitigate security events, which can cause distress for populations that historically have been mistreated by police.⁴ While it has been well-established that racial and ethnic disparities exist in patient treatment, few studies have looked at the inter-

section of policing and health care that exists as hospital security.⁵ An internal investigation conducted at Seattle Children’s Hospital found that security was disproportionately called on patients and families who identify as Black or African American.⁶ Similar findings also were documented at two other large academic hospitals, demonstrating the number of observed security calls for Black patients to be significantly greater than expected based on hospital population representation.^{7,8}

There are usually consequences in place for patients involved in security encounters, including limited visitation, continuous monitoring, or placement of a flag on their electronic medical record. These flags alert clinicians to potential unwanted behaviors to help guide future patient interactions. One study found that placing flags on the charts of high-risk patients resulted in a 91% reduction of violent incidents, which was attributed to improved staff awareness when interacting with these patients.⁹ Flags might also be placed after safety events to identify risk-averse patients who would not necessitate a call to security but still put themselves or staff in danger. Research in this area is relatively new, with limited literature.

Our primary objectives were to explore the types and frequency of such flags at an academic medical center. Secondary objectives included examining whether differences exist among patients with flags and flag patterns over time.

METHODS

Study Design and Setting

This retrospective data analysis focused on a tertiary academic medical center in Milwaukee, Wisconsin. The medical center is the region's only level I trauma center. In fiscal year 2019, the majority of patients serviced were White (73.8%), followed by African American (15.5%).¹⁰ As of June 2022, the medical center had over 72000 emergency visits, over 37000 admissions, and nearly 950000 outpatient visits for that year. This study was approved by the Medical College of Wisconsin Institutional Review Board.

Study Sample

Participants were identified through the Epic Clarity database, a dedicated reporting database within the Epic electronic health record system (Epic Systems, Verona, Wisconsin). Patients of the medical center age 18 years or older with a flag in their chart comprised the study population. Data from April 2009 through March 2022 were used.

Data Collected

Flags are placed on patients' charts to alert staff to details about the patient and travel across encounters. Any member of the health care team involved in the patient's care who has access to their electronic medical record (EMR) can place flags. At our institution, the specific flags identified were "communication alert," "risk management," and "vulnerable/unsafe behavior." These flags were first used in 2009, 2016, and 2021, respectively. Flags are most often placed on a patient's chart after a safety event, which is an incident that puts a patient or staff at risk for harm. Communication alert flags are used for various reasons ranging from reporting use of inflammatory language to noting a patient's desired contact person. Risk management flags are used to identify high-risk patients, for example, those who are more likely to

fall or leave against medical advice. Of the 3 flag types, there is a clear protocol in place only for placement of a vulnerable/unsafe behavior flag. This is outlined in the hospital employee handbook, which states that a vulnerable/unsafe behavior flag should be considered for any verbal, physical, or emotionally threatening action by a patient. The protocol includes a review of the incident by security and the charge nurse to determine if a flag is appropriate. It also suggests appropriate precautions and interventions that could be implemented when interacting with the flagged patient.

The following demographic information was extracted: age, sex, race/ethnicity, county, language, Epic risk score (identifies patients at increased risk of postoperative mortality, complication, readmission, and long-term intensive care unit stay); medications including narcotics, anti-anxiety agents, antidepressants, antipsychotics, and stimulants; medical diagnoses including AIDS, HIV, alcohol abuse, depression, drug abuse, liver disease, metastatic cancer, neurologic disorder, peripheral vascular disease, psychoses, and renal failure; and comorbidity count. The department and specialty where the safety event occurred also was obtained.

Analyses

Because the flags were utilized in varying years, 2 separate data sets were created for further exploration. One data set consisted solely of patients with the communication alert flag, which was the only flag used throughout the entire study period (2009 through 2022). The second data set included patients with either a communication alert flag or a vulnerable/unsafe behavior flag from quarter 3, 2021, to quarter 2, 2022, the period when both flags were in use. Descriptive statistics were used to explore patient data. Demographics of the study population with a communication alert flag were summarized with mean and standard deviation for continuous variables and count and percentages for categorical variables. Comparison of the communication alert flag population and the vulnerable/unsafe behavior flag population from quarter 3, 2021, to quarter 2, 2022, utilized 2 sample *t* tests for continuous variables and chi-square goodness of fit tests for categorical variables. The type of patient safety events that occurred was summarized with counts and percentages. The statistical significance was assessed at $P < 0.05$. Complete analyses were performed using R.4.1.3 (R Core Team, 2022).

RESULTS

Communication alert flags were used in every year of the study ($n = 4162$). Risk management flags were recorded only in 2016 ($n = 6$) and 2021 ($n = 1$) and, therefore, due to the limited number, were not incorporated into the analysis. Vulnerable/unsafe behavior flags ($n = 631$) were first used in quarter 3, 2021, and are not included in the following demographic analysis because they were not in use over the entire study period.

The average patient age was 57 years at the creation date of

Table 1. Population Demographics of Patients With Communication Alert Flags, 2009 – 2022

Mean age at flag creation	56.5 (SD = 20.5)
Sex, n (%)	
Male	1980 (47.6%)
Female	2181 (52.4%)
Unknown	1 (0.0%)
Race/ethnicity, n (%)	
White	2786 (66.9%)
Black	1046 (25.1%)
Hispanic	173 (4.2%)
Other	120 (2.9%)
Unknown	37 (0.9%)
Primary language, n (%)	
English	4009 (96.6%)
Spanish	55 (1.3%)
Hmong	10 (0.2%)
Russian	5 (0.1%)
American Sign Language	10 (0.2%)
Other	63 (1.5%)
Unknown	10 (0.2%)
Most common medications, n (% of patients prescribed) ^a	
Narcotics	2890 (88.5%)
Anti-anxiety agents	1873 (57.4%)
Antipsychotics	1546 (47.4%)
Antidepressants	1652 (50.6%)

^aSome patients were prescribed multiple medications.

a communication alert flag. There were slightly more female patients (n=2181, 52.4%) and the majority of patients were White (n=2786, 67.5%), followed by Black (n=1046, 25.4%) and Hispanic (n=173, 4.2%). Table 1 provides complete demographics for patients with communication alert flags. The most prescribed medication classes during admission for patients with a communication alert flag were narcotics (n=2890, 88.5%), anti-anxiety agents (n=1873, 57.4%), antidepressants (n=1652, 50.6%), and antipsychotics (n=1546, 47.4%).

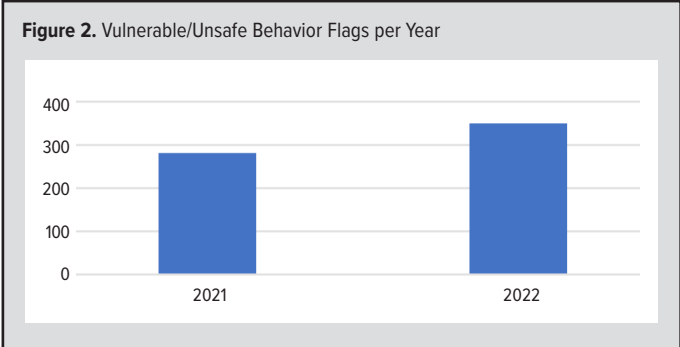
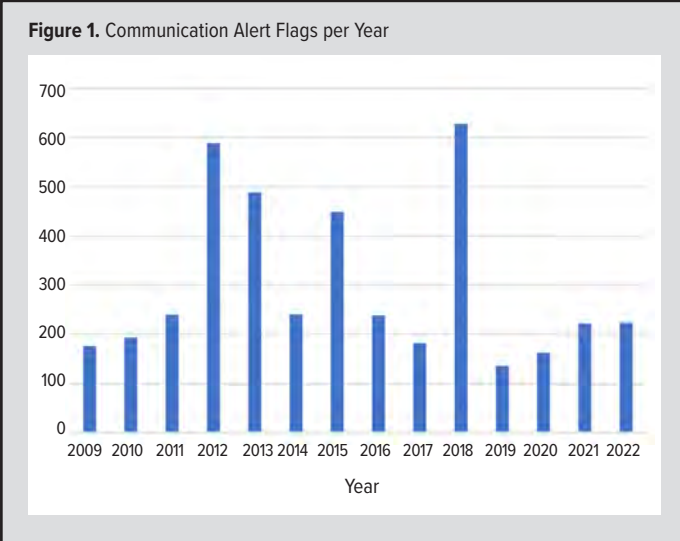
The average number of communication alert flags per year was 297 (SD +/- 160). The most common time of year for creation of communication alert flag was quarter 3 (July-September), with 37.7% (n=1551) of all communication alert flags being created during these months (Table 2). The incidence of flags peaked in 2012 (n=588) and 2018 (n=627) (Figure 1).

Vulnerable/unsafe behavior flags were seen only during quarter, 2021 through quarter 2, 2022 (Figure 2). Therefore, patients with these flags were compared with a subset of patients with communication alert flags, specifically those from quarter 3, 2021 through quarter 2, 2022. There were more males identified with vulnerable/unsafe behavior flags than communication alert flags, which was statistically significant (Table 3). Other factors that were significantly different between the 2 flags included race/ethnicity; the use of anti-anxiety, antidepressant, anti-psychotic, psychotherapeutic medications; and neurologic disorders.

Table 2. Communication Alert Flags per Quarter, 2010^a– 2021

Quarter	Flags
Q1 (January – March)	769
Q2 (April – June)	800
Q3 (July – September)	1515
Q4 (October – December)	888

^aData from 2009 have been omitted from this table because communication alert flags were not in used until Quarter 2 of that year.



DISCUSSION

There are multiple ways to interpret the overall number of flags added to medical records per year. In comparison to the cumulative number of hospitalizations, emergency, and outpatient visits, the incidence of flags is less than 0.02% for all patient encounters in 2022. However, if looking at sheer numbers, flags were created anywhere from 1 every half-day to 1 every 2.5 days.

The definition of the vulnerable/unsafe behavior flag and its protocol suggest some amount of medical worker harm. Literature notes that “workers in the medical field encounter more nonfatal incidents of WPV [workplace violence] than workers in any other profession.”¹¹ Workplace violence refers to not only physical acts but also includes harassment and any other behavior that is threatening.¹² The Association of American Medical Colleges, US

Bureau of Labor Statistics, Occupational Safety and Health Administration, and American Association of Critical-Care Nurses have reported on the alarming rise in violence experienced by health care workers.¹³⁻¹⁵ Nonetheless, the actual number of events that occur remains uncertain. This is primarily because information and data on this topic comes almost exclusively from surveys and interviews.^{16,17} Furthermore, the interpretation of verbal remarks is subjective, the result of each individual's background and personal experience. What may make one individual feel threatened or uncomfortable may not be the case for another. In this study, flags are placed in patient charts by medical center staff. The determination of whether a flag is needed is largely, if not completely, up to individual medical center personnel, which makes it challenging to accurately quantify and collect information on patient-related safety events.

Vulnerable/unsafe behavior flags were found only in 2021 and 2022, which suggests a likely change in documentation practices. It is possible that the communication alert flag was used previously as a catch-all for any adverse event that occurred. Interestingly, there were more vulnerable/unsafe flags than communication alerts when the former came into use in 2021 and 2022. A more standardized process for flag documentation is needed, including further guidance on which behavior solicit which flag type. It should be noted that most vulnerable/unsafe behavior flags follow a specific format that includes prompts, such as recommended safety practices, known triggers, behavior exhibited, and de-escalation methods, that can be filled out by the flag creator. This provides a more robust picture of the unsafe behavior while giving clinicians necessary insight for proper patient care. It would be beneficial to approach all types of flags in this systematic manner, as prompts could encourage the flag creator to describe the incident in a way that might prevent future conflict and promote safety for all involved.

There were differences between patients with communication alert flags in 2021 and 2022 compared to those with vulnerable/unsafe behavior flags. The latter flag had a significantly higher proportion of male and Black patients. Additionally, patients with this flag were prescribed more anti-anxiety agents, antidepressants, antipsychotics, and psychotherapeutic drugs than patients with the communication alert flag. Coincidentally, diagnoses of neurologic disorders or psychoses were more prevalent with the vulnerable/unsafe behavior flag. It is important to consider the implications behind flag types. While it was not possible to ascertain the exact

Table 3. Comparison of Demographic Factors Between Communication Alert Patient Group and Vulnerable/Unsafe Behavior Patient Group From Quarter 3, 2021 – Quarter 2, 2022

	Communication Alert (n = 337)	Vulnerable/Unsafe Behavior (n = 631)	P value
Mean age (SD)	53 (20)	52 (9)	0.5
Sex, n (%)			<0.001
Female	167 (49.6%)	233 (36.9)	
Male	170 (50.4%)	398 (63.1%)	
Race/ethnicity, n (%)			<0.001
White	208 (61.7%)	303 (48.0)	
Black	87 (25.8%)	285 (45.2)	
Hispanic	26 (7.7%)	24 (3.8)	
Other	16 (4.7%)	15 (2.4)	
Epic risk score (mean)	3.7 (2.4)	5.1 (2.4)	<0.001
Medications, n (% of patients prescribed) ^a			
Anti-anxiety	173 (57.3%)	490 (79.9)	<0.001
Antidepressants	160 (53.0%)	415 (67.7)	<0.001
Antipsychotics	190 (62.9%)	534 (87.1)	<0.001
Psychotherapeutics	45 (14.9%)	232 (37.8)	<0.001
Medical diagnosis, n (%)			
Metastatic cancer	16 (4.7%)	7 (1.1)	<0.001
Neurologic disorder	25 (7.4%)	100 (15.8)	<0.001
Psychoses	6 (1.8%)	65 (10.3)	<0.001

^aSome patients were prescribed multiple medications.

reason for the placement of each flag, by its own protocol definition, vulnerable/unsafe behavior flags are used when a patient's conduct is felt to be threatening. The differences seen between flags may not be surprising given historical stereotypes, research on implicit bias, its effect on health care workers' perceptions, and, subsequently, health care inequalities.¹⁸⁻²² There is also an abundance of literature that demonstrates the stigmatization of patients with mental health conditions, both by those in health care and the public.²³⁻²⁵ However, it is possible that the underlying neurologic and psychiatric conditions themselves predispose patients to certain behavior.²⁶

It is interesting that for multiple years, most flags were placed during quarter 3 (July-September), which is when new interns and fellows start at academic medical centers. This raises questions as to whether house staff turnover could factor into flag placement. Literature on "the July effect" notes important concerns with each new academic year, including increased patient mortality and decreased efficiency attributed to the inexperience of trainees.²⁷

Limitations

Our study has several limitations. First, this study serves to better understand and identify patterns in security interactions at a single academic medical center in Wisconsin. Whether these results can be generalized to community practices or other academic centers is unclear. Further, there are some gaps in the data collected that prevented full analysis of flags. There were so few risk management flags recorded over the course of the study (n = 7) that this category

was not included in the analysis. Additionally, vulnerable/unsafe behavior flags were not in use prior to July 2021, preventing the investigators from making comparisons before that time. Finally, out of the 3 flags, recommended protocols and workflows are in place only for the vulnerable/unsafe behavior flag. There are no clear guidelines for the remaining flags as to what behavior would justify their use. This, in turn, provides little context as to what it truly means to have these specific flags placed on a chart. Future steps should explore health care staff experiences to better understand their thresholds and reasons for flagging patients.

CONCLUSIONS

Patients with certain diagnoses and characteristics were more likely to be labeled with specific flags compared to others. How often hospital safety events happen remains inconclusive. Standardized processes and procedures for reporting events across all health care systems could help with quantifying and providing transparency to this issue.

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Data Availability: Datasets used in this study were pulled from the medical record and cannot be shared with individuals outside the approved Institutional Review Board protocol.

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Service Line Director Appraisal: Evaluating Impact on Provider Satisfaction in a Rural-Based Clinic

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ABSTRACT

Introduction: Rural-based health care systems face unique concerns, including the struggle to recruit and retain quality clinicians. We evaluated health care providers' perceptions of their service line directors (SLDs) in the Marshfield Clinic Health System to understand how these perceptions affect job satisfaction in a rural health care setting.

Methods: Utilizing quantitative and qualitative methods, we reached out to providers within the health system, excluding SLDs to prevent bias. The survey, with a 43% response rate, encompassed 14 questions focusing on 8 domains of engagement. Data analyses included chi-squared tests, *t* tests, analysis of variance, and correlation matrices. To delve deeper into perceptions, a qualitative approach was employed, analyzing open-ended feedback.

Results: Of the 457 respondents, 70% reported satisfaction with their SLDs. High meeting frequencies with SLDs were positively correlated with satisfaction. The majority acknowledged the positive attributes of SLDs in domains like availability, recognition, and feedback. However, significant variations in perceptions arose between physicians and advanced practice clinicians and between surgeon and non-surgeon SLDs. Qualitative feedback elucidated themes including engagement, communication, and advocacy. Positive attributes, such as competence and proactivity, were mentioned frequently, while negatives highlighted disconnectedness and being uninformed.

Conclusions: The quality of interactions with SLDs significantly influences clinician satisfaction. Regular, meaningful interactions—especially recognizing and providing feedback—enhance satisfaction. However, certain groups like advanced practice clinicians under surgeon SLDs felt less engaged. Our findings underscore the importance of tailored leadership training for SLDs and suggest organizational strategies to boost satisfaction, potentially affecting recruitment and retention in rural health care settings.

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INTRODUCTION

Rural-based health care systems face unique challenges: vast service areas, variable regional health care needs, and the struggle to provide uniform access to services.^{1,2} These health care systems also can struggle to recruit and retain the quality health care providers who are crucial for aligning services with organizational mission and vision.^{3,4} To balance patient and provider satisfaction with a range of services, rurally based health care systems must reckon with many impacting factors.^{3,5}

Service line directors (SLDs) have emerged as a significant solution in navigating these challenges.^{4,6-9} First introduced in the 1980s, the concept of service line management is not monolithic, and various leadership structures exist.⁸ In complex regional health care settings, where each specialty service line can have distinct demands, SLDs provide strategic oversight and leadership.^{7,9,10} Evidence suggests that SLD effectiveness significantly affects the satisfaction and retention of service line providers, which in turn improves patient satisfaction and overall health care delivery.^{4,5,11} For clarity, “service line providers” generally refer to professionals delivering patient care specific to a certain medical specialty or department within the health care system; the term encompasses physicians, surgeons, and other advanced practice clinicians (APCs).⁶ The SLD model

centralizes the role of service line leadership within the health system infrastructure, providing agility in a dynamic rural health care landscape.^{4,5,7,12}

One survey found various models for service line leadership structures in health care organizations, over 75% of which implemented a dyad structure.¹³ By comparison, our institution, Marshfield Clinic Health System (MCHS), utilizes a single SLD, implemented in approximately 10% of organizations surveyed.¹³ Notably, that survey reported inconclusive results with respect to the dyad model; ours identified both positive and negative characteristics of the single SLD model. Considering MCHS's expansive regional footprint and diverse service offerings, our study can offer some perspectives for similar institutions navigating the challenges of rural health care delivery.

METHODS

Clinical Environment

MCHS ranks among the largest, private, multidisciplinary, multispecialty private group practices in the United States. It covers a largely rural service area in central, northern, and western Wisconsin, spanning more than 45 000 square miles and including multiple regional settings designated as health professional shortage areas. Recent studies have provided a more detailed description of MCHS.¹⁴⁻¹⁶ Leadership includes the chief medical officer (CMO) and the credentialing and privileging officer. Collaborative discussions between MCHS's CME, chief operating officer, and service line representatives envisioned an operational model integrating regional operations with service and support lines to improve operational and provider functions. Appendix 1 shows areas of emphasis under each focus area. Appendix 2 shows service line/support infrastructure involving physician and administrative leadership, stratified by the 6 organizational constructs.

Study Design and Measures

Using a retrospective cross-sectional design, a survey approach was applied to query the service line provider population and test the validity of 3 hypotheses posited by the MCHS leadership. Our study aimed to validate these hypotheses: (1) physicians who perceive heightened engagement from their SLDs are more likely to report elevated job satisfaction levels; (2) a positive experience with the leadership qualities of SLDs across 8 pivotal performance domains is positively linked to job satisfaction; and (3) the duration of SLDs' service and their experience at MCHS are directly proportional to the perceived level of SLD engagement in their service line. Our hypotheses were rooted in both the existing literature and the unique organizational priorities of MCHS.

The CMO designed a survey tool comprising 14 questions to gather perspectives from service line providers about their experiences (Appendix 3). To ensure survey content validity, we

engaged in informal iterative discussions and collected feedback from domain experts. A pilot test was carried out involving select service line providers not included in the final study, leading to refinements in the survey. For distribution, the survey was sent via Survey Monkey to identify participants using their official MCHS email addresses. The survey was emailed in September 2020 to 1143 physicians and APCs. All service line providers within MCHS formed our sampling frame. However, to eliminate potential bias and conflicts of interest, SLDs were deliberately excluded from the survey, aligning with best practices in survey research to avoid potential bias.⁷⁻⁹ Responses were collected through October 2020. To boost the response rate, we sent weekly reminder emails after the initial distribution. We had a 43% response rate, as determined by American Association for Public Opinion Research definitions.¹⁷ Participation was voluntary and anonymous. The study received an Institutional Review Board exemption.

To articulate service line provider perspectives, we defined 8 domains of SLD engagement that corresponded to specific questions (questions 5-12) in our survey tool. These questions captured sentiments about the availability of the SLD to the provider, the degree of respect experienced, recognition of work, provision of feedback, awareness of policy changes, fostering a conducive work environment, fairness in policy application, and support towards professional development. Each of these domains was evaluated with a binary yes/no format. A pivotal differentiation was made between "physician" and "non-physician/APCs." Dentists were included under the "physician" category. The "non-physician" or APCs included certified registered nurse anesthetists (CRNA), certified nurse midwife, nurse practitioners, and physician assistants. We segmented our participants based on their tenure length at MCHS: providers with 1 to 4 years were categorized under "early career," those who had been with MCHS for 5 to 15 years fell into the "mid-career" bracket, and those with more than 15 years of service were labeled "mature career." We separated the professional background of the SLDs themselves into "surgeon" and "non-surgeon" SLDs. Surgeon SLDs belonged to specialties such as otolaryngology, gynecology, anesthesia, general surgery, dentistry, cardiology, and orthopedics. Non-surgeon SLDs originated from diverse service lines such as primary care, core support services, and regional support services. We categorized the frequency of meetings between providers and their SLDs as a measure of engagement. Over the preceding year, meetings that occurred 0 to 1 time were labeled as "low," those that happened 2 to 3 times were termed "intermediate," and sessions that convened 4 or more times were defined as "high." For satisfaction metrics, we employed a 3-tier system: "satisfied" combined responses of "extremely satisfied" and "satisfied," the "neutral" designation remained consistent, and "unsatisfied" combined "extremely unsatisfied" and "unsatisfied." We delved into the correlations between meeting frequency, the 8 domains, and reported satisfaction.

Analyses

We adopted a mixed-methods approach. Quantitatively, we utilized descriptive statistics, chi-squared tests, *t* tests, analysis of variance, and correlation matrices, among others, consisting of 457 individuals. Using SAS version 9.4 (SAS Institute Inc), we conducted chi-squared tests for categorical data to compare responses based on different classification criteria. We employed *t* tests or analysis of variance to assess the 8 domains of engagement and the frequency of SLD meetings. For deeper exploration, we transformed the levels of satisfaction numerically, allowing us to carry out correlation testing. Using the correlation matrix, we investigated associations among the number of meetings, the 8 domains of engagement, and the overall satisfaction level. All the analyses set a statistical significance threshold of ≤ 0.05 .

Also, we embarked on a comprehensive qualitative analysis using Word Cloud Generator,¹⁸ similar to previous studies.^{19,20} Among 491 respondents, 212 provided open-ended feedback to question 14. Comments of respondents ($N = 16$) who worked at MCHS for less than 1 year were excluded, because comments generally were limited to statements pointing to the short duration of their employment. Thus, of the 457 respondents who have been working at MCHS 1 year or more, 196 provided feedback in the open-ended question. However, commentary by some providers ($N = 16$) contributed no relevant insights into SLD characteristics and were not analyzed further. Hence, qualitative analysis was achievable on comments from 180 of 196 of respondents. Of the respondents, 212 provided feedback on an open-ended question; 180 of these were analyzed thoroughly. A thematic analysis of these responses identified central themes and subthemes related to dissatisfaction/satisfaction with SLDs. Two of our team members initially reviewed a subset of the comments independently to pin down emergent themes. We then

Table 1. Characteristics and Survey Responses Study Participants ($N = 457$)

Variables	Descriptive Statistics		Bivariate Analysis	
	N (%)	APCs, ^a n (%)	Physician, n (%)	P value
Job title				
Certified registered nurse anesthetist	14 (3)			
Certified nurse midwife	4 (1)			
Nurse practitioner	73 (16)			
Physician assistant	41 (9)			
Physician	304 (67)			
Dentist	21 (5)			
Service line directors				
Chief medical officer	13 (3)			
Core support lines	99 (22)			
Credentialing and privileging	21 (5)			
Primary care service lines	164 (26)			
Regional support lines	3 (1)			
Specialty service lines	147 (32)			
I am not sure	10 (2)			
Frequency of meeting in past year				
Low (0–1 time)	182 (40)	75 (57)	107 (33)	< 0.0001
Intermediate (2–3 times)	123 (27)	36 (27)	87 (27)	
High (4 and more)	152 (33)	21 (16)	131 (40)	
Years of working at MCHS				
1–4 years (early career)	122 (27)	37 (28)	85 (26)	0.0008
5–15 years (mid-career)	187 (41)	69 (52)	118 (37)	
>15 years (mature career)	145 (33)	26 (20)	119 (37)	
Level of satisfaction				
Satisfied	319 (70)	79 (60)	240 (74)	0.0002
Neutral	71 (16)	35 (26)	36 (11)	
Unsatisfied	67 (15)	18 (14)	49 (15)	
Q5 – Available: my SLD is available to me when I have suggestions or concerns to address				
No	37 (8)	17 (13)	20 (6)	0.0157
Yes	412 (92)	116 (87)	300 (94)	
Q6 – Respectful: my SLD treats me with respect				
No	27 (6)	11 (9)	16 (5)	0.1624
Yes	419 (94)	118 (91)	301 (95)	
Q7 – Recognition: my SLD recognizes me for a job well done				
No	83 (19)	39 (30)	44 (14)	< 0.0001
Yes	360 (81)	90 (70)	270 (86)	
Q8 – Feedback: my SLD provides me with constructive advice/feedback				
No	104 (23)	46 (36)	58 (18)	< 0.0001
Yes	339 (77)	81 (64)	258 (82)	
Q9 – New policy: my SLD keeps me informed of MCHS policy changes and initiatives				
No	70 (16)	31 (24)	39 (12)	0.0015
Yes	379 (84)	97 (76)	282 (88)	
Q10 – Environment: my SLD works to provide an environment promoting success				
No	86 (20)	30 (24)	56 (18)	0.1487
Yes	355 (80)	96 (76)	259 (82)	
Q11 – Unbiasedness: my SLD applies policy and directives fairly				
No	54 (12)	23 (18)	31 (10)	0.0146
Yes	384 (88)	102 (82)	282 (90)	
Q12 – Supportive: my SLD supports my development as a professional				
No	81 (18)	29 (23)	52 (17)	0.1024
Yes	359 (82)	96 (77)	263 (83)	

Abbreviations: APC, advanced practice clinician; MCHS, Marshfield Clinic Health System; SLD, service line director; Q, question.

^aAPCs include certified registered nurse anesthetist, certified nurse midwife, nurse practitioner, physician assistant, dentist.

Table 2. Classification by the Level of Satisfaction: Satisfied, Neutral, and Unsatisfied

Variables	Satisfied n (%)	Neutral n (%)	Unsatisfied n (%)	P value
Frequency and number of meetings in past year				
Low (0–1 time)	92 (29)	52 (73)	38 (57)	<0.0001
Intermediate (2–3 times)	100 (31)	8 (11)	15 (22)	
High (4 and more)	127 (40)	11 (16)	14 (21)	
Years of working at MCHS				
1–4 years (early career)	88 (28)	25 (35)	9 (14)	0.0399
5–15 years (mid-career)	124 (39)	29 (41)	34 (52)	
>15 years (mature career)	106 (33)	17 (24)	22 (34)	
Q5 – Available: my SLD is available to me when I have suggestions or concerns to address				
No	1 (0)	11 (17)	25 (38)	<0.0001
Yes	317 (100)	55 (83)	40 (62)	
Q6 – Respectful: my SLD treats me with respect				
No	1 (0)	6 (9)	20 (31)	<0.0001
Yes	314 (100)	61 (91)	44 (69)	
Q7 – Recognition: my SLD recognizes me for a job well done				
No	13 (4)	35 (54)	35 (54)	<0.0001
Yes	300 (96)	30 (46)	30 (46)	
Q8 – Feedback: my SLD provides me with constructive advice/feedback				
No	19 (6)	40 (63)	45 (69)	<0.0001
Yes	295 (94)	24 (37)	20 (31)	
Q9 – New policy: my SLD keeps me informed of MCHS policy changes and initiatives				
No	12 (4)	29 (45)	29 (43)	<0.0001
Yes	306 (96)	35 (55)	38 (57)	
Q10 – Environment: my SLD works to provide an environment promoting success				
No	8 (3)	29 (48)	49 (73)	<0.0001
Yes	305 (97)	32 (52)	18 (27)	
Q11 – Unbiasedness: my SLD applies policy and directives fairly				
No	5 (2)	16 (26)	33 (53)	<0.0001
Yes	309 (98)	46 (74)	29 (47)	
Q12 – Supportive: my SLD supports my development as a professional				
No	10 (3)	27 (44)	44 (68)	<0.0001
Yes	303 (97)	35 (56)	21 (32)	

Abbreviations: MCHS, Marshfield Clinic Health System; Q, question; SLD, service line director.

proceeded to align the remaining comments under these themes with follow-up discussions and consensus-building. The comments provided insights into what leadership qualities providers value. After streamlining synonyms and similar concepts and arriving at a list of positive and negative leadership attributes, we generated word clouds that allowed stakeholders to quickly identify and understand the most valued leadership traits and areas for improvement.

RESULTS

Quantitative Analysis

As shown in Table 1, respondents included 304 physicians (67%), 73 nurse practitioners (16%), 41 physician assistants (9%), and 14 CRNAs (3%). Satisfaction was reported by 70% of respondents, with 16% neutral and 15% unsatisfied. Most respondents noted SLD availability (92%) and respectful treat-

Table 3. Classification by the Years of Working at Marshfield Clinic Health System: Early, Mid and Mature Careers

Variables	Early Career ^a n (%)	Mid Career ^b n (%)	Mature Career ^c n (%)	P value
Frequency of meeting in past year				
Low (0–1 time)	40 (33)	73 (39)	67 (46)	0.0165
Intermediate (2–3 times)	46 (38)	49 (26)	28 (19)	
High (4 and more)	36 (29)	65 (35)	50 (35)	
Q5 – Available: my SLD is available to me when I have suggestions or concerns to address				
No	7 (6)	17 (9)	11 (8)	0.5675
Yes	112 (94)	167 (91)	132 (92)	
Q6 – Respectful: my SLD treats me with respect				
No	3 (3)	13 (7)	10 (7)	0.2077
Yes	114 (97)	171 (93)	132 (93)	
Q7 – Recognition: my SLD recognizes me for a job well done				
No	17 (14)	37 (21)	28 (20)	0.3567
Yes	102 (86)	143 (79)	113 (80)	
Q8 – Feedback: my SLD provides me with constructive advice/feedback				
No	23 (19)	43 (24)	25 (26)	0.5033
Yes	95 (81)	138 (76)	105 (74)	
Q9 – New policy: my SLD keeps me informed of MCHS policy changes and initiatives				
No	17 (14)	31 (17)	22 (15)	0.8139
Yes	102 (86)	152 (83)	122 (85)	
Q10 – Environment: my SLD works to provide an environment promoting success				
No	17 (14)	36 (20)	32 (23)	0.2404
Yes	101 (86)	142 (80)	110 (77)	
Q11 – Unbiasedness: my SLD applies policy and directives fairly				
No	10 (9)	28 (15)	16 (12)	0.2045
Yes	106 (91)	153 (85)	122 (88)	
Q12 – Supportive: my SLD supports my development as a professional				
No	16 (14)	38 (21)	26 (19)	0.2683
Yes	101 (86)	142 (79)	114 (81)	
Level of satisfaction				
Unsatisfied	9 (7)	34 (18)	22 (15)	0.0399
Neutral	25 (21)	29 (16)	17 (12)	
Satisfied	88 (72)	124 (66)	106 (73)	

Abbreviations: MCHS, Marshfield Clinic Health System; Q, question; SLD, service line director.

^aEarly career: 1–4 years, N=122, 26.9%.
^bMid-career: 5–15 years, N=187, 41.2%.
^cMature career: >15 years, N=45, 31.9%.

ment (94%), with 81% feeling recognized and 77% receiving constructive feedback. Most respondents also reported awareness of new policies (84%), fairness (88%), and feeling supported (82%). Meeting frequency varied, with 40% reporting low, 27% intermediate, and 33% high meeting frequency. Significant differences were observed in meeting frequency between APCs and physicians. Low meeting frequency was reported by 57% of APCs versus 33% of physicians, while 40% of physicians reported high meeting frequency compared to 16% of APCs ($P<0.0001$). APCs also reported lower recognition (70% vs 86%; $P<0.0001$) and feedback (64% vs 82%; $P<0.0001$). Satisfaction levels differed, with 60% of APCs satisfied compared to 74% of physicians ($P=0.0002$). APCs were less likely to feel informed about

new policies (76% vs 88%; $P=0.0015$) and perceived lower fairness (82% vs 90%; $P=0.0146$).

Satisfaction levels were significantly associated with meeting frequency (Table 2), with 40% of respondents in the high-frequency group expressing satisfaction compared to 29% in the low-frequency group ($P<0.0001$). Satisfaction also varied across career stages, with 28% of early-career, 39% of mid-career, and 33% of mature-career providers reporting satisfaction ($P=0.0399$). Respondents who felt recognized (96%) or informed about policies (96%) were significantly more likely to be satisfied ($P<0.0001$). Respectfulness (100% satisfaction; $P<0.0001$) and feedback (94% satisfaction; $P<0.0001$) were also strongly associated with satisfaction.

As shown in Table 3, meeting frequency differed significantly across career stages, with 46% of mature-career providers reporting low frequency compared to 33% of early-career providers ($P=0.0165$). Perceptions of availability (94% early, 91% mid, 92% mature) and respectfulness (97% early, 93% mid, 93% mature) did not vary significantly. Recognition rates were slightly higher for early-career respondents (86%) compared to mid-career (79%) and mature-career (80%), though not statistically significant.

Table 4 demonstrates that perceptions of non-surgeon SLDs were generally more favorable than those of surgeon SLDs. Non-surgeon SLDs were reported as available by 95% of respondents compared to 89% for surgeon SLDs ($P=0.0289$). Recognition was also higher under non-surgeon SLDs (86% vs 74%; $P=0.0017$), as was feedback (81% vs 70%; $P=0.0093$). Satisfaction levels were significantly higher under non-surgeon SLDs, with 42% extremely satisfied compared to 32% under surgeon SLDs ($P=0.0227$). Surgeon SLDs were perceived as less effective in keeping respondents informed about new policies (78% vs 90%; $P=0.0005$).

Table 5 highlights correlation analysis findings, which revealed significant positive relationships between meeting frequency and recognition ($r=0.48$, $P<0.0001$) and feedback ($r=0.48$, $P<0.0001$). Satisfaction was moderately correlated with meeting frequency ($r=0.35$, $P<0.0001$) and feedback ($r=0.57$, $P<0.0001$). Strong correlations were observed between feedback and recognition ($r=0.71$, $P<0.0001$), emphasizing the interdependence of these domains. Respectfulness had a lower correlation with satisfaction ($r=0.39$, $P<0.0001$), suggesting it is less predictive of satisfaction than other domains.

Qualitative Analysis

The qualitative analysis identified key themes of leadership qualities, engagement, communication efficacy, advocacy, and supportiveness, while highlighting systems issues that challenge SLDs. As shown in Appendix 4, among the 6 main service lines, leaders under “specialty service lines” had the lowest satisfaction; leaders under “regional support lines” had the highest. Word clouds depicted in Appendix 5A (positive) and Appendix 5B (negative)

Table 3. Classification by Surgeon Versus Non-surgeon Service Line Directors (SLDs)

Variables	Non-Surgeon SLDs n (%)	Surgeon SLDs n (%)	P value
Job Title			
Advanced practice clinicians	73 (26)	55 (32)	0.1940
Physician	203 (74)	116 (68)	
Frequency and numbers of meeting in past year			
Low (0–1 time)	104 (37)	70 (41)	0.7088
Intermediate (2–3 times)	75 (27)	47 (27)	
High (4 and more)	97 (38)	54 (32)	
Years of Working at MCHS			
1–4 years (early career)	69 (25)	50 (29)	0.5647
5–15 years (mid-career)	116 (43)	65 (38)	
>15 years (mature career)	88 (32)	56 (33)	
Q5 – Available: my SLD is available to me when I have suggestions or concerns to address			
No	14 (5)	18 (11)	0.0289
Yes	258 (95)	150 (89)	
Q6 – Respectful: my SLD treats me with respect			
No	17 (6)	9 (5)	0.7402
Yes	256 (94)	156 (95)	
Q7 – Recognition: my SLD recognizes me for a job well done			
No	37 (14)	42 (26)	0.0017
Yes	234 (86)	122 (74)	
Q8 – Feedback: my SLD provides me with constructive advice/feedback			
No	51 (19)	49 (30)	0.0093
Yes	219 (81)	116 (70)	
Q9 – New policy: my SLD keeps me informed of MCHS policy changes and initiatives			
No	28 (10)	38 (22)	0.0005
Yes	244 (90)	131 (78)	
Q10 – Environment: my SLD works to provide an environment promoting success			
No	41 (15)	42 (26)	0.0057
Yes	230 (85)	120 (74)	
Q11 – Unbiasedness: my SLD applies policy and directives fairly			
No	23 (9)	27 (17)	0.0126
Yes	244 (91)	136 (83)	
Q12 – Supportive: my SLD supports my development as a professional			
No	40 (15)	38 (23)	0.0270
Yes	229 (85)	125 (77)	
Level of satisfaction			
Extremely satisfied	115 (42)	54 (32)	0.0227
Satisfied	91 (33)	56 (33)	
Neutral	37 (13)	30 (18)	
Unsatisfied	15 (5)	22 (12)	
Extremely unsatisfied	18 (7)	9 (5)	

Abbreviations: MCHS, Marshfield Clinic Health System; Q, question. Sample size: surgeon SLDs (N=171, 39.0%); non-surgeon SLDs (N=276, 63.0%).

illustrate the prominence of these qualities, with terms like “competent” and “receptive” dominating positive feedback, while “disconnected” and “ineffective” were central to negative perceptions. Physicians and non-physicians attributed 199 and 59 positive qualities, respectively, with physicians noting more negative attributes (Appendix 6). Surgeons described fewer positive qualities (41 citations) compared to non-surgeons (151 citations), while negative attributes like “disconnected” and “uninformed” were more

Table 5. Correlations Among Numbers of Meeting, Eight Domains of Engagement, and Level of Satisfaction

	Meeting No.	Available	Respectful	Recognition	Feedback	New Policy	Environment	Unbiasedness	Supportive	Satisfaction
Meeting No.	1									
Available	0.28	1								
Respectful	0.23	0.51	1							
Recognition	0.48	0.48	0.43	1						
Feedback	0.48	0.51	0.42	0.71	1					
New Policy	0.35	0.57	0.33	0.46	0.58	1				
Environment	0.39	0.51	0.47	0.63	0.64	0.64	1			
Unbiasedness	0.34	0.56	0.50	0.50	0.59	0.60	0.64	1		
Supportive	0.35	0.51	0.50	0.64	0.65	0.57	0.67	0.63	1	
Satisfaction	0.35	0.46	0.39	0.50	0.57	0.45	0.60	0.52	0.57	1

prevalent among surgeon-led SLDs (Appendix 7). Word clouds stratified by professional experience showed “competent” as a universally valued quality, while terms like “disconnected” and “ineffective” appeared frequently among mid- and late-career groups, reflecting detailed perceptions across tenure (Appendix 8). Positive leadership qualities, including “competent” (97 mentions), “receptive” (26 mentions), and “proactive” (16 mentions) were cited frequently, alongside negative attributes such as “disconnected” (28 mentions) and “uninformed” (21 mentions) (Appendix 9).

DISCUSSION

Our evaluation of service line providers’ perceptions of their SLDs in MCHS’s rural health care setting uncovered several significant findings. First, a substantial 70% of respondents expressed satisfaction with their SLDs. Many reasons for this contentment may exist, as provided in our second finding: that regular, meaningful interactions from SLDs (ie, recognizing and providing feedback) significantly boost provider satisfaction levels. This finding was corroborated by a positive correlation between meeting frequencies and increased satisfaction. Third, while most respondents acknowledged SLDs for positive attributes (availability, feedback, etc), our analysis exposed distinct variations in perceptions—particularly between physicians and APCs. This divergence was more pronounced between surgeon and non-surgeon SLDs. Certain groups—especially APCs under surgeon SLD—reported less engagement. These results accentuate a need for tailored SLD leadership training. Strategic organizational shifts might enhance satisfaction, ultimately influencing provider recruitment and retention for rural health care settings.

Regarding the 3 hypotheses, our exploration also unearthed useful outcomes. The first hypothesis receives support from the 70% respondent satisfaction. In terms of the second hypothesis, we found that while most domains associated with leadership qualities of SLDs were positively tied to job satisfaction, nuances existed. For instance, consistent recognition and constructive feedback from SLDs were strong determinants of satisfaction, but respectful treatment—though significant—correlated rela-

tively lower with overall satisfaction. The frequency of meetings with SLDs was only moderately correlated with satisfaction, suggesting that meeting quality mattered more than sheer frequency. Our third hypothesis postulated a direct correlation between the tenure of SLDs at MCHS and their perceived engagement levels, but such an association was not found. This insight challenges the presumption that tenure of leadership serves as a proxy measure of effectiveness.

Our findings both resonate with the existing medical leadership literature and contribute novel insights. Our results showed that effective SLDs were seen as credible experts by service line members; a systematic review of medical leadership in hospital settings likewise found lower levels of satisfaction correlated with a perceived lack of credibility.²¹ Our study reinforces findings around the struggle for rural health care institutions to provide uniform access, and the role leadership plays navigating such struggles.^{1,2} Our observed 70% satisfaction rate with MCHS SLDs also emphasizes their recognized role in aligning service delivery with organizational objectives and effective communication.^{4,6,8} Other research has found that leadership roles and competencies impact the service line management approach or that such leadership impacts quality of health care service provided, while others have examined various service line models, including the dyad.^{5,8,15} To these insights we add that the frequency and quality of SLD interactions deeply impact provider satisfaction. In analyzing the single SLD model, we find that the social nature of leadership itself manifests in meeting quality and perceived positive SLD characteristics. Thus, we emphasize the importance of continuous leadership development irrespective of tenure, challenging preexisting notions about the nature of leadership and encouraging a much-needed shift in leadership training.²²

Conducting surveys among health care professionals poses intrinsic challenges in fast-paced settings like ours. Among providers, a survey’s length and its perceived relevance significantly affect participation rate. Our moderate response rate (43%), then, suggests the importance of the SLD to their service line. Previous

research has revealed a median response rate of approximately 54% in physician surveys,²³ indicating that surveys in analogous settings could register below-median response rates. Thus, we characterize our 43% response rate as “moderate” based on the literature and our sense of achievement in response uptake from extraordinarily busy professionals.

Study Limitations

We acknowledge several study limitations. Response rates across service lines differed, and whether those who responded represent the whole is unknown. Service line size (which varies considerably) could impact these rates, but so could service line functions, as some represent support services and others deliver patient care. Any of these factors may affect the perception of an SLD’s relative capabilities.

Our qualitative approach also had limitations. Though we found our survey tool effective, more delicate tools such as a Likert scale might capture the intensity of perceptions. The word clouds we generated only represent the frequency of words for leadership attributes and do not include themes that could be identified by other qualitative analyses. Usage of synonyms, umbrella terms, and other connotations might erase some nuance or overrepresent certain terms. More granular methods of presenting such data may emerge in future research.

We note that certain groups may have been over- or underrepresented in our subgroups. In the “job title” category, “physicians” were notably overrepresented, making up 67% of the responses. This representational imbalance may influence generalizability. Additionally, this study involves a single center, encompassing employees from 1 distinct geographic region and entailing limited generalizability.

We also note the potential for selection bias. Respondents might predominantly consist of the more engaged portion of the workforce. Those with stronger feelings—positive or negative—about the SLDs could have been more inclined to respond. This limitation should be considered when interpreting our study or comparing it with others.

CONCLUSIONS

Our evaluation of service line providers’ perceptions of their SLDs within MCHS, set against the backdrop of a rurally based health care environment, made several discoveries. An overwhelming 70% of our participants expressed satisfaction with their SLDs. Crucially, the frequency and quality of interactions—especially those emphasizing recognition and constructive feedback—stood out as primary drivers. Conversely, disparities emerged, particularly between physicians and APCs. APCs under surgeon-led SLDs reported notably less engagement. This divergence underscores a pressing need for personalized leadership training catered to specific provider groups. Our findings suggest implications for policy and practice: tailored leadership development for SLDs (irrespec-

tive of tenure) and informed organizational strategies could markedly elevate provider satisfaction levels. These evidence-backed strategies can help rural health care institutions improve provider recruitment and retention.

Compliance with Ethical Standards: The Institutional Review Board (IRB) deemed the study did not meet the definition of research and was not subject to IRB oversight.

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Next Steps: Teaching Future Generations an Interprofessional Approach to Diabetic Foot Ulcer Care

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ABSTRACT

Background: We aimed to assess the effectiveness of interprofessional teaching sessions focused on the care of patients with diabetic foot ulcers.

Methods: We conducted a pre-/post-intervention, quasi-experimental study with repeat evaluations on either side of the teaching sessions (n=28). Surveys and chart reviews were used to assess changes in attitude, knowledge, practice, and patient outcomes.

Results: All 5 infectious disease fellows favorably reviewed the sessions. Positive baseline attitudes towards interprofessional care further improved with respect to shared learning and teamwork (5-point Likert scale scores pre- and post-session: 4.13 vs 4.44, respectively, $P < 0.01$). No other significant changes were observed.

Discussion: Our sessions were associated with improved attitudes toward interprofessional care but likely need to be augmented with experiential learning to achieve practice and outcome improvements.

BACKGROUND

Health care delivery today requires physicians to practice within interprofessional teams. The importance of this skillset is recognized increasingly, including mandates to teach interprofessional skills in graduate medical education.^{1,2} However, educational strategies that best hone these skills are nascent.^{3,4} Educators need efficient, effective means of teaching interprofessional skills with limited time and resources.

To help meet this need in our infectious disease (ID) fellowship, we designed 2 interprofessional teaching sessions centered on the care of patients with diabetic foot ulcers and incorpo-

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rated them into the existing curriculum. Fellows are optimal targets for such curricula, because they are still early enough in their training to maximize clinical practice habit change while past the point of focusing on pathophysiology. We chose diabetic foot ulcers as the physiologic topic because interprofessional teams have been associated with improved patient outcomes.⁵ Further, our Veterans Affairs (VA) training site also houses a podiatry residency—a keystone profession for diabetic foot ulcer care.

Through our brief curriculum, we sought to change attitudes toward interprofessional care among our ID fellows

and increase their knowledge of diabetic foot ulcer care, all in service of improving practice habits and patient outcomes.

METHODS

Setting and Participants

We conducted interprofessional teaching sessions at a VA tertiary care hospital in the Midwest, with a co-located ID fellowship and podiatry residency. Sessions were delivered in person during regular curricular time to 5 ID fellows in January 2023, the academic year midpoint. Podiatry residents and individuals from other professions participated in the sessions, detailed below.

Interprofessional Teaching Sessions

Teaching sessions were informed by the 2011 Interprofessional Education Collaborative Core Competencies for Interprofessional Collaborative Practice and followed best practice for case-based, cooperative learning (Table 1).^{3,5} Each 1-hour session was mandatory for ID fellows. The first introduced interprofessional principles and their importance in ID. Cases (injection drug

Table 1. Five Key Concepts of Cooperative Learning and How They Were Applied to Case-based Teaching Sessions on Interprofessional Collaboration³

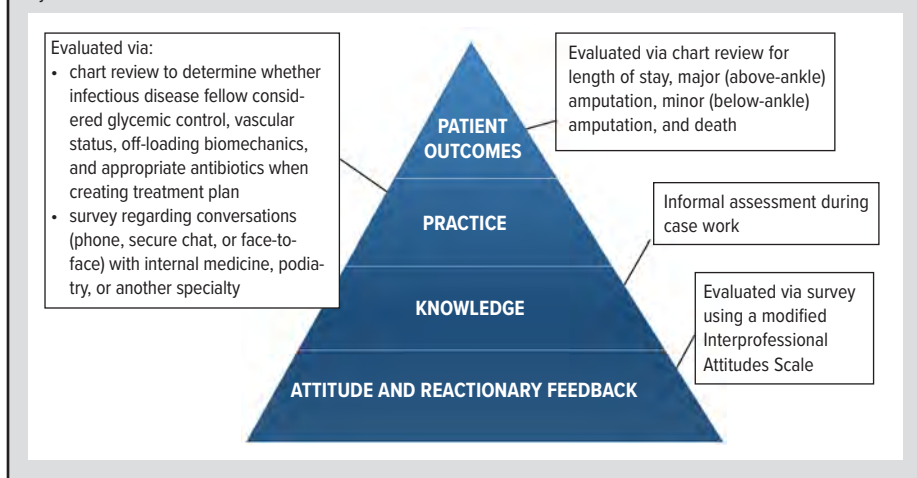
Key Concept	Abstract Description	Concrete Application
Positive interdependence	Students have complementary roles and share a common goal	<i>Session 1:</i> Infectious disease (ID) fellows participated in 20-minute small group discussions with nurses, case managers, pharmacists, and an advanced practice provider with the shared goal of delivering high quality care to: a) a person who injects drugs with endocarditis or b) a person receiving palliative care with a central line-associated bloodstream infection. Results were shared back to the larger group in the ensuing 10 minutes. <i>Session 2:</i> ID fellows paired with podiatry residents to develop a collaborative care plan for patients with diabetic foot ulcers, sharing the goal of limb salvage (20 minutes to develop a plan; 10 minutes to share the plan with the larger group).
Face-to-face promotive interaction	Close, usually synchronous, activities such as discussion or joint decision-making where learners help each other succeed	<i>Sessions 1 and 2:</i> Case-based learning was held synchronously and face-to-face. Cases required input from all professions to achieve the desired goal. Each case packet contained a written description of the initial clinical presentation, photographs of the wound, pertinent labs/microbiology/pathology, and radiographic images.
Individual accountability	Each individual is held responsible for contributing a fair share to the group's success	<i>Session 2:</i> Cases of patients with diabetic foot ulcers were chosen so that they contained principles of biomechanics that would be well known to the podiatry residents but unfamiliar to the ID fellows, and principles of antibiotic selection that would be well known to the ID fellows but outside the expertise of the podiatry residents. Facilitators ensured members of each discipline contributed to the group's success by addressing these principles.
Interpersonal and small group skills	Team skills	<i>Session 1:</i> Four learning objectives aligned with the 2011 Interprofessional Education Collaborative Core Competencies for Interprofessional Collaborative Practice: ⁵ 1. Review the process of professional socialization and recognize how it influences your perspective of interprofessional team members (information available at the UW Center for Interprofessional Practice and Education: www.cipe.wisc.edu). 2. Describe the principles of effective interprofessional healthcare teams (information available at UW Center for Interprofessional Practice and Education: www.cipe.wisc.edu). 3. Engage members of your interprofessional team to develop care plans to meet specific patient needs. 4. Communicate with team members to better understand their responsibility in executing a treatment plan.
Group processing	Reflecting on how the group functioned and what might make it work better	<i>Session 2:</i> The closing 10 minutes were spent actively eliciting learners' response to the collaborative case work and how they might apply this approach to clinical practice.

use-associated endocarditis and catheter-associated bloodstream infection) emphasized the importance of interprofessional care across the spectrum of infectious disease. They facilitated perspective sharing among fellows and other invited professionals: nurses, case managers, pharmacists, and an advanced practice provider. The second session was co-facilitated by an ID physician and a podiatrist. ID fellows were paired with podiatry residents to work through diabetic foot ulcer cases with the intent of fostering appreciation of each other's expertise.

Study Design and Curriculum Evaluation

We designed a pre-/post-intervention, quasi-experimental study with repeat evaluations on either side of the teaching sessions to reduce maturation threats and regression to the mean. We collected 14 weeks of pre-intervention data and 14 weeks of post-intervention data on attitudes, practice, and patient outcomes—an assessment approach informed by Miller's pyramidal framework (Figure).⁶ Each time ID fellows finished their weeklong VA consult rotations, they completed a 3-part survey. First, attitudes were assessed using a modified interprofessional attitudes scale.

Figure. Impact of Curriculum on Attitude, Knowledge, Practice, and Patient Outcomes, Following Miller's Pyramidal Framework for Clinical Assessment.⁶



Items were subcategorized into shared learning and teamwork, patient-centeredness, interprofessional biases, diversity and ethics, and community-centeredness.⁷ Responses were based on a 5-point Likert scale, with 5 corresponding to strongly positive. Second, fellows were asked to identify a patient with a diabetic foot ulcer for whom they provided care. A study team member then abstracted 2 ID-specific and 10 non-ID-specific care practices from clinical documentation by the fellows and patient outcomes assessed at 1 month via chart review (Table 2). Third, fellows who cared for a

patient with a diabetic foot ulcer that week were asked to name the disciplines with which they collaborated. Fellows received monetary compensation for completing the surveys. Knowledge was assessed informally during the teaching sessions, and post-session surveys were distributed for participant feedback. ID fellows provided written informed consent; patient consent was waived. The University of Wisconsin Health Sciences Institutional Review Board and William S. Middleton Memorial VA Research and Development Committee approved this study.

Statistics

We aggregated care metrics into the percentage of applicable ID-specific and non-ID-specific metrics met. We used nonparametric, Fisher's exact, and Mann-Whitney U tests due to our small sample size and lack of independence between observations.

RESULTS

All fellows participated in the curriculum and pre- and post-assessments (n = 5) and cared for 7 and 4 patients with diabetic foot ulcers in the pre-intervention and post-intervention phases, respectively. Evaluations suggest the teaching sessions were viewed favorably. The first session was rated 4.38 on average (n = 4). One participant said, "I learned that everyone looks at a case study differently based on their level of expertise and role... [The session] strongly showed that every member of the team can bring a different perspective to the table."

The second session was rated 4.95 on average (n = 5). One participant said that they learned to "use efficient but often [frequent] communication."

Fellows demonstrated strongly positive attitudes toward interprofessional collaboration, which improved following the teaching sessions, particularly in the domain of shared learning and teamwork (4.13 pre-intervention vs 4.4 post-intervention, $P < 0.01$, Table 2). ID fellows provided all ID-specific care metrics over the course of the study. They provided fewer non-ID care practices at baseline, and this did not increase over the course of the study. Patient outcomes, including length of stay, amputations, and death, did not change.

DISCUSSION

We saw improved attitudes towards shared learning and teamwork following delivery of our interprofessional teaching sessions. We

Table 2. Multilevel Assessment of the Teaching Sessions on Interprofessional Collaboration Following Miller's Pyramidal Framework⁶

Assessment Level	Pre-intervention ^a	Post-intervention ^b	P value
Attitude			
Shared learning, mean (range)	4.13 (2-5)	4.44 (3-5)	<0.01
Patient-centeredness, mean (range)	4.67 (4-5)	4.69 (4-5)	0.86
Interprofessional biases, mean (range)	3.33 (1-3)	3.38 (2-4)	0.91
Diversity and ethics, mean (range)	4.86 (4-5)	4.82 (5-5)	0.61
Community-centeredness, mean (range)	3.87 (2-5)	3.89 (2-5)	0.93
Practice			
Interprofessional communication			
with primary team, n (%)	7 (100)	4 (100)	—
with podiatry, n (%)	4 (57)	1 (25)	0.35
Percent of applicable ID-specific care metrics met, ^c mean (range)	100 (100-100)	100 (100-100)	--
Percent of applicable non-ID-specific care metrics met, ^d mean (range)	20 (0-75)	11 (0-43)	0.30
Patient outcomes			
Death, n (%)	0 (0)	0 (0)	—
Major amputation (above-ankle), n (%)	0 (0)	0 (0)	—
Minor amputation (below-ankle), n (%)	3 (43)	1 (25)	1.00
Length of hospital stay in days, mean (range)	19.3 (7-36)	22.0 (15-29)	1.00

Abbreviations: IPC, interprofessional care; ID, infectious disease.

^aFellows completed 14 attitudinal surveys and saw 7 patients with foot ulcers in the pre-intervention phase.

^bFellows completed 14 attitudinal surveys and saw 4 patients with foot ulcers in the post-intervention phase.

^cID-specific care metrics were (1) interpretation of culture results and (2) appropriate antibiotic use.

^dNon-ID-specific care metrics were: (1) mention of hemoglobin A1C, (2) addressed hemoglobin A1C values >7.5%, (3) recorded pedal pulses, (4) mentioned ankle-brachial index values, (5) recommended vascular diagnostics, if applicable, (6) recorded statin use, (7) recommended statin use, if applicable, (8) recorded tobacco use, (9) recommended tobacco cessation, if applicable, and (10) mentioned off-loading.

hope this may portend more interprofessional care and improved patient outcomes, but our small sample size and brief follow-up did not allow us to fully investigate this. Teaching sessions might offer an efficient, effective means of fostering positive attitudes toward interprofessional collaboration, which tend to wane as training progresses, with more profound drops among surgical colleagues.⁸ Therefore, our findings of improved attitudes among fellows—especially embarking on medical-surgical collaborations—is noteworthy.⁸ However, we need to further investigate the durability of this improvement and its impact on clinical practice and patient outcomes.

Our teaching sessions represent a first—and not final—step toward attaining high-caliber interprofessional skills. While we improved attitudes toward interprofessional care, the effect on practice patterns and patient outcomes has not been realized. A particular increase in attitudes regarding shared learning and teamwork makes sense given that teaching sessions focused on cooperative learning between members of different disciplines. The education literature supports cooperative learning as an effective strategy to teach teamwork skills.³ It consists of 5 key concepts, which we reified in our teaching sessions (Table 1). These same concepts are also important aspects of interprofessional teamwork in health care.⁹ Cooperative learning provides a way of instilling

core teamwork skills, but experiential, service-driven learning is likely necessary to habitualize interprofessional collaboration into a learner's clinical practice.³ As a next step, therefore, our team intends to model and guide interprofessional collaborations during bedside care of patients with diabetic foot ulcers. We hope to gather feedback from non-ID learners, such as podiatry residents, involved in these interprofessional collaborations. We hypothesize that experiential learning will help ID fellows and their collaborators improve non-ID care metrics in particular, as their interprofessional focus precipitates more comprehensive care.

While promising, our study has significant limitations worthy of acknowledgement. First is its small sample size. Although we had 100% participation amongst our ID fellows, the cohort was small. Furthermore, they cared for few patients with diabetic foot ulcers. Even when we included all patients with diabetic foot ulcers cared for by our fellows in the pre- and post-intervention periods, we captured data on only 11 patients. This reduced our ability to detect statistically and clinically significant changes. We used multiple measures of curriculum evaluation to strengthen our work, from reactionary feedback to patient outcomes. However, if fellows had cared for 1 patient with a diabetic foot ulcer each week—resulting in 28 hypothetical patients rather than 11 actual patients—and no one (0%) sustained a minor (below ankle) amputation in the post-intervention group, we still would be underpowered to detect a statistically significant difference in minor amputations given our pre-intervention rate of 30% (hypothetical *P* value of 0.22). Second, we cannot comment on the durability of attitudinal improvements beyond 14 weeks. The effect of brief interventions—especially those without bedside teaching follow-up—may wane with time. However, our 14-week post-intervention period is longer than most interprofessional education studies, leaving us cautiously optimistic that a brief intervention might sustain improvements.⁴ Third, we focused exclusively on ID fellows. Capturing attitudinal changes and experiences of those with whom they were collaborating, such as podiatry and internal medicine residents, would be an important next step in evaluating this curriculum. Reactionary feedback from non-ID fellows attending the teaching sessions was positive, although more in-depth data similar to that obtained from the fellows are lacking. Fourth, we assessed non-ID care metrics by abstracting notes written by the ID fellows. Fellows may have thought that it was unnecessary to reiterate this information in an ID note. While our practice-level evaluation may have underestimated non-ID-specific care provided, the low level of formal documentation suggests ample room for improvement.

CONCLUSIONS

A brief educational intervention emphasizing interprofessional care for patients with diabetic foot ulcers was well received by ID fellows and associated with improved attitudes toward shared learning and teamwork in the 14 weeks following curriculum deliv-

ery. More robust shared learning within the clinical environment may be needed to achieve clinically significant improvements in practice and outcomes for patients with diabetic foot ulcers.

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A Case of Travel-Associated Tick-Borne Relapsing Fever in Wisconsin

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ABSTRACT

Introduction: Tick-borne relapsing fever is a zoonotic infection caused by members of the *Borrelia* genus of spirochetes found predominantly in the southwestern United States.

Case Presentation: A 65-year-old woman presented to a Wisconsin emergency department with a 2-day history of fevers and altered mental status after returning from a 5-week stay in Colorado. Initial labs were notable for elevated transaminases, thrombocytopenia, mild hyponatremia, mild hypokalemia, and elevated procalcitonin.

Discussion: Rapid identification of patients with tick-borne relapsing fever is essential to minimize morbidity and mortality. Peripheral blood smear—especially during a febrile episode—can serve as a quick and accurate way to diagnose the illness with direct visualization of spirochetes.

Conclusions: Early analysis of a peripheral blood smear can lead to a swift diagnosis of tick-borne relapsing fever, particularly in nonendemic states such as Wisconsin.

INTRODUCTION

Tick-borne relapsing fever (TBRF) is a zoonotic infection caused by members of the *Borrelia* genus of spirochetes.¹ While cases have been reported throughout the continental United States, from 1990 to 2011, approximately 70% of cases were localized to California, Washington, and Colorado. TBRF is classically transmitted by soft ticks, such as *Ornithodoros spp*, which live in close proximity to mammal hosts and feed rapidly compared to

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the “wait and feed” approach of hard tick species. In contrast to Lyme disease, where tick attachment for 24 to 48 hours is necessary for transmission, TBRF transmission can occur in as little as 15 to 90 minutes.^{2,3} Given the quick feeding time and susceptibility to be caused by nymph bites, patients often do not associate symptoms with a tick bite. The most commonly associated exposure with the illness is cabin-based lodging.⁴⁻⁷

Clinically, presentation of TBRF is characterized by fever presenting 4 to 18 days after exposure, most commonly with headache, myalgias, chills, and vomiting.¹ The fever pattern is recurrent, with the initial

febrile episode typically lasting for 4 to 7 days. Subsequent febrile episodes are classically interspaced by up to 7 febrile-free days.⁸ Neurologic involvement can manifest as meningismus, radiculopathy, facial palsy, and encephalitis. Neuropsychiatric disturbances such as apathy or delirium also have been reported. Ocular manifestations are rare and can manifest as iritis, choroiditis, and optic neuritis with rapid deterioration of vision.⁹ Gastrointestinal manifestations of TBRF commonly involve nausea and vomiting but also can include abdominal pain, diarrhea, jaundice, and hepatosplenomegaly. On physical examination, localized neurologic findings, hepatomegaly, or splenomegaly can be suggestive of TBRF.¹⁰ Laboratory findings can be nonspecific and include leukocytosis, thrombocytopenia, elevated liver enzymes, elevated erythrocyte sedimentation rate (ESR), and prolonged prothrombin time (PT) and partial thromboplastin time (PTT).

Fourteen *Borrelia* species have been found to cause tick-borne relapsing fever, with *B hermsii*, *B turicatae*, and *B parkeri* being the dominant forms in North America. *B miyamotoi* is transmitted by hard-bodied ticks and is the species identified to locally transmit

TBRF in Wisconsin.⁸ The first confirmed case of *B miyamotoi* in Wisconsin was in 2016, and there were a total of 23 cases reported from 2016 through 2022.¹¹ Here, we report a case of TBRF identified at an academic medical center in Wisconsin, with polymerase chain reaction indicating a *Borrelia* infection.

CASE PRESENTATION

In August 2023, a 65-year-old woman presented to an emergency department (ED) in Madison, Wisconsin, after a 2-day history of fevers and altered mental status. She had returned to Wisconsin the day prior from a 5-week solitary meditation retreat in Colorado, where she was staying in a cabin at an elevation of 8900 feet. During the initial 2 weeks of her trip, she had experienced headaches, polyuria, and skin dryness that she attributed to the elevation and which self-resolved. After returning to her usual state of health for the majority of the trip, she first experienced a subjective fever on the day prior to leaving Colorado. While driving to Wisconsin the following day, she reported continued subjective fevers and new urinary incontinence, in addition to neurological concerns such as confusion, forgetfulness, and difficulty completing tasks. She even described herself as having an uncharacteristically flat affect, which was concerning for her.

The following day, symptoms had progressed to include intermittent headaches, nausea, and bleeding gums while brushing teeth, which prompted her to self-present to the ED. While enroute, she experienced a low-impact motor vehicle collision after veering off the road. She could not recall the details surrounding the crash, though noted having no emotional reaction to crashing her car. She had no focal neurologic changes. An extensive history was collected related to her recent time in Colorado, which was notable only for multiple insect bites of unclear source and proximity to deer. She denied any tick exposures. Past medical history was notable only for asthma and migraines with aura.

During her initial presentation, the patient was found to be febrile to 38.8°C. Physical exam revealed a small, well-circumscribed, erythematous lesion with central clearing on the lateral aspect of her right thigh. No bleeding gums were noted. The neurological exam was unremarkable. Her presenting labs were notable for elevated transaminases, thrombocytopenia, mild hyponatremia and hypokalemia, and elevated procalcitonin (Table 1). A workup of altered mental status included computed tomography (CT) head to rule out structural causes, chest x-ray, and CT abdomen/pelvis to evaluate for sources of infection—all of which were without acute abnormalities. She was started on cefepime and vancomycin initially and admitted to a general medicine service.

Upon admission, ESR was 44 and C-reactive protein (CRP) was 22.3. A peripheral blood smear was sent for review, and the patient was started empirically on doxycycline given high concern for tick-associated pathology. She continued to worsen clinically

Table. Pertinent Lab Values at Time of Admission

Lab	Result	Normal Range	Units
Complete Blood Cell Count			
White blood cell count	6.3	(3.8–10.5)	K/ μ L
Red blood cell count	3.8	(3.8–5.2)	M/ μ L
Hemoglobin	12	(11.6–15.6)	g/dl
Hematocrit	35	(34–46)	%
Mean corpuscular volume	92	(80–97)	fL
MCHC	34	(32–36)	g/dL
RDW-CV	12.3	(11.7–14.7)	%
RDW-SD	41.7	(36–46)	fL
Platelet count	103	(160–370)	K/ μ L
Comprehensive Metabolic Panel			
Sodium	132	(136–145)	mM/L
Potassium	3.1	(3.5–5.1)	mM/L
Chloride	103	(98–107)	mM/L
Carbon dioxide	20	(22–29)	mM/L
Anion gap	9	(7–14)	mM/L
Blood urea nitrogen	12	(7–19)	mg/dL
Creatinine	0.84	(0.55–1.02)	mg/dL
Glucose	235	(70–99)	mg/dL
Calcium	8.7	(8.4–10.2)	mg/dL
Magnesium	1.8	(1.6–2.6)	mg/dL
Bilirubin (total)	2.1	(0.0–1.4)	mg/dL
Alkaline phosphatase	91	(40–150)	U/L
Aspartate aminotransferase	106	(5–34)	U/L
Alanine aminotransferase	116	(0–55)	U/L
Albumin	3.0	(3.5–5.0)	g/dL
Protein, total	6.0	(6.4–8.3)	g/dL
Other			
Thyroid-stimulating hormone	0.82	(0.35–4.94)	μ U/mL
Ammonia	24	(0–71)	μ U/mL
Procalcitonin	2.26	(<0.25)	ng/MI

Abbreviations: MCHC, mean corpuscular hemoglobin concentration; RDW-CV, red blood cell distribution width coefficient of variation; RDW-SD, red blood cell distribution width standard deviation.

overnight, becoming mildly tachycardic and hypotensive with systolic blood pressure in the 70s to 80s refractory to multiple liters of fluid. Evaluation for intensive care unit (ICU) admission for vasopressor support was performed, though she did not meet ICU admission criteria. Shortly thereafter, blood smear demonstrated the presence of spirochetes (Figure 1), and a presumptive diagnosis of TBRF was made. Lumbar puncture demonstrated <10/LPF mononuclear cells and no neutrophils or organisms. She was continued on ceftriaxone and doxycycline.

Further negative infectious workup included murine typhus Ab titer (<1:64), Rocky Mountain Spotted fever Ab titer (<1:64), cerebrospinal fluid (CSF) bacterial culture (no growth at 5 days), CSF fungal culture (no growth at 7 days), blood culture (2/2 no growth at 5 days), urine culture (negative), *Borrelia burgdorferi* Ab (negative), Lyme PCR (not detected), *Babesia* IgG (<1:16), *Babesia* IgM (<1:20), *Anaplasma phagocytophilum* IgG (<1:80), *A phagocytophilum* IgM (<1:16), *E Chaffeensis* IgG (1:64), *E Chaffeensis* IgM (<1:16), and CSF meningitis/encephalitis panel. Relapsing fever

Borrelia species PCR was positive, with results obtained 5 days after presentation.

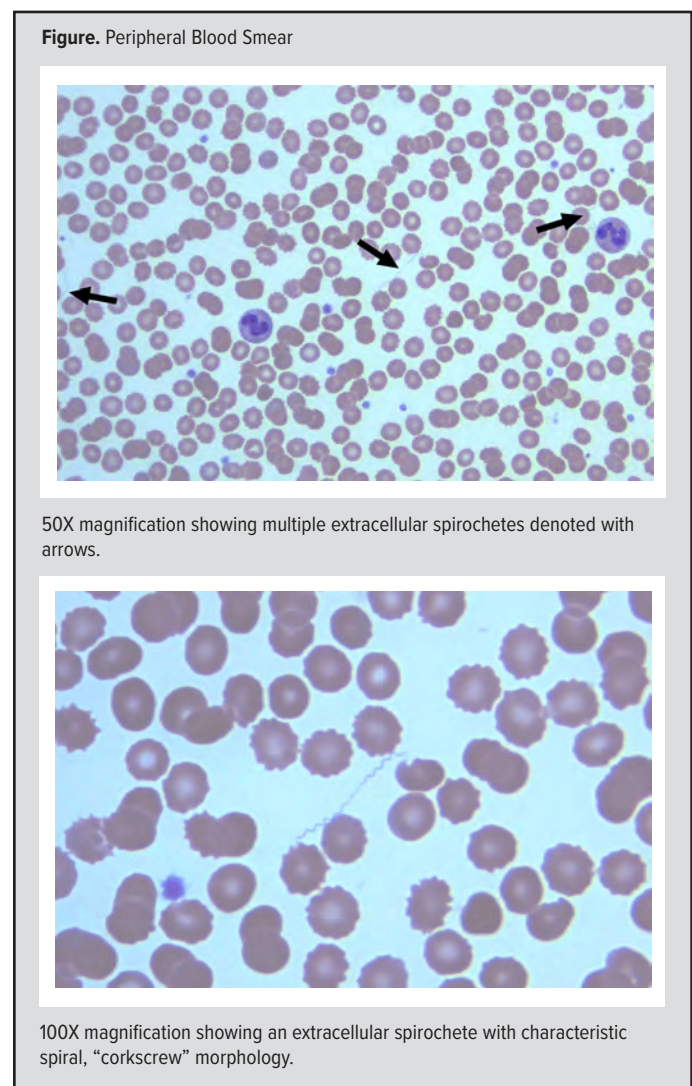
The patient's neurological status quickly improved with doxycycline, and there was low concern for central nervous system involvement. She was discharged on hospital day 1 with a 10-day course of oral doxycycline. Liver function tests (alanine aminotransferase [ALT] 59, aspartate aminotransferase [AST] 55, total bilirubin 0.5, and thrombocytopenia (platelets 334 000) improved at time of discharge. She was seen in the primary care clinic a few days later with near complete resolution of symptoms and normalization of labs. She was seen for follow-up by Infectious Disease 1 month postdischarge, where she reported improved brain fog-giness and word recall but continued balance issues treated with physical therapy.

DISCUSSION

We describe a case of tick-borne relapsing fever identified in Madison, Wisconsin. Although transmission in this case most likely occurred secondary to travel to the endemic area of Colorado, current trends predict increasing prevalence of tick-borne infections to previously nonendemic parts of the country due to climate change.¹² This is attributed to more temperate winters and increasing overall precipitation, which promotes increased survival and activity of ticks, as well as their animal hosts. Since 2016, multiple cases of "nontraveler" TBRF have been identified in Wisconsin alone, suggesting that endemic expansion to the Midwest already may be occurring.¹¹

Tick-borne illnesses such as TBRF can present with many non-specific symptoms. As the name implies, the most prevalent symptom of TBRF is relapsing fever, which is estimated to occur in nearly 100% of cases.¹ The oscillating nature of fever is attributed to antigenic variation of the organism to evade the initial IgM immune response.¹ Other commonly identified symptoms include flu-like symptoms, such as headache (94%), myalgias (92%), nausea/vomiting (>70%), and chills (88%).¹³ As observed in this present case, the presenting concern may be primarily neurologic. The exact mechanism of neurologic involvement is unclear but thought to be indirectly related to fevers and spirochetemia, rather than direct CNS involvement, as brain imaging and lumbar punctures often do not indicate pathology.¹ The described neurologic symptoms, including confusion, lethargy, or apathy, often occur in the absence of any localized neurologic findings.¹ Interestingly, our patient's presentation included amnesia and a self-described uncharacteristic flat affect and apathy to her recent motor vehicle collision while enroute to the hospital.

Transmission of TBRF occurs through tick bite, although only 25% of patients can identify a tick given the quick latch and unlatch time exhibited by soft shell ticks. Cabin-related exposures are highly associated with the infection, with 34% of patients identifying this risk factor in systematic review.¹⁴ Our patient had taken a picture of one of the bites she had received



in the days prior to her symptoms, which was somewhat targetoid in appearance, albeit small and unchanging. TBRF has been associated with erythema migrans in only about 10% of cases, all of which have occurred in regions with hard shell *Ixodes* ticks. Regardless of the identified tick exposure, she did note staying in a remote cabin during her trip. In terms of laboratory studies, the presence of thrombocytopenia is the only finding that has been reported relatively frequently (approximately 55% of cases), although elevation of ESR and CRP can occur approximately 25% of the time.¹ In this case, elevated procalcitonin without clinical features of pneumonia was a key lab value that suggested acute inflammation.¹⁵

Overall, if there is concern for TBRF, prompt blood smear can aid rapid diagnosis. Peripheral blood smear—especially during a febrile episode—is, on average, 80% sensitive for identifying spirochetes in cases of TBRF.¹ Peripheral blood smear is most useful in the diagnosis of TBRF, anaplasmosis, ehrlichiosis, and babesia. It is less useful in the diagnosis of Lyme disease and may not be a first-line diagnostic test for all cases of suspected tick-borne disease. PCR is the most sensitive test; however, it is time-intensive

and more expensive. Due to the high molecular similarity between different *Borrelia* species, with reported 16S rRNA gene sequence variability $\leq 1\%$, it is challenging to provide exact species identification even with current PCR methods.¹

When concern for tick-borne pathology is high, empiric treatment with doxycycline is warranted. Within hours of presenting to our institution, the patient in our case began to develop refractory hypotension, concerning for potential septic shock. Hours after administration of doxycycline, she had improved back to near baseline. Doxycycline is the most common agent used to treat TBRF and is administered as an oral regimen of 100 mg twice daily for 10 days.¹³ Additional options may include macrolides and fluoroquinolones. It is important to note, however, that initiation of antibiotics in spirochete-based infections can result in Jarisch-Herxheimer reaction due to systemic release of cytokines. This reaction is demonstrated also by high fevers and hypotension and, therefore, can be difficult to separate from the infection itself.

CONCLUSIONS

Clinicians should consider tick-borne pathogens in patients with nonspecific symptoms, especially if fever, neurologic changes, and/or thrombocytopenia are present, regardless of travel history. Recent travel to the southwestern United States, presence of tick, and/or cabin exposure are notable risk factors for TBRF. Peripheral blood smear is an easy and inexpensive test that can help lead to a quick diagnosis of TBRF. Empiric treatment with doxycycline may be warranted if clinical suspicion for TBRF is high. Jarisch-Herxheimer reactions can occur with treatment of any spirochete infection, so it is important to monitor patients for worsening fever and hypotension after the initial dose of antibiotics.

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Fibrocartilagenous Embolism Spinal Cord Infarction, Mistaken for Glial Fibrillary Acidic Protein Autoimmune Transverse Myelitis: A Case Report

Felix E. Chukwudelunzu, MD, MBA; Timothy Young, MD

ABSTRACT

Introduction: Fibrocartilagenous embolism causing spinal cord infarct is rare, and a high index of clinical suspicion is needed for accurate diagnosis.

Case Presentation: A 65-year-old woman presented to our hospital with back pain, paraparesis, and neurogenic bladder. Magnetic resonance imaging showed a T4-T7 signal abnormality that was misdiagnosed initially and treated as autoimmune myelitis.

Discussion: Fibrocartilagenous spinal cord infarction is rare and remains a clinical diagnosis with supportive imaging findings. The imaging findings may be nonspecific, and other etiologic diagnostic considerations must be excluded.

Conclusion: Fibrocartilagenous embolism causing spinal cord infarct can be mistaken for transverse myelitis. A high index of clinical suspicion with clinical and radiologic correlation is necessary to make accurate diagnosis and avoid unnecessary treatment.

INTRODUCTION

Spinal cord infarctions are uncommon when compared to their cerebral counterpart. Unlike cerebral infarctions, spinal cord infarct due to fibrocartilagenous embolism (FCE) from intervertebral nucleus pulposus is a rare but well-recognized phenomenon. It was first described by Naiman in 1961.¹ This condition often affects a broader age range, including young adults and pediatric patients without obvious stroke risk factors.

The spinal cord has a complex arterial blood supply with significant individual variability. A single large anterior spinal artery runs ventrally in the midline from vertebrobasilar junction

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to the filum terminale. The spinal cord receives auxiliary supply from an inconsistent array of variable numbers of radiculomedullary and descending aorta branches.² Posteriorly, there are paired posterior spinal arteries that primarily supply the dorsal spinal cord, which are fed by similar radicular branches at every spinal level.² Spinal cord blood supply can be divided into 4 semi-distinct territories. The first extends from C1 to T3 and derives blood supply from the vertebral artery. The second region, which extends from T3 to T7, is often supplied by the left intercostal artery. The third region, which extends from T8 to T12, receives

supply from the artery of Adamkiewicz; and the fourth region, which includes the conus, sometimes is supplied by branches from the internal iliac artery.³ FCE causes spinal cord infarction when dislodged material from fibrocartilagenous nucleus pulposus causes occlusion of a spinal radicular artery at or near the level of disc extrusion. Identification of an associated vertebral body infarction is suggested to be a confirmatory sign of FCE-associated spinal cord ischemia.⁴

CASE PRESENTATION

A 65-year-old woman presented to our hospital with a 1-day history of mid back pain, numbness from the upper thorax to bilateral feet, subjective bilateral leg weakness, and difficulty emptying her bladder.

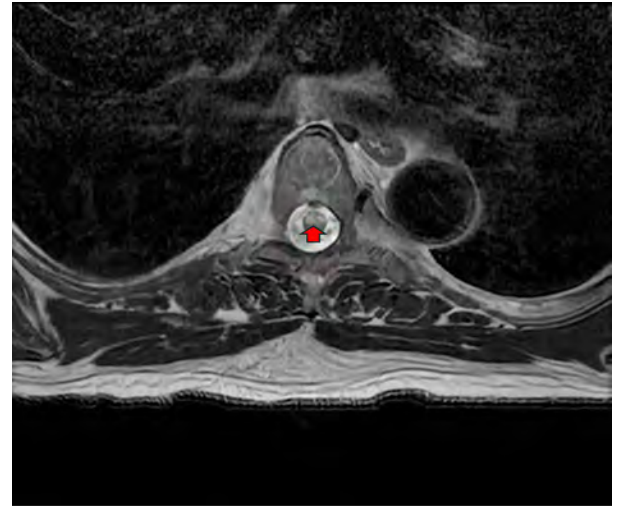
A few days prior to presentation, she was engaged in house painting but otherwise reported no physical trauma. Her prior medical history included stage IV low grade B-cell lymphoma diagnosed in 2022 but now in remission, diet-controlled diabetes, hypertension, tobacco use, obstructive sleep apnea, and

Figure 1. Sagittal T2 Magnetic Resonance Imaging Scan



Scan showing increased signal abnormality involving the ventral aspect of the cord from T4-T7 (yellow solid arrow) and T2 prolongation signal abnormality of the T6 vertebral body (solid red arrow).

Figure 2. Axial T2 Thoracic Spine Magnetic Resonance Imaging



Scan showing hyperintense signal abnormality predominantly involving the ventral aspect of the cord at T6 (red arrow).

cervical laminectomy with fusion from C4-C5 and C5-C7 14 years earlier. She had a retained bone growth stimulator from this procedure.

Initial neurologic examination showed normal cranial nerve testing, normal strength of proximal and distal upper and lower extremity muscles, diffuse hypoactive reflexes, sensory deficit to mild noxious stimulation to thoracic spinal cord level 4 (T4) with preserved position and vibratory sensation (proprioception), as well as urinary retention with a 220 cc post-void residual volume. Planned magnetic resonance imaging (MRI) was delayed due to patient safety concerns related to the bone stimulator, and the patient was provided supportive care.

On hospital day 3, she continued to report mid back pain and diffuse weakness. Neurologic examination revealed mild bilateral proximal lower extremities with Medical Research Council (MRC) grade 4/5 weakness and normal deep tendon reflexes but persistent T4 sensory level to mild noxious stimuli with preserved proprioception.

MRI of the cervical spine showed expected postsurgical changes without spinal canal narrowing. Thoracic spine MRI showed a T2-signal hyperintensity ventrally from T4-T7, with associated disc extrusion at T6-T7. There was no cord compression. A linear T2-signal prolongation abnormality involving the posterior aspect of the T6 vertebral body with marrow enhancement was noted (Figures 1 and 2). Preliminary cerebro-

spinal fluid (CSF) study showed albuminocytologic dissociation (red blood cells 2, nucleated cells 4, and protein 102 mg/dl). Infectious, inflammatory, and autoimmune laboratory markers were ordered. Brain MRI performed on hospital day 4 was normal. Based on the patient's clinical presentation of subacute motor deficits, sensory level, autonomic dysfunction, and initial MRI thoracic spine results and CSF findings, a preliminary diagnosis of transverse myelitis was made. Viral etiologies returned negative. She was started on high-dose intravenous methylprednisolone, 1 gram daily for 3 days. Her symptoms of proximal leg weakness improved to normal, and she was discharged home with a plan for outpatient follow-up.

The patient was re-admitted to the hospital 3 days postdischarge for progressively worsening bilateral lower extremity weakness and numbness. Neurologic examination now revealed MRC grade 2/5 proximal and 3/5 distal bilateral lower extremity weakness with hyperactive reflexes associate with nonsustained (2 beats) ankle clonus on the right side. Also, sensory level to T4 persisted. Upper extremity strength and reflexes were normal. An additional 3 days of high-dose methylprednisolone was initiated.

Further testing included a negative lumbar spine MRI. Computer tomography (CT) scan of chest, abdomen, and pelvis showed mild prominent axillary and mediastinal adenopathy. Fluorodeoxyglucose positron emission (FDG-PET) scan was stable, without signs of recurrent lymphoma. Extensive laboratory testing was negative for human immunodeficiency viruses 1 and 2, leukemia/lymphoma immunotyping by flow cytometry, hepatitis panel, Powassan virus, West Nile virus, and Lyme serologies. CSF bacteria, fungal, and viral cultures/serologies were negative. Multiple sclerosis panel showed elevated immunoglobulin kappa free light chain at 0.4760 (reference <0.1000) and oligoclonal

bands at 3 (reference <2). Myelopathy autoimmune panel was negative except for positive glial fibrillary acidic protein (GFAP) antibodies by immunofluorescence assay. A preliminary diagnosis of GFAP-positive autoimmune transverse myelitis was made pending confirmatory cell-based assay. The patient was started on a 5-day plasmapheresis regimen due to persistent paraparesis. Several days later, the GFAP confirmatory cell-based assay returned negative. Repeat thoracic MRI 17 days after the initial study showed stable findings. However, upon further careful review of both thoracic MRI studies by Neuroradiology, it was observed that the T2-signal abnormality involving the T6 vertebral body represented a subacute ischemic bone infarct. Given the proximity and overlapping vascular distribution to the spinal cord lesion and the associated disc extrusion at or near the same level, a final diagnosis of FCE spinal cord infarction was made. The patient was started on aspirin 81 mg and rosuvastatin 20 mg daily. Alternative stroke mechanism was excluded with negative hypercoagulable profile, transthoracic echocardiogram, and a 30-day cardiac event monitor.

Upon hospital discharge 25 days after the initial admission, the patient's lower extremity paraparesis had improved. The sensory deficit descended to T6 level with preserved proprioception. On outpatient follow-up evaluation 1 month after discharge, she required intermittent catheterization for neurogenic bladder, and her lower extremity showed trace proximal muscle weakness with mild ataxic gait on rapid turns only.

DISCUSSION

Histopathologic evidence for thrombosis of radicular spinal arteries due to fibrocartilaginous nucleus pulposus leading to spinal cord infarction have been well-documented.^{5,6} Our patient presented with back pain without specific trauma, followed by subacute onset of fluctuating bilateral lower extremities paraparesis, persistent sensory level, and neurogenic bladder. The initial fluctuating weakness made this case more difficult to identify as an ischemic process.

A study of 41 histopathologically confirmed cases of spinal cord infarctions due to FCE showed 64% were female. Average age was 41 (range 14–78 years) with clinical picture at presentation of transient neck or back pain, followed by syndrome of myelopathy with abnormal sensory level, neurogenic bladder, and paraplegia in cases involving the thoraco-lumbar spinal cord or quadriplegia in cases of cervical spinal cord involvement. Time to symptom peak ranged from 15 minutes to 21 days.⁶

Our case was notably different from previous reports regarding fluctuating paraparesis. Our patient received high-dose methylprednisolone on admission with presumptive diagnosis of transverse myelitis. The steroid effect may have played some role in the fluctuating nature of the initial symptoms. Additionally, clinical presentation of spinal cord ischemia can vary depending on location and extent of infarction. A rapid decline of function

Table. Proposed Schematic Approach to Diagnosis of Fibrocartilaginous Embolism (FCE) Causing Spinal Cord Infarction

Steps	Description
1	Establish clinical syndrome of myelopathy, sensory level most important
2	Exclude traumatic and compressive etiologies of myelopathy by history and imaging using MRI (preferred) or CT scan with and without contrast
3	Exclude inflammatory etiologies of myelopathy using CSF. Absence of pleocytosis or increased IgG index
4	Establish the diagnosis of spinal cord infarction. Requires steps 1-3 plus 1 "major" criterion or 2 "minor" criteria
Major Criteria	
<ul style="list-style-type: none"> • Clear vascular distribution by exam such as sparing of proprioception • Clear vascular distribution on imaging, axial views MRI • Radiologic changes, MRI T2-hyperintensity in the vertebral body or inter-vertebral disc adjacent to the cord infarction 	
Minor Criteria	
<ul style="list-style-type: none"> • Accompanying new onset neck or back pain • Symptom progression to nadir or near nadir in 4-8 hours • Initial unremarkable MRI of the spinal cord with subsequent evolution of an intra-parenchymal lesion 	
5	Establish the high likelihood of FCE. This requires the absence of other more common etiologies of spinal cord infarction, mainly being aortic pathologies, plus presence of one or more of the following: <ul style="list-style-type: none"> • Temporal relation to heavy lifting or minor neck or back injury or any event that can cause increase intra-disc or intra-vertebral pressure like axial falls, or events that can reverse the venous drainage of the spinal column away from the heart and to the spinal cord instead such as Valsalva maneuver. • Presence of degenerative disc disease especially protrusions or Schmorl's nodes at or near the infarction • Absence of more than 1 vascular risk factor.

Abbreviation: MRI, magnetic resonance imaging; CT, computed tomography; CSF, cerebrospinal fluid; IgG, immunoglobulin.

within 12 hours of onset with severe neurologic deficit is characteristic; however, up to 17% of patients have biphasic syndrome with transient or mild symptoms followed by deterioration.⁷ We also observed initial hyporeflexia in our patient, as was the case in multiple other studies.^{4-6,8} Flaccid paraparesis with hyporeflexia is the dominant initial finding in spinal cord ischemia due to spinal shock. Over time, hyperreflexia, spasticity, and extensor plantar reflexes prevail.

Our patient had elevated immunoglobulin CSF free kappa light chain and 3 oligoclonal bands, suggesting possible intrathecal immunoglobulin synthesis commonly found in multiple sclerosis, as well as other infectious, autoimmune, and inflammatory central nervous system pathologic states known to trigger a humoral immune response. She also has a history of B-cell lymphoma, although in remission. Interestingly, elevated immunoglobulin free light chain is present in 27% of patients with diffuse B-cell lymphoma,⁹ and systemic immunoglobulins may cross the blood-brain-barrier by passive transfer,¹⁰ necessitating a cautious and careful interpretation of abnormal levels in CSF.

Spinal cord ischemic infarct can be mistaken for and treated as an inflammatory or autoimmune transverse myelitis. FCE-

associated spinal cord infarction is rare and remains a clinical diagnosis with supportive imaging findings. The imaging findings may be nonspecific, however, and other etiologic diagnostic considerations need to be excluded, such as autoimmune, inflammatory, infectious, and metabolic transverse myelitis.

A schematic approach to the diagnosis of FCE (Table) as proposed by AbdelRazek et al⁶ serves as a useful template for the diagnosis of this elusive disorder. Our case meets the major steps and all 3 elements of the major criteria of this schematic, including evidence of vertebral body infarction.

CONCLUSIONS

As demonstrated by this case, spinal cord infarction due to FCE can be mistaken for an inflammatory or autoimmune transverse myelitis. A high index of clinical suspicion, cautious interpretation of laboratory findings, and multidisciplinary review of the spinal cord imaging is essential. Correlation with a detailed patient history and clinical symptoms as they evolve are needed to arrive at the correct diagnosis.

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Periorbital Dermatitis Induced by Apixaban

Kelsey Koenig, MD; Grace Tews, BA; Aleksander Downs, MD

ABSTRACT

Introduction: Periorbital dermatitis can be due rarely to an adverse drug reaction. We present a case of a patient whose periorbital dermatitis was caused by apixaban.

Case Presentation: A 76-year-old female presented with severe periorbital dermatitis 3 weeks after starting apixaban. Varying potencies of antihistamines, topical steroids, calcineurin inhibitors, and emollients were used over a 20-month span with no relief of symptoms. Upon discontinuing apixaban and switching to rivaroxaban, she experienced complete resolution of her symptoms.

Discussion: Periorbital dermatitis is a lesser-known adverse effect of apixaban. To our knowledge, there has only been 1 other reported case of periorbital dermatitis induced by apixaban.

Conclusions: We report this case to increase awareness among clinicians of adverse effects of apixaban and to encourage consideration of drug side effects as part of the differential diagnosis for new skin complaints.

INTRODUCTION

Adverse drug reactions, including drug hypersensitivity reactions, are common in the primary care setting and affect up to 20% of outpatients. In 1 meta-analysis, cardiovascular drugs were found to be the most common cause of adverse drug reactions.¹ Cutaneous manifestations are the most common drug hypersensitivity reactions. In 2017, Vu and Gooderham reported a variety of cutaneous drug reactions associated with direct oral anticoagulants.² However, at the time of that study, there were no reports of dermatologic eruptions associated with apixaban. More recent

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research has linked apixaban to lichenoid eruption, vesicular urticarial dermatosis, hypersensitivity reactions, and periorbital edema.³⁻⁶ These reactions usually are diagnosed clinically; thus, it is essential for clinicians to maintain a high index of suspicion to avoid prolonged symptoms as occurred in this case.

CASE PRESENTATION

A 76-year-old female with a medical history significant for congestive heart failure, atrial fibrillation, gastroesophageal reflux disease, myelofibrosis, prior stroke, and pulmonary hypertension presented to outpatient primary care clinic with ongoing severe periorbital dermatitis. Twenty

months prior, she had been admitted to the hospital due to pneumonia and recurrent atrial fibrillation. Apixaban was prescribed on discharge.

One month after discharge, the patient presented to urgent care with a 3-week history of eyelid irritation, redness, edema, and itchiness. She was using multiple over-the-counter creams (including antibacterial and anti-itch creams) to treat this and, thus, was diagnosed with contact dermatitis and told to use only 0.1% triamcinolone cream. Symptoms did not improve with cessation of all over-the-counter treatments and triamcinolone cream alone. She sought care multiple times from several specialists, including dermatology, ophthalmology, optometry, and allergy. She had been using makeup (foundation, mascara, rouge, eyebrow pencil) and was advised to stop all makeup, nail polish, and facial products/creams. Doing so for months did not resolve her symptoms. She denied any new exposures to laundry detergents, household products, hobby related products, etc. Various treatments were tried for periorbital dermatitis, including a daily

antihistamine (fexofenadine and cetirizine), topical steroids of varying potencies (hydrocortisone 2.5% cream, triamcinolone 0.1% cream), calcineurin inhibitors (pimecrolimus, tacrolimus), and emollient creams (chilled petroleum jelly, La Roche-Posay Toleriane eye cream, Cetaphil cream), none of which resolved her symptoms. She also was treated for possible seborrheic dermatitis with ketoconazole 2% cream, which did not resolve her symptoms. A skin biopsy was not done. Standard allergy patch testing was negative. She improved briefly with a 7-day course of oral prednisone prescribed in urgent care, but symptoms reoccurred after cessation.

Twenty months after her symptoms began, the patient saw her primary care physician and reported that she was having ongoing extremely bothersome symptoms. She reported that the skin around her eyes was itchy, burning, red, and swollen every day (Figure). She said that her symptoms started after her hospitalization, and the physician identified that she was started on apixaban at that time. Literature review found 1 case report of a similar patient who had “periorbital swelling and pruritus limited to her eyes” after starting apixaban.³ All of this patient’s other medications were reviewed and no other possible drug reactions were identified. Apixaban was discontinued and she was started on rivaroxaban. She reported complete resolution of her symptoms at her follow-up visit 2 weeks later, and symptoms did not recur over the next 2.5 years.

DISCUSSION

Using the Naranjo scoring system⁷ for adverse drug reactions, this patient’s reaction scores a 7, rating it as a “probable” reaction. Points were given for previous reports of this reaction (+1), the adverse event appearing after the suspected drug was given (+2), resolution of the reaction when the drug was discontinued (+1), no known alternative causes of the reaction (+2), and objective evidence (physical exam, +1) of the reaction.

Direct oral anticoagulants are prescribed increasingly over vitamin K antagonists due to their wide therapeutic window and fixed dosage without need for monitoring.⁸ In product information literature, apixaban was reported to have a hypersensitivity rate of <1%.⁹ In addition to the previously mentioned periorbital edema case, several other apixaban-induced cases of cutaneous hypersensitivity reactions have been identified in the literature. Isaq et al reported 4 cases of hypersensitivity reactions, including possible drug-induced lupus, 2 cases of IgA vasculitis, and 1 case with palpable purpura and acute kidney injury.⁴ An additional case report describes a woman who “developed a vesicular-urticated erythematous rash initially located on her right upper extremity, progressing to her face” from apixaban.⁵ Our case, along with recent case reports, indicates that cutaneous reactions from apixaban have a wide range of presentations, and it is important to be aware of these risks.

Figure. Periorbital Dermatitis



CONCLUSIONS

Apixaban is a frequently prescribed drug and, increasingly, adverse cutaneous effects are being reported. Early recognition of cutaneous side effects will allow for improved medication management. We hope that presenting this case will help physicians consider the possibility of cutaneous adverse effects from apixaban in future cases and maintain a high index of suspicion for other drug-induced cutaneous side effects.

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Prostatic Abscess Presenting as Penile Discharge: A Case Report

Jenna Wettstein, MS; Whitney Lynch, MD; Mary Beth Graham, MD

ABSTRACT

Introduction: While prostatic abscess formation is often mitigated by initiating antibiotics for prostatitis, early recognition and treatment are important to avoid risk of sepsis and death.

Case Presentation: A 79-year-old male presented with milky-white penile discharge during bowel movements. He had no fever, dysuria, or perineal pain. The discharge culture grew multidrug resistant *Escherichia coli*. Computed tomography of abdomen/pelvis showed a heterogeneous, enlarged prostate leading to diagnosis of a prostatic abscess. The abscess was treated successfully with cystourethroscopy, transurethral unroofing, and a course of intravenous ertapenem.

Discussion: Previous research shows patients with prostatic abscesses present with perineal pain, dysuria, and fever. This case demonstrates the importance of considering a prostatic abscess in a patient with penile discharge alone.

Conclusions: We report a unique presentation of prostate abscess to educate and improve clinical suspicion of a rare, yet potentially fatal urological complication.

INTRODUCTION

The incidence of prostatic abscesses is bimodal, typically occurring in patients aged 20 to 40 and those over 60. Prostatic abscesses usually result from accumulation of purulent fluid within the prostate due to progression of acute bacterial prostatitis. When cultured, the most common pathogen is *Staphylococcus aureus*.^{1,2} Over 50% of patients with a prostatic abscess have diabetes, and younger men who develop prostatic abscess also have been found to have undiagnosed diabetes.³ Other risk factors include chronic catheter placement, immunomodulatory conditions including end-stage renal disease, liver cirrhosis, immunodeficiencies, urinary tract infections, and those who are status post prostate biopsy.² Common symptoms

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include perineal pain, difficulty urinating, and dysuria, along with systemic infection symptoms such as fever, chills, and myalgias.^{2,3} For one-third of patients, management with antibiotics alone will treat the abscess, while two-thirds of patients will require antibiotics and surgical drainage for resolution.¹

CASE PRESENTATION

A 79-year-old male with end stage renal disease (ESRD) secondary to hypertensive nephropathy on dialysis, anemia, rheumatoid arthritis, coronary artery disease, seizure disorder, rectal prolapse, and glaucoma presented to the internal medicine clinic for a hospital follow-up. He recently had been

admitted for management of rectal bleeding secondary to known rectal prolapse. The rectal bleeding had resolved with plan for continued conservative management under the care of colorectal surgery due to his poor surgical candidacy.

However, despite this clinical improvement, the patient developed a new concerning symptom over the ensuing 2 to 3 weeks. When attempting to have a bowel movement, he noted a painless, milky-white discharge from the penis. Given that he had not produced urine in over 6 years, he was concerned about this clinical change, which had been occurring consistently during bowel movements. He had not experienced fevers, dysuria, penile, testicular, rectal, or perineal pain. He also had no recent sexual partners and was without a history of sexually transmitted infections. Four months prior to presentation, he was started on prednisone 10 mg once daily for management of rheumatoid arthritis newly diagnosed in the setting of neck and arm pain, joint deformities, and erosive changes on computed tomography (CT) of the cervical spine. He was not a candidate for disease-modifying antirheumatic drugs due to ESRD status and had not been initiated on any other immu-

nosuppressive therapies. On examination, he was well-appearing, afebrile, and normotensive without tenderness to palpation over the penis, testicles, epididymitis, or perineum. No penile lesions or discharge from the urethral meatus were appreciated.

Upon attempting to provide a sample for urinalysis, a mucous discharge was excreted from the penis. The specimen sent for culture grew 4+ *Escherichia coli* (*E coli*) susceptible only to amikacin, ertapenem, and meropenem. A retrospective review of a CT abdomen and pelvis obtained during the aforementioned hospitalization noted a heterogenous, enlarged prostate with multiple areas of low attenuation. Given concern for prostatic abscess versus pyocystis on account of this clinical picture and the aforementioned CT scan, the patient was admitted for intravenous (IV) antibiotic management.

Initial complete blood cell count showed a white blood cell count of 11 600 μL (normal range, 3900–11 200 μL), which later decreased to 5700 μL with treatment. Based on culture sensitivities showing multidrug-resistant *E coli*, ertapenem 500 mg every 24 hours was initiated. During admission, the patient remained hemodynamically stable but did ultimately endorse groin pain. Blood culture (1 of 2) also grew multidrug-resistant *E coli*. Early into the admission, repeat CT scan of the abdomen and pelvis with and without contrast obtained to differentiate between pyocystis and a prostatic abscess and showed a presumed prostatic abscess (4.2 x 2.9 cm in size) that had enlarged since prior imaging (previously 2.8 x 2.9 cm). Given enlargement, urology advised unroofing.

The patient underwent cystourethroscopy and transurethral unroofing of the prostatic abscess on hospital day 2 with continuation of ertapenem 500 mg every 24 hours for 7 days. Ertapenem was then transitioned to 1000 mg every 24 hours post-hemodialysis on Mondays, Wednesdays, and Fridays. He ultimately completed 4 weeks of treatment (500 mg daily for 7 days followed by 1000 mg 3 times weekly for 3 weeks) with abscess resolution noted on a repeat CT scan.

DISCUSSION

Prostatic abscesses are less common since the development of antibiotics, with a 0.5% incidence, and often may be overlooked.² Approximately 6% of acute bacterial prostatitis coalesce to become an abscess. The clinical presentation, medical history, and physical exam findings of acute bacterial prostatitis and prostatic abscesses are similar, making them difficult to distinguish.² If not caught early, there is a high risk of sepsis, with a mortality rate from 1% to 16%.² Antibiotics are the initial treatment for prostatic abscess. However, 75% of abscesses are resistant to first-generation antibiotics, making cultures with antibiotic sensitivities essential to care. If the abscess does not respond to antibiotics, surgical drainage becomes essential.^{1,3} In this case, surgical drainage was initiated early for source control. As previously noted, the patient was started on prednisone in the setting of rheumatoid arthritis around 4 months before presentation, which may have contributed to abscess development.

While many pathogens may cause prostatic abscesses, *Staphylococcus aureus* is the new leading cause of abscess, with others being *E coli*, *Klebsiella*, *Pseudomonas*, *Proteus*, *Enterobacter*, *Serratia*, and *Enterococcus*. Most hospital-acquired infections are due to *Pseudomonas aeruginosa*, *Enterococcus*, and *Staphylococcus aureus*.^{1,2,4} A 2016 study showed that 10% of men with prostatic abscess had recent prostate biopsies performed.² These nosocomial pathogens are associated with more aggressive symptomology, a higher likelihood of developing into a prostatic abscess, and a higher risk of sepsis.⁴

Our patient came in with unique symptoms of milky-white penile discharge but no initial perineal pain, dysuria, or fever. Typical disease presentation is perineal pain, dysuria, fever, chills, and muscle aches. Creating a differential for milky-white penile discharge would include lower urinary tract infection (pyocystis), inflammation of the head of the penis (balanitis), and sexually transmitted infections, such as *Neisseria gonorrhoea* or *Chlamydia trachomatis*. Our patient denied perineal pain, fevers, new sexual partners, or history of sexually transmitted infections, decreasing the likelihood of a *Neisseria gonorrhoea* or *Chlamydia trachomatis* infection. Balanitis was less likely due to the absence of tenderness, erythema, or ulcerations on the glans on examination of the penis. Pyocystis should be considered given its association with anuria. Imaging can help distinguish pyocystis from a prostatic abscess.

The repeat CT showed an increase in the size of the presumed prostatic abscess, further confirming our suspicion. Subsequently, a cystourethroscopy and transurethral unroofing of the prostatic abscess was performed, and the patient continued ertapenem for 4 weeks. At the time of treatment completion, a repeat CT scan showed abscess resolution.

CONCLUSIONS

While prostatic abscesses are rare, the consequences of a missed, untreated, or intervention-resistant abscess can be fatal. In this case report, we provide insight into a unique presentation of prostatic abscesses to educate and improve clinical suspicion of a potentially fatal urological issue.

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Sarcoidosis Masquerading as Breast Implant-Associated Anaplastic Large Cell Lymphoma – The Importance of Definitive Pathology to Guide Therapy

Riley Young, BMSc; Emelyn Zaworski, MD, Melissa Hart, MD; Bradley Grewe, MD; Ellen Liang, MD; Yvonne Pierpont, MD

ABSTRACT

Introduction: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare critical outcome of breast implantation that typically presents 8 to 10 years after textured-implant placement with periprosthetic seroma. Treatment consists of implant removal and capsulectomy, which is typically curative. But in rare case, malignant infiltration through the capsule results in disseminated disease, necessitating aggressive treatment with systemic chemotherapy. Sarcoidosis, a chronic systemic granulomatous disease characterized by noncaseating granulomas, is another rare cause of periprosthetic seroma.

Case Presentation: A 61-year-old female with a history of invasive ductal carcinoma of the breast status post textured implant-based reconstruction presented with late periprosthetic seroma and overlying rash. Cytology of seroma aspirate was suggestive of BIA-ALCL, and positron emission tomography-computed tomography was concerning for invasive disease. Surgical specimen pathology of the implant-capsule complex and skin punch biopsy of the overlying rash revealed only granulomatous inflammation. The patient was diagnosed with sarcoidosis and spared systemic chemotherapy treatment for disseminated BIA-ALCL.

Conclusions: BIA-ALCL should be ruled out in all cases of late periprosthetic seroma. Definitive surgical pathology is necessary to prevent misdiagnosis and inappropriate treatment of masquerading entities, such as sarcoidosis.

which is typically curative. However, in rare cases, there may be malignant infiltration through the capsule resulting in disseminated disease. In these cases, the two-year survival rate is 52.5%, necessitating aggressive treatment with systemic chemotherapy.²

Another rare cause of late periprosthetic seroma is sarcoidosis, a chronic systemic granulomatous disease characterized by noncaseating granulomas.³ Sarcoidosis demonstrates a wide range of presentations, but breast involvement is reported in less than 1% of cases.⁴ Diagnosing sarcoidosis can be difficult as it is a disease of exclusion. To differentiate between BIA-ALCL and sarcoidosis of the breast, flow cytometry, immunohistochemistry, and surgical pathology must be evaluated.³

INTRODUCTION

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare critical outcome of breast implantation. Defined as a subtype of T-cell lymphoma with monoclonal expansion of CD30-positive cells, BIA-ALCL typically presents 8 to 10 years after textured-implant placement with periprosthetic seroma.¹ Treatment consists of implant removal and capsulectomy

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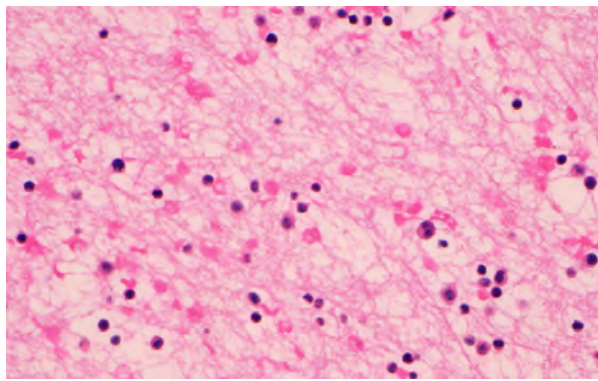
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CASE PRESENTATION

A 61-year-old female with past medical history of invasive ductal carcinoma of the left breast status post textured implant reconstruction 7 years prior presented to plastic surgery clinic for evaluation of acute onset swelling of her left breast. She was afebrile, with marked left breast swelling and a linear rash overlying her surgical scar consisting of light brown, nonblanching, shiny, fibrous papules.

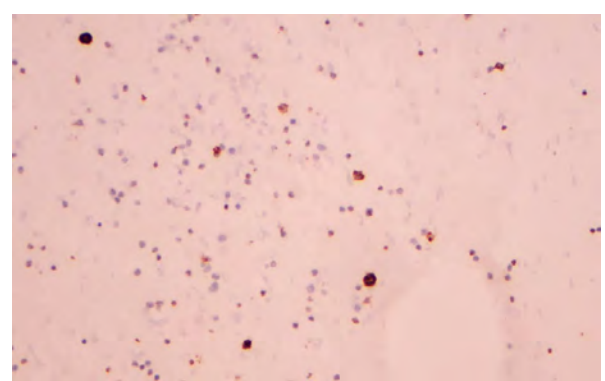
Ultrasound-guided aspiration of the periprosthetic seroma yielded 200 cc of transparent, yellow fluid sent for cytology, immunohistochemistry, and culture. Microbiology culture was negative. Effusion fluid was processed using standard cytospin and cell block preparations. The formalin fixed paraffin imbedded block was used for immunohistochemical stains. Microscopic examination revealed an admixture of small lymphocytes and large, atypi-

Figure 1. Cell Block Preparation From the Breast Fluid Aspiration at 40X Objective (400X magnification)



Scattered large, atypical cells are present.

Figure 2. CD30 Immunohistochemical Stain of Breast Fluid Aspirate at 20X Objective (200X magnification)



Large cells are strongly positive for CD30.

cal lymphocytes with pleomorphic nuclei and background histiocytes (Figure 1). By immunohistochemistry, the large, atypical cells were positive for CD3, CD4, CD30, CD43, and CD45, but negative for CD20, ALK, and EMA (Figure 2). This cytology pattern was suspicious, but not confirmatory, for BIA-ALCL.

Positron emission tomography-computed tomography (PET-CT) for baseline staging of presumed BIA-ALCL demonstrated hypermetabolic activity around the left breast implant with uncertain chest wall involvement and multiple hypermetabolic lymph nodes within the mediastinum, bilateral hilar, and internal mammary chain, suspicious for advanced disease.

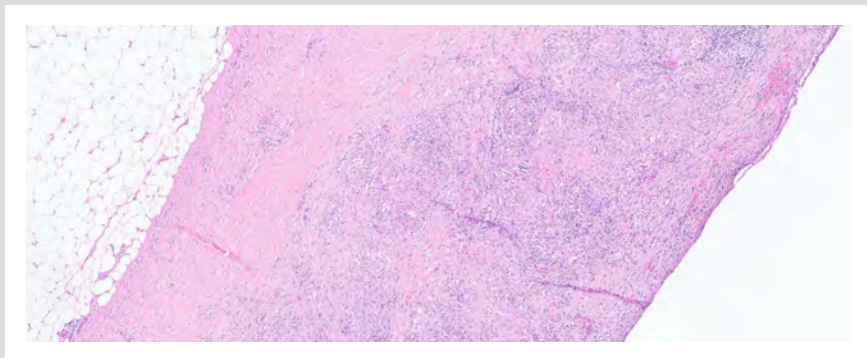
Biopsies of mediastinal, hilar, and internal mammary lymph nodes all demonstrated noncaseating granulomas without evident lymphoproliferative disease. Punch biopsy of the breast rash also revealed noncaseating granulomas.

Bilateral surgical implant removal and capsulectomy were performed, and specimens were sent for postoperative pathology. The capsulectomy specimen was assessed using standard grossing procedures, with any suspicious areas of thickening submitted as formalin fixed paraffin embedded tissue that was utilized for immunohistochemical stains. Pathology showed florid granulomatous inflammation with no evidence of lymphomatous involvement in either specimen (Figure 3). These results were sufficient for the exclusion of BIA-ALCL and diagnosis of sarcoidosis.

DISCUSSION

Late seromas occur greater than 1 year after implant placement and may be caused by BIA-ALCL, which must be ruled out due to the mortality risk associated with disseminated disease. The most sen-

Figure 3. Breast Capsule Excision at 10X Objective (100X magnification)



Fibrous tissue from the breast capsule contains diffuse non-caseating granulomatous inflammation.

sitive diagnostic test for BIA-ALCL is cytopathological evaluation with a CD30-positive, ALK-negative phenotype.⁵ In most etiologies of seromas, the majority of cells are CD30-negative with possible rare reactive CD30-positive immunoblasts. In comparison, BIA-ALCL is characterized by numerous CD30-positive T cells. Current guidelines for the evaluation of suspected BIA-ALCL are outlined by the National Comprehensive Cancer Network.⁶

Previously, a suggestive cytopathologic phenotype was considered diagnostic of BIA-ALCL.⁷ Surgical excision of the implant and capsule was completed with curative intent, and pathology was sent primarily to evaluate for invasive disease.

This case demonstrates the diagnostic importance of surgical pathology in all cases of suspected BIA-ALCL. Sarcoidosis is an entity also known to be associated with silicone breast implants and can contain reactive CD30-positive cells. It should, therefore, be included as a differential diagnosis for late seroma with CD30-positive aspirate suggestive of BIA-ALCL.⁸

In this case, surgical pathology revealed noncaseating granulomas consistent with sarcoidosis rather than lymphomatous deposits expected in BIA-ALCL. Correct diagnosis is imperative

due to disparate treatments. Treatment for sarcoidosis ranges from immunosuppressive therapy to observation, whereas treatment of advanced BIA-ALCL requires chemotherapy.

The similar clinical presentation between BIA-ALCL and sarcoidosis with breast involvement should be highlighted as there is growing evidence that breast implants may be associated with an increased risk for sarcoidosis.⁹ Waiting for specimen pathology prior to initiation of treatment saved this patient from unnecessary, potentially harmful chemotherapy, as well as the deleterious impact of a second cancer diagnosis. Furthermore, implant removal and specimen pathology are necessary to adequately evaluate the etiology of a late seroma to guide proper treatment.

CONCLUSIONS

Our case demonstrates an atypical presentation of sarcoidosis of the breast initially thought to be BIA-ALCL in a woman with a late periprosthetic seroma status post textured implant-based reconstruction. In cases of late seroma, sarcoidosis must be considered as a differential diagnosis, and proper diagnostic pathways must be followed to confidently rule out BIA-ALCL. First, seroma aspirate should be sent for cytology to evaluate for CD30 positivity. However, CD30 positivity alone is insufficient for diagnosis of BIA-ALCL. Other entities, such as sarcoidosis, have also been known to cause CD30-positive seromas. If seroma aspirate is CD30 positive, surgical pathology of the implant and capsule is necessary to correctly elucidate an etiology. Misdiagnoses can greatly impact therapeutic management, success of treatment, and the psychological well-being of patients.

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Statistical Thinking in Medicine Part 4: Probability, Statistics, and the Central Limit Theorem

Robert A. Calder, MD, MS; Jayshil J. Patel, MD

Probability is a key concept when interpreting diagnostic tests and explaining data to patients.¹ Stephen Jay Gould (1941-2002) stated, “Misunderstanding of probability may be the greatest of all general impediments to scientific literacy.” Therefore, we think that it is important to gain a deeper understanding of probability and how it relates to statistics. In this installment of the Statistical Thinking in Medicine series, we aim to (1) define and interpret probability, (2) describe independent events and the relationship between probability and statistics, (3) define and exemplify the central limit theorem, (4) outline normal and t-distributions, and (5) introduce the regression to the mean.

Definition of Probability

Probability is the extent to which an event is likely to occur and has its origins in games of chance. As we understand it today, the modern concepts of probability were first described in a series of letters in the mid-17th century between Pascal and Fermat.² In essence, for

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equally likely events, they defined the classical approach to probability by stating that if an event can occur in “ k ” different ways out of a total of “ n ” attempts, the probability of it occurring is k/n .³ The main problem with this definition is that “equally likely” is vague. What does “equally likely” mean?

To address this question, the “frequency approach” to probability was developed. In that approach, if an event occurs k times out of n possible occurrences, where n is a large number, the probability is k/n as with the classical approach described above.⁴ However, the term large number is vague and now the question is: what is a large number?

To address these issues and to put probability on a firmer mathematical footing, Andrey Kolmogorov proposed three axioms for probability in 1933.⁴ An “axiom” is a statement accepted without proof. The three axioms have been described as a “wish list”⁵ to define probability functions. That is, if a function satisfies the wish list, it is a probability function. Recall that in mathematics, a function is a mathematical operation in which an “input” is provided, and for each input, a unique “output” is returned. In probability, the input is an “event” eg, heads or tails, and the output is a number between zero and 1. Kolmogorov’s axioms usually are expressed as follows:

1. The probability of an event (among all events in some outcome space) is ≥ 0 , that is, it is non-negative. There are no negative probabilities.

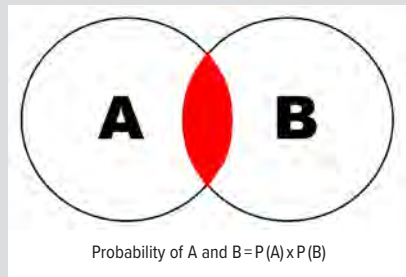
2. The sum of the probabilities of all mutually exclusive events in some sample space is 1. Mutually exclusive events cannot occur at the same time, eg, the flip of a coin is either heads or tails, it has to be one or the other, they cannot both occur at the same time.
3. If two events are mutually exclusive, the probability that either occurs is the sum of the two probabilities. This is referred to as the “additive rule.”

Probability Interpretations

Although Kolmogorov’s axioms put probability on a firmer mathematical footing (as Euclid’s axioms did for geometry), the interpretation of this number between zero and 1 is still unclear. As discussed in part 2 of our series, the two most common interpretations of probability are the “frequentist” and the Bayesian interpretations.⁴ The frequentist interpretation is that probability is a long-run frequency of the occurrence of an event over a large number of repetitions of an experiment performed under similar conditions. The Bayesian view is that probability is a degree of belief about an event, which can then be modified with additional data.

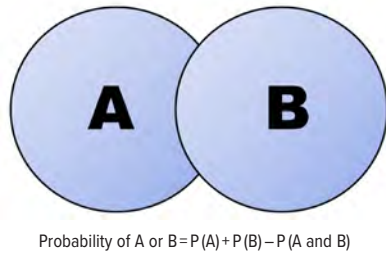
As we discussed in part 3, the Bayesian approach to probability is very useful when evaluating diagnostic tests. However, the Bayesian approach to data analysis presents mathematical challenges beyond the scope of this article. In essence, one either has to find mathematical functions that are “updateable” with additional data (of which the beta distribu-

Figure 1. Probability of A and B (both independent events)



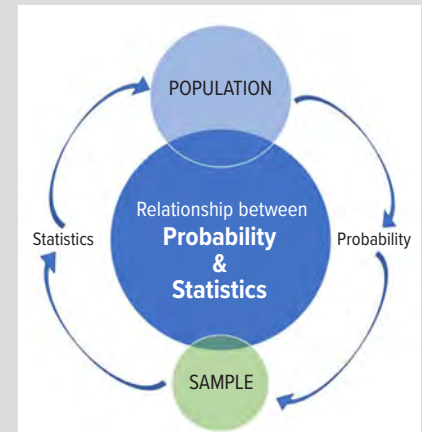
If events are independent, the probability of both occurring is the product of their probabilities, denoted in the intersection of A and B (shaded area) of the Venn diagram.

Figure 2. Probability of A or B



The probability of A or B equals the sum of each $[P(A) + P(B)]$ minus the probability of both happening together $[P(A \text{ and } B)]$, if A and B are independent, the probability of both happening is the product of their probabilities.

Figure 3. The Relationship Between Probability and Statistics



tion is one)⁶ or use other methods well beyond this brief summary and our expertise. A principal reason for the frequentist approach to data analysis, which is by far the most common approach today, is that no assumptions are required regarding the “prior probability” of some event. The frequentist approach is also computationally more straightforward, in general. Bland provides examples and an accessible introduction to this topic.⁷

Independent Events

Kolmogorov’s axioms describe single events. If two events are of interest, they are considered “independent” if the probability that they both occur is the product of their independent probabilities.⁴ For example, suppose the probability of a positive diagnostic test is 0.5 and that tests done on separate days are independent. Then the probability of positive tests two days in a row is: $0.5 \times 0.5 = 0.25$. Venn diagrams are very helpful for visualizing such intersection probabilities as shown in Figure 1. The product of independent events is often called the “multiplicative rule.” Again, this rule only applies to independent events. Another way to describe independence is when the occurrence of one event provides no information whatsoever about the occurrence of another (independent) event.

In medicine, we frequently are interested in the “union” of two events. For example, as above, if the probability of a positive test is 0.5 and the test is done two days in a row, what is the probability that the test is positive on either (or both) days? Again, Venn diagrams are very helpful. The probability of at least one

positive test is the probability of being positive on day 1 plus the probability of being positive on day 2, MINUS the probability of being positive on both days (to avoid counting this twice): $0.5 + 0.5 - 0.25 = 0.75$. This is easy to visualize in Figure 2. An alternative way to calculate such probabilities is to calculate the “complement” of a positive test on one or the other day, ie, the probability of being negative on both days. That probability is $0.5 \times 0.5 = 0.25$. This complement is then subtracted from 1 to arrive at the probability of being positive at least once (ie, 1 minus the probability of being negative on both days means that the test was positive on at least one day).

A large number of problems in probability can be solved by using the additive and/or the multiplicative rules as appropriate.

The Relationship Between Probability and Statistics

We turn now to the relationship between probability and statistics (Figure 3).⁸ Probability takes us from some population to any given sample. For example, given a “population” of red and white marbles, probability theory can tell us the exact probability of any given sample (eg, 5 white and 2 red marbles) whenever we randomly sample from the population (either with or without replacement).

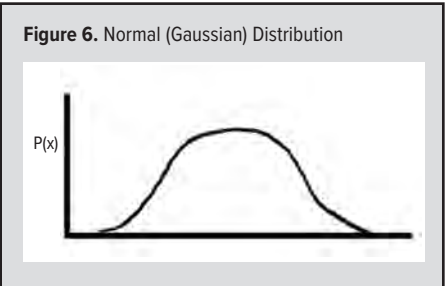
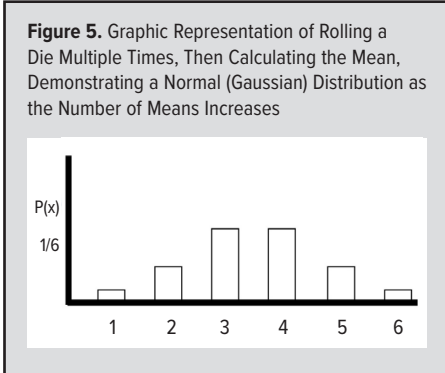
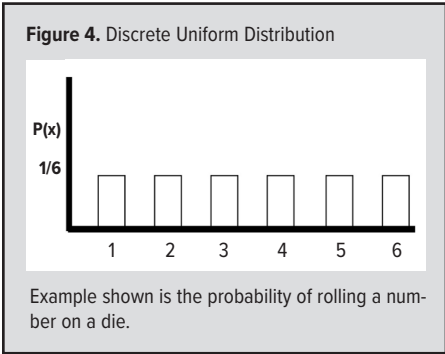
Moreover, a random sample allows us to infer about the true nature of a population. For example, if as above, our random sample contains a certain proportion of red marbles, statistics allows us to estimate the range within which the true proportion of red marbles is

likely to be with any desired level of confidence. As the sample size increases, the precision of the estimate also increases.

The Central Limit Theorem and Normal Distribution

The reason we are able to infer about a population from a random sample is because of the central limit theorem (CLT). In essence, this theorem states that if some given population distribution has a finite mean and variance (to be defined in the next article), the means of random samples from that distribution become normally distributed as the number of samples becomes large.⁵ What does this mean? This deceptively simple principle allows us to learn about a population from a random sample. In a very real sense, without the CLT, science would not be possible!

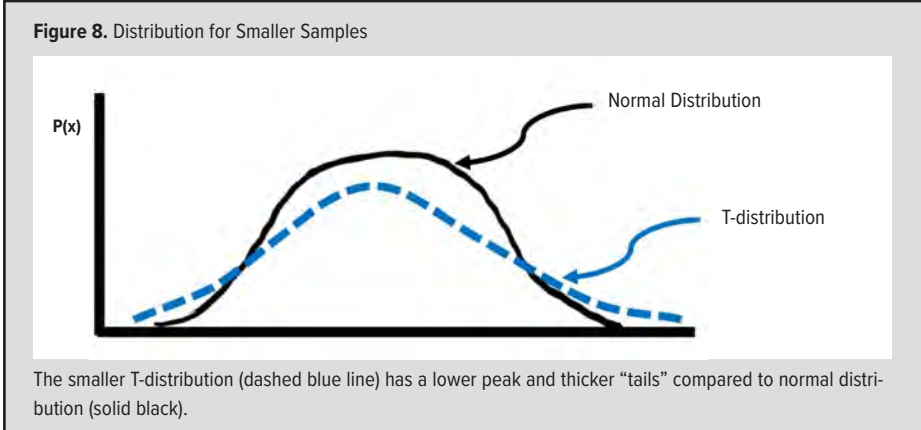
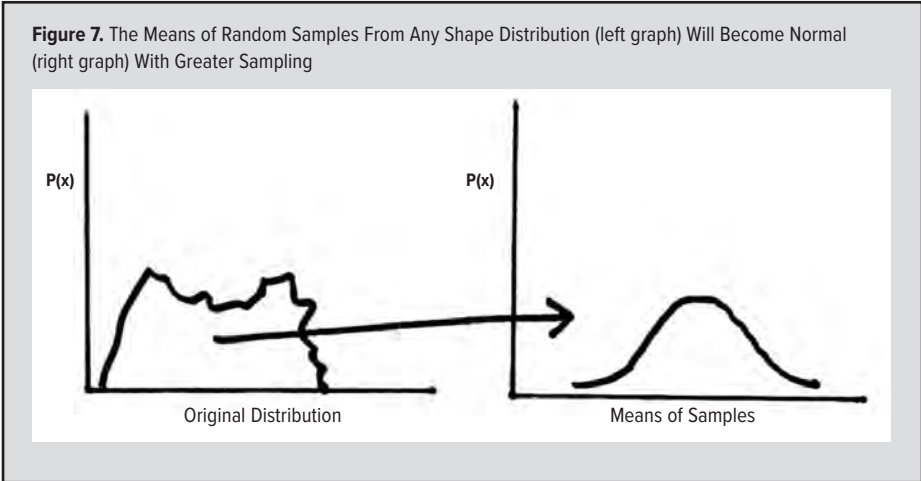
A nice way to demonstrate the CLT is to roll a die several times and calculate the average of these rolls. For each number on the die, the probability is 1/6. The distribution for the values of the die is a “discrete uniform” distribution (Figure 4). This discrete uniform distribution, however, changes to a normal distribution if we graph the means of many rolls of the die. For example, if I roll a die five times, the average of these rolls is usually about 3 or 4 (when rounding to the nearest whole number), occasionally 2 or 5, and, very rarely, 1 or 6. If we graph the mean values of many rolls of a die, that graph will begin to take the shape of a normal (or Gaussian) distribution as the num-



ber of means increases (Figure 5). This is why the normal distribution is the most important distribution in statistics (Figure 6). Yes, many physical parameters are normally distributed in and of themselves, such as height and weight, but the means of ANY physiological parameter will have a normal distribution. Therefore, the means of random samples from any shape distribution will become normal as the number of samples becomes large (Figure 7). Thus, the CLT allows us to learn about a population from a random sample.

T-Distribution

The smaller the sample, the less likely it will be to closely follow the normal distribution. That is why W.S. Gosset, who wrote under the pseudonym “Student” developed the t-distribution. (He was working for the Guinness Brewing Company at the time and found the need to



analyze small samples of yeast and related components of beer).⁹ The t-distribution is very similar to the normal distribution, except that it has thicker “tails” and a lower peak (Figure 8).⁵ Unusual values can easily skew a small distribution, and when the sample size is under about 30, most statisticians prefer using the t-distribution since it accounts for this distortion seen in small samples.

Regression to the Mean

Closely related to the CLT is the concept of “regression to the mean,” first described by Sir Francis Galton.¹⁰ In essence, results become more “average” over time. For example, in 1961, Roger Maris broke Babe Ruth’s home run record by hitting 61 home runs. However, in 1962, Maris hit 33 home runs, a number much more typical for him. He had one exceptional year and that was followed by a more average year. This is a great example of regression to the mean. Other examples are that tall parents are likely to have children more average in height. One high blood pressure reading is likely to be followed

by lower, more average, readings. Also, one low test score is likely to be followed by higher, more typical scores. Regression to the mean explains many surprising occurrences.

Summary

In summary, probability is a number between zero and 1 that satisfies three axioms. If events are independent, the probability of both occurring is the product of their probabilities (multiplicative rule). If events are mutually exclusive, the probability that at least one occurs is their sum (additive rule). Probability takes us from a population to a sample, and statistics allows us to infer about a population from a random sample. The CLT and the normal distribution are two important links in the chain connecting a random sample and a population. Finally, regression to the mean answers many probability curiosities.

In part 5 of this series, we will use these principles of probability to determine whether something is unusual. Is an individual value unusual? Is the mean of some group unusual? Is the difference between two or more means

unusual? In order to do this, we must have ways to define the “average” and to quantify variation. However, before turning to that topic, you may want to test your ability to put probability concepts to work by thinking about the questions below. (Answers will be provided in part 5.)

Probability Practice Questions

1. When rolling a die, what is the probability of rolling a 1 or a 2?
2. If the probability that a laboratory test is positive is 40%, assuming test results on different days are independent, what is the probability of at least one positive test when testing is done on two separate days?
3. As with the conditions in question 2, what is the probability that at least one test is positive if tests are done 5 days in a row?
4. To make a diagnosis, suppose you order 20 independent laboratory tests, each of which is “normal” in 95% of people. What is the probability that at least 1 test is abnormal?
5. How many ways are there to shuffle a standard deck of 52 cards?

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High-Value Imaging in an Era of Uncertainty, Growth, and Disruptive Technologies

Scott B. Reeder, MD, PhD, and Robert N. Golden, MD

The discovery of x-rays by Wilhelm Röntgen, PhD, in 1895¹ launched the field of medical imaging and revolutionized medicine in ways he would never have imagined. The ways in which modern X-ray and derivative technologies like computed tomography (CT), digital subtraction angiography, and bone mineral density and other technologies such as ultrasound, magnetic resonance imaging (MRI), and positron emission tomography have transformed health care are myriad. Gone are the days of exploratory laparotomies and diagnostic burr holes for suspected epidural hematomas. Arrived is a new era of imaging-based molecular diagnosis, staging, and treatment monitoring of cancer, as well as imaging-guided therapies such as histotripsy and theranostic.

Imaging is now a fundamental technology for many key research approaches related to Alzheimer's disease and other neurological and psychiatric diseases. Drug discovery trials increasingly use quantitative imaging as endpoints and eligibility for new, expensive drugs

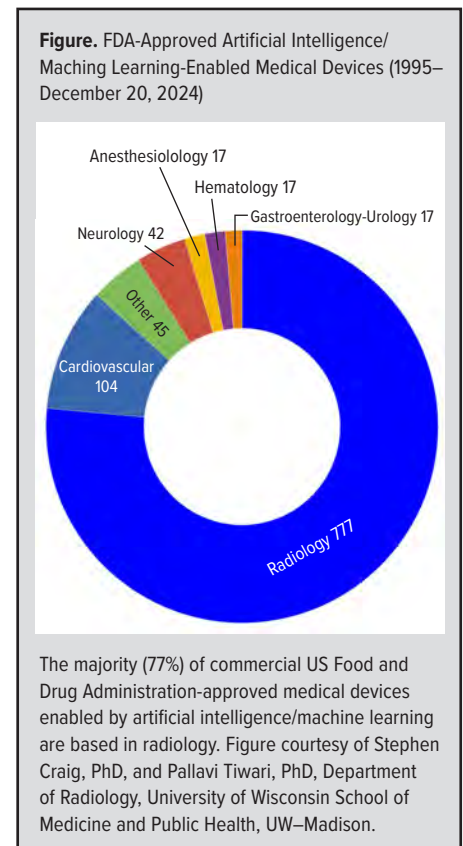
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require imaging assessment.² Imaging is the main portal of entry for many facets of tertiary care, whether it involves cancer, cardiovascular disease, or prenatal diagnosis of congenital heart disease. Indeed, the widely cited survey by Fuchs and Sox of physicians on the importance of medical innovations identified MRI and CT as the most impactful for patient care, ahead of angiotensin-converting enzyme inhibitors, statins, coronary bypass, and other discoveries in modern medicine.³ It is no wonder that the use of diagnostic imaging and image-guided therapies has skyrocketed in recent years. At UW Health, we expect to perform more than 1 million exams per year by the time we celebrate our Department of Radiology's centennial anniversary in 2027.

With such utilization comes great cost in capital equipment and in the rapidly growing workforce needed to operate equipment, interpret exams, and treat patients. From a global sustainability perspective, by some estimates, health care represents 9% of carbon emissions, led by radiology with approximately 0.8% of all carbon emissions from CT and MRI alone, compared to aviation at 2.5%.⁴ We urgently need sustainable ways to provide imaging-based care. As stewards of these precious resources, the radiology community must rethink how we deliver imaging-based care.

We also are witnessing a revolution through the emergence of artificial intelligence (AI)/machine learning (ML). Applications of AI have



profoundly impacted all areas of medicine, but perhaps imaging has seen the greatest initial penetrance, with more than 77% of the over 1000 US Food and Drug Administration-approved AI-related technologies based in radiology (Figure).⁵ We view this disruption as a generational opportunity to transform imaging technologies and to “bend the curve” to ensure a sustainable future.

In parallel with the development of AI are new paradigms such as “opportunistic screening,” whereby actionable information can be derived from medical images to benefit patients. Perry Pickhardt, MD, a University of Wisconsin School of Medicine and Public Health (SMPH) faculty member who is a leader in this field, has led the charge using CT scans performed for other reasons (eg, abdominal pain) to derive bone mineral density, aortic calcium scoring, and body composition as biomarkers and prognostic predictors of osteoporosis, major adverse cardiac events, and cardiometabolic diseases, among others.⁶ Enabled by AI-based algorithms, the application of automated technologies to routine imaging exams poses a unique opportunity to increase the information content, or value, of imaging at little or no additional cost. For the first time, we also are witnessing the use of AI-based algorithms to move us toward the realization of population-based precision imaging as a cornerstone for precision health.

The confluence of economic and sustainability pressures, strains on the workforce, continued success and growth of medical imaging, and emergence of advanced analytics and disruptive AI-based technologies all converge toward a new paradigm of “high-value imaging.” We define high-value imaging as a comprehensive strategy for patient-centered imaging aimed at maximizing access, efficiency, patient experience, and actionable imaging-derived information. Developing strategies for delivering imaging care in more efficient ways is fundamental to good stewardship of important human and technological resources.

Closely related to this opportunity is the need to translate the remarkable discoveries of the University of Wisconsin–Madison and local biotechnology and medical technology (medtech) industries — such as GE HealthCare, Epic, and Exact Sciences — into widespread clinical practice. This tenet is central to the Wisconsin Idea to bring discoveries of the university to the citizens of Wisconsin and beyond, and to the principles of high-value imaging. How do we create the infrastructure and foster a mindset to accelerate discoveries in imaging

into practical solutions that benefit patients everywhere?

Transforming any field involves both major challenges and enormous opportunities. This is why the SMPH and UW Health are launching the Center for High Value Imaging (CHVI), an initiative aimed at transforming the way diagnostic imaging and image-guided therapies are delivered. Through the use of data science and AI, the CHVI will bring together key stakeholders within the university and academic medical center and will partner with external collaborators to address challenges and opportunities in medical imaging. A central feature of the CHVI is the “command center” in which a nexus of analytics and real-time dashboards will enable decision-making and create a process of continuous, data-driven improvements for increased efficiency, access, and the best possible patient experience. Human factors engineering will aim to create the best working environment for professionals, maximizing their career fulfillment, reducing burnout, and maximizing their potential to the betterment of our patients. The CHVI also will create the technological and regulatory infrastructure to accelerate translation of innovations into clinical operations. In this way, “Innovation to Operations (I2O)” will be the guiding mantra of the CHVI. The unique medtech ecosystem of Wisconsin, in combination with the Isthmus Project and Wisconsin’s designation as a Regional Technology and Innovation Hub (Tech Hub), will help fully realize this vision. All of the factors will enhance the training of future generations of medical imaging engineers, technologists, radiologists, and others in related fields.

A CHVI pilot launched in 2024 has focused on MRI operations at the new Eastpark Medical Center, which opened in October 2024. Initial results have exceeded all expectations. This has been achieved through advanced analytics characterizing the utilization of MRI resources and an innovative architectural design of a “Smart Suite” pair of MRI scanners, each with two doors and two tables to optimize on-time starts and patient access. Since the beginning of the pilot, we have reduced MRI wait times to less than a

week and achieved more than 50% increase in patient throughput, effectively providing the services of three MRI scanners with just two. Patient feedback has been overwhelmingly positive, and the teamwork and energy from the CHVI team has been inspiring.

Beyond the initial pilot for MRI, the CHVI will expand to all radiology subspecialties through the leadership of Dania Daye, MD, PhD, associate professor of radiology. Recently recruited from Mass General Brigham, Dr Daye is an internationally recognized leader in the use of AI-based technologies for quality and operations. She also will serve as the SMPH Department of Radiology’s vice chair for practice transformation and will lead the strategy and implementation of the CHVI, taking transformation to the national level. We welcome collaboration with stakeholders for whom medical imaging plays a role in their practice or research. Together we will expand the impact of the CHVI, most importantly maximizing patients’ access and experience, as well as the value of the lifesaving diagnostic and image-guided treatments they receive.

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