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2024 • volume 123 • issue 4

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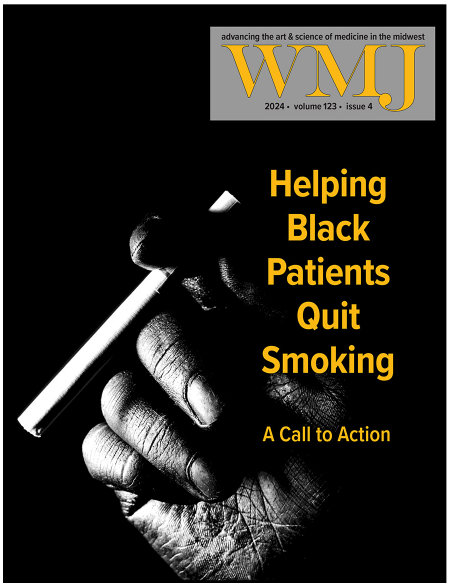

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WMJ

advancing the art & science of medicine in the midwest

COVER THEME

Helping Black Patients Quit Smoking

Data from 2022 show that in Wisconsin, over 20% of Black adults smoked compared to about 14% of non-Hispanic White adults—a disparity that results in higher rates of smoking-caused morbidity and mortality among Black adults in the state. A commentary in this issue of WMJ *explores some of the reasons behind this disparity and calls for a renewed focus on clinical interventions to help Black individuals who smoke to quit.*

Cover design by Kendi Neff-Parvin

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BRIEF REPORTS

CASE REPORTS

LIMITED SERIES

The Effectiveness of the URM Mentorship Platform in Promoting Scholarly Productivity

Dear Editor:

Scholarship and mentorship play a vital role in academic medicine. However, previous literature has demonstrated that many medical students underrepresented in medicine (URM) often need additional support to engage in scholarly activities. To this end, the URM Mentorship Platform at the Medical College of Wisconsin (MCW) is a peer and faculty mentoring program designed to foster collaborative networks, promote peer support, and facilitate interactions between students and faculty.

This platform, which started as a pilot program supported by Kern Institute in the 2020-2021 academic year with 2 peer mentors and 4 mentees, has now completed its third year. We have found this platform effective in increasing scholarly productivity.[1] The program is an innovative platform to promote mentorship and scholarship among URM medical students at MCW with support from general internal medicine (GIM) faculty members who volunteer their time and expertise, along with student leads. With ongoing departmental faculty support, despite the end of funding in 2021, the efforts have continued to flourish.

Over the past 3 years, the program has seen substantial growth, with over 60 URM students and more than 15 faculty mentors participating, resulting in national and regional presentations, publication in peer-reviewed journals, acquisition of research opportunities and funding, and securing leadership roles at the regional and national levels. The student participants perceive benefits to this mentorship platform, most notably through increased scholarly productivity including case reports, quality improvement projects, letters to editors, and research projects.

Next steps for program improvement include accommodating a larger student body, facilitating additional formal engagement opportunities between students and faculty, diversifying mentee-mentor pairings across classes, and incorporating cases from various subspecialties. Through this, we hope to increase the formal mentorship and training opportunities that previously have been proven crucial to the process of forming new and adept student mentors out of previous mentees and perpetuate the cycle of peer support for future classes.[2]

Based on the effectiveness and the success of the mentorship platform, we anticipate the incorporation of this innovative structured mentorship platform into medical education curriculum to promote scholarship amongst the medical class.

—Naisarg Vanani, BSc; Devesh Kumar, BSc; Nana Danso, BSc; Mark Ehioghae, MSc; Pinky Jha, MD, MPH

REFERENCES

1. Chandratre S, Marfowaa G, Abdel-Reheem AR, Jha P. Promoting mentorship and scholarship among underrepresented minority medical students. *WMJ*. 2022;121(3):171. PMID: 36301638.

2. Ehioghae M, Danso N, Jha P. Lessons learned from a mentorship platform for underrepresented minority medical students. *Acad Med.* 2024;99(9)938-939. doi:10.1097/acm.0000000000005790

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Promoting the Effectiveness of Low-Carbohydrate/ Time-Restricted Diets in the Management of Diabetes

Dear Editor:

Having read "Feasibility Study of a Low-Carbohydrate/Time-Restricted Eating Protocol for Insulin-Using Type 2 Diabetic Patients" by Zimmermann et al,[1] we acknowledge the significant effort and valuable contributions made in this area of research. The writers' outstanding work provides a strong basis, and our suggestions are meant to expand its impact and reach in this area.

Diabetes is a major health problem and a significant risk factor for cardiovascular diseases, chronic kidney disease, peripheral arterial disease, and diabetic retinopathy.[2] Behind these interventions' clinical outcomes, the article could benefit from a deeper exploration of the mechanistic underpinnings.

Different mediators, such as insulin-like growth hormone receptor, growth factor-1, and insulin-like growth factor binding protein, affect carbohydrate metabolism under the influence of growth hormone secretions. These growth hormone mediators may have a direct or indirect effect on insulin sensitivity and insulin secretion, which could lead to type 2 diabetes formation and its natural history.[3] Addressing the effect of growth hormone on this method could have improved the study, especially given the wide age range of 18 to 80 years among the participants.

Although the study covers a range of measures, such as A1c levels, body weight, and mental well-being, thorough analysis of further relevant factors like mean glucose level, time in euglycemic range, medication effect score,[1,2] body composition (measured by dual-energy x-ray absorptiometry), plasma lipid levels, dietary intake, dietary adherence, and weekly adverse events among the time-restricted eating could have further enhanced the research.[4] Also, the study does not consider potential confounders, such as lifestyle changes or drug changes made outside the prescribed regimen, because an intensive diet intervention maintained glycemic control in individuals with type 2 diabetes, averting an increased requirement for glucose-lowering medication.[5]

To develop new approaches for improving patient outcomes, understanding how a low-carbohydrate/time-restricted eating regimen affects the gut microbiota's composition and function could be crucial. The possible role of gut bacteria in modulating this link is a chance to investigate, even though how glycemic management in insulin affected by nutrition has been studied extensively.

—Saim Mahmood Khan, MBBS; Jawairya Muhammad Hussain, MBBS; Iman Azam, MBBS

REFERENCES

1. Zimmermann PN, Baier Manwell LM, Osman F, Feldstein D. Feasibility study of a low-carbohydrate/ time-restricted eating protocol for insulin-using type 2 diabetic patients. *WMJ*. 2024;123(1):11-17.

2. Suthutvoravut U, Anothaisintawee T, Boonmanunt S, et al. Efficacy of time-restricted eating and behavioral economic intervention in reducing fasting plasma glucose, HbA1c, and cardiometabolic risk factors in patients with impaired fasting glucose: a randomized controlled trial. *Nutrients*. 2023;15(19):4233. doi:10.3390/nu15194233

3. Lu C, Wolfs D, El Ghormli L, et al. Growth hormone mediators and glycemic control in youths with type 2 diabetes: a secondary analysis of a randomized clinical trial. *JAMA Netw Open*. 2024;7(2):e240447. doi:10.1001/jamanetworkopen.2024.0447

4. Pavlou V, Cienfuegos S, Lin S, et al. Effect of time-restricted eating on weight loss in adults with type 2 diabetes: a randomized clinical trial. *JAMA Netw Open.* 2023;6(10):e2339337. doi:10.1001/jamanetworkopen.2023.39337

5. Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an intensive lifestyle intervention on glycemic control in patients with type 2 diabetes: a randomized clinical trial. *JAMA*. 2017;318(7):637-646. doi:10.1001/jama.2017.10169

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Driving in Cars with Viral Transport Medium

Maureen D. Goss, MPH

It's an early morning in late 2020, and the quiet is thick inside the car. The roads are icy and lonely; the occasional whoosh of a passing car on the two-lane highway keeps me awake. The sun has just become visible, and light trickles slowly over barren fields. There are usually a million things to do the week before Christmas, but this year the list is shorter, the days feel longer, the exhaustion a little deeper – arthralgia, not myalgia.

I'm driving out past the suburbs of Oregon, Wisconsin, to collect Ziploc bags filled with nasal specimens languidly floating in viral transport medium from families with sick children. This was how I began working in respiratory disease research 5 years ago; now I'm usually behind a desk, thinking more about methodology and less about why I missed my turn for the third time. When it gets busy and there are enough people on vacation, I get to go back.

The frost creeps back toward the edges of my windshield like a reverse freeze as my car warms. Fingers stiff with cold, I flex them on the steering wheel and am reminded of an evening a few years ago driving down the same road, when I watched the sun move in the opposite direction on the way to a stranger's house.

It was an evening – I won't perseverate on the date, but it was cold. The sun had almost completed its descent, casting long, gnarled shadows on the road before me. The trees were empty, their naked limbs twisting ever so slightly in the wind. It was early in the study, and I was finally feeling comfortable traipsing into unfamiliar houses – acting like I belonged there, at least briefly.

It was a bizarre and intimate thing, being invited into someone's home to ask questions and carefully stick a flocked swab up a child's nose and another down their throat. I knew what kind of tea this mom drank, where this father traveled for work every month, which show this kid had been glued to 3 years ago and exactly when they grew out of it. After COVID hit the Midwest though, things changed overnight. Instead of sitting across from a child and squinting as they cough-sneezed directly into our eyes, we left a bag of collection kits and consents on their doorstep. We would return 3 times to pick up their specimens and forms over the next 2 weeks – sometimes never setting eyes on a single household member.

When the temperature drops, these pickups feel like a race against the bone-chilling air. I hop out of my car, sprint up to the front door, swipe the bag of specimens from the stoop and book it back, sliding into the driver's seat as a puff of breath engulfs my vision for a moment. What used to take an hour, condensed to 12 seconds and a single exhale.

After COVID hit the Midwest...things changed overnight. Instead of sitting across from a child and squinting as they cough-sneezed directly into our eyes, we left a bag of collection kits and consents on their doorstep.

Sometimes I miss the moments when I could briefly step into these families' lives: I watched a kid pull his rotund cat around on a blanket singing "I can show you the world" from *Aladdin*; another lined up 13 stuffed animals and recited their names and favorite foods, punctuating each with a rattling cough. One child gagged when I swabbed his throat, then sprinted to the bathroom to puke in the shower. *Not the toilet?* I'd thought at the time.

Although our study looks very different, it is, shockingly, mostly the same. Our roles have changed, but the data continue to flow in uniform lines, collected by the participants instead of us, swabs performed by parents instead

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of researchers. What would have seemed an unthinkable jump was actually just a step, abridged by necessity and a global emergency. Our relationships with families have changed, the connections less personal, but once you've been invited in, there is a lasting warmth that spans even the reaches of pandemic distance. We are no longer strangers, and in this chapter of the world, it is a comforting thought.

COVID-19 has been given nicknames, claimed millions of lives, and sandwiched public health directives firmly between embattled political parties. The pandemic has been described as a collective experience, a global phenomenon, and yet we all have survived the last several years in vastly different ways.

The one constant I always come back to is adaptability: of people, of protocols, of communities. Our research team has shrunk and expanded over the years, undulating like a jellyfish. Students have moved on, some stay; new people join and realize what a miracle it is to leave your house and find another family waiting for you at work, inducted by time and exigent circumstances. Some of us have been here since the beginning, others are a couple years in; but it feels like whatever state we're in, we've always been this way. Accepting and letting go, absorbing both the changes and the enduring, repetitive nature of research together.

I secure the specimens and watch the pink liquid surge around the swabs, then settle. As I start my car, the engine makes a noise as if unsure it's worth continuing. I think about the temperature specimens are archived at –70 °C. Much colder than today, but right now it doesn't feel that way. If my car does decide to give up, I know the specimens will be okay. And I can always go back and knock on the door.

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Experience as IMGs Applying for US Clinical Experience

Rabbia Irfan, MD; Shamayel Safdar, MD

Who leaves behind all they have ever known and ever had for the love of a profession and for the love of a land that promises the freedom to be their best self? An International Medical Graduate or "IMG."

Being new to the US health care system, it is almost mandatory for IMGs to have some sort of US clinical experience before applying for what is euphemistically termed the "Match," a residency affiliation with a hospital/school institution.

Applying for a match in the United States is a stressful process. Visas, financial burdens, and incompatibility with the home institution's curriculum all present impediments that must be confronted and overcome. Adding to these is the limited number of schools offering international students visiting electives. Indeed, just before the COVID-19 pandemic, only 21 medical schools offered spots for IMGs from institutions without affiliation agreements.

In a good year, the match rate is unlikely to exceed 70%, although the pandemic saw a significant reduction to little more than 57% – probably due to the difficulty of obtaining US clinical experience, the economic impact of the pandemic, and the increased competition for residency spots.

As mentioned already, US clinical experience is a crucial component of the matching process. Being a requirement for many residency programs, it allows IMGs to gain exposure to the US health care system and to network with potential mentors. However, with travel restrictions and other pandemic-related challenges, it has been challenging for IMGs to obtain US clinical experience in recent times. For example, the economic upset, lack of visa appointments, and hospitals and clinics being overwhelmed by dealing with the pandemic were among the many hurdles to overcome. Meanwhile, even as IMGs have had to pay for their own US clinical experience, the pandemic made it more difficult to find the required funding and get an appointment for a visa interview. Even when visa offices opened up, the wait times remained hopelessly long.

As IMGs, we continued searching online to find any opportunity, but none was in sight for a long time. For those of us in our final years of medical school during the first 2 years of the pandemic, we lost our chances of getting an elective – considered the best form of US clinical experience. Many hospitals and clinics closed their doors to visitors, and those that were open were operating at reduced capacity. As a result, we could not find any observerships for several months. We finally applied to a few places when the world started opening up. At first, mostly clinics were available, not hospitals, and those accepting applications for observerships had a long wait time.

We want to share our story to help other IMGs who are struggling to find US clinical experience during these difficult times. We emailed many doctors as well as hospital and university administrators. The response was overwhelmingly negative, and as days passed, while searching web pages and social media groups for opportunities without any promising response, a cloud of hopelessness began to overshadow our dreams. However, our passion for this noble profession was fierce enough to illuminate those dark days and help us through this challenging time, aided in part by a focus on other meaningful activities like telerotation and research projects to continue moving toward of our shared dream.

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Fahad Aziz, MD, FASN

Mastering Communication: Key Strategies for Trainee Physicians to Enhance Patient Care

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

It is no secret that effective communication is essential for quality patient care. It not only encourages collaboration among health care professionals and leads to more efficient care, error reduction, and well-informed team participation in treatment, it also helps establish trust between patients and their clinician.

However, due to their dual roles as learners and caregivers, trainee physicians can face distinct communication hurdles. Navigating the clinical setting involves interacting with myriad health care professionals with differing areas and levels of expertise. Trainees also must manage emotional and practical communication obstacles with patients and their families, frequently in high-pressure situations. Striking a balance between competence and approachability demands a profound grasp of both medical knowledge and interpersonal skills. Thus, mastering the following qualities and skills will help ensure successful communication with patients and colleagues.

Clarity and Transparency

George Bernard Shaw said the main issue in communication is the mistaken belief that it has occurred. Indeed, clarity and transparency are essential, especially in medical settings where effective communication--or a lack thereof—can significantly impact patient care.

Clinicians must convey medical information in a way that patients can easily understand. This includes using simple language, avoiding medical jargon with patients, and providing specific, concise instructions to both patients and colleagues to avoid any confusion. Being transparent involves sharing comprehensive information about treatment options, risks, and uncertainties, and also includes seeking advice from experienced colleagues when needed. Communicating with clarity and transparency will help empower patients to make informed decisions about their care while building their trust, and it fosters a supportive health care environment where learning is continuous.

Understanding Nonverbal Cues

Nonverbal cues are an integral part of communication, especially in the medical field. Clinicians can use them to convey empathy (see below), attentiveness, and confidence. At the same time, patients' nonverbal clues, such as avoiding eye contact or slumped posture, can reveal valuable information about their emotional well-being. By acknowledging and responding to patients' nonverbal signals, clinicians can enhance patient care and improve communication—ultimately creating an environment conducive for healing.

> "The simplest and most powerful method to establish a connection with another individual is to listen. Just listen. Maybe the most crucial thing we ever offer each other is our attention."
>
> –Rachel Naomi Reme

Empathy and Active Listening

"The simplest and most powerful method to establish a connection with another individual is to listen. Just listen. Maybe the most crucial thing we ever offer each other is our attention," writes Rachel Naomi Reme.

Showing empathy toward patients – listening, understanding, being aware of, and being sensitive to their thoughts, feelings, and experiences helps reduce their stress and anxiety, and – as demonstrated in various studies – it is crucial for improved health outcomes and patient satisfaction.[1] Showing empathy also helps create a stronger bond between the patient and the clinician, resulting in quicker

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recovery, increased independence, and reduced need for intensive care.[2,3] Establishing an environment where patients feel heard and understood can significantly improve their adherence to medical advice.

Unfortunately, in today's fast-paced clinical environment, demonstrating empathy is not always intuitive. According to Stephen R. Covey, "Most people do not listen with the intent to understand; they listen with the intent to reply." Trainee physicians can easily fall into this pattern. Ideally, training programs that incorporate scenarios or role-playing exercises can assist in honing trainee physicians' communication skills, including empathy. Deliberate practice and mindfulness also can help.

Empathy requires active listening – being fully present, maintaining eye contact, interpreting nonverbal signals, acknowledging emotions, and offering feedback to confirm or clarify information. Proficiency in this skill allows clinicians to collect accurate patient histories, identify unspoken concerns, and tailor treatments accordingly. Moreover, it promotes a collaborative atmosphere where feedback from peers and mentors can be utilized effectively to improve practice and patient results.

Respect and Cultural Sensitivity

Closely related to empathy are respect and cultural sensitivity. Demonstrating these qualities to patients, colleagues, and other staff alike is vital for creating a positive clinical environment and building trust and professionalism in medical practice – especially in the diverse landscape of modern health care.

Showing respect goes beyond being polite. Like empathy, it involves active listening, valuing input, and having dialogues that foster understanding and collaboration. It also includes being sensitive to nonverbal cues and responding well to feedback. For trainee physicians, communicating respectfully with the entire health care team can improve teamwork and help navigate health care complexities, contributing positively to their work environment and upholding integrity and trust in medical practice.

Embracing cultural sensitivity helps clinicians address social and cultural factors affecting the delivery of patient-centered care. This means understanding and respecting cultural differences influencing patient values, beliefs, and behaviors and integrating this awareness into every interaction to ensure appropriate and respectful medical advice and treatments. By doing so, clinicians can build rapport with patients from various backgrounds and foster inclusivity to enhance patient compliance and satisfaction.

Cultural sensitivity is also important in interactions among health care professionals. Trainees who value diverse perspectives can improve team dynamics and patient care collaboration. This sensitivity enhances problem-solving by considering various viewpoints, leading to comprehensive treatment plans that meet all patient needs. Training programs should include scenarios that promote cultural competence development, helping clinicians navigate cultural identity complexities related to health beliefs. Ultimately, embracing cultural sensitivity enhances patient outcomes and enriches a clinician's professional growth in a globalized world.

Ultimately, trainee physicians should recognize the dignity of each person, regardless of their health, culture, or beliefs. Demonstrating respect and cultural sensitivity nurtures a positive physician-patient bond that encourages patients to be open and compliant, which is vital for accurate diagnosis and successful treatment.

Adaptability

Although perhaps not traditionally thought of as a communication skill, adaptability is another vital quality for trainee physicians. Being adaptable allows clinicians to adjust their interactions with patients to navigate complex health care situations and meet their diverse needs. Moreover, adaptability is integral to effective collaboration among multidisciplinary teams as it fosters a flexible mindset, helping physicians manage uncertainties and complexities in clinical environments while maintaining resilience and effectiveness in high-pressure situations.

Managing Difficult Conversations

From delivering bad news to engaging with skeptical patients regarding treatment options, managing difficult conversations is inevitable for physicians and not an easy skill for trainees to master. Such scenarios require not only medical knowledge, but a high degree of emotional intelligence. Douglas Stone, the writer of Difficult Conversations, says, "Difficult conversations are almost never about getting the facts right. They are about conflicting perceptions, interpretations, and values."

Delivering bad news, such as a terminal diagnosis or the failure of a treatment, demands sensitivity, empathy, and transparency. Similarly, discussing treatment plans with skeptical patients involves addressing their concerns and doubts effectively, ensuring they feel heard and respected. These conversations can significantly affect patient trust and treatment adherence.

Successfully managing these complex interactions with grace and professionalism requires one to stay calm. This establishes the mood for the conversation and promotes constructive dialogue. As noted earlier, it is also important to communicate clearly and empathetically, avoiding complex medical terms that might confuse or distance patients. Furthermore, it is important to confirm that patients grasp the information shared. This might entail restating critical details and prompting patients to voice their comprehension or worries. By engaging in difficult discussions with empathy, tolerance, and courtesy, physicians can cultivate a nurturing atmosphere that stimulates honest communication, ultimately enhancing patient care and satisfaction.

Conclusion

Communication is a cornerstone of a strong physician-patient relationship and a high-functioning health care team. Thus, it is imperative that as trainee physicians hone their medical expertise, they also master communication skills, such as active listening and clear messaging. By doing so, they will be better prepared to work effectively in medical teams and to provide high-quality patient-centered care throughout their careers.

REFERENCES

1. Doohan I, Saveman BI. Need for compassion in prehospital and emergency care: a qualitative study on bus crash survivors' experiences. *Int Emerg Nurs.* 2015;23(2):115-119. doi:10.1016/j.ienj.2014.08.008

2. van der Cingel M. Compassion in care: a qualitative study of older people with a chronic disease and nurses. *Nurs Ethics.* 2011;18(5):672-685. doi:10.1177/0969733011403556

3. Lown BA, Muncer SJ, Chadwick R. Can compassionate healthcare be measured? The Schwartz Center Compassionate Care Scale. *Patient Educ Couns.* 2015;98(8):1005-1010. doi:10.1016/j.pec.2015.03.019

Helping Black Patients in Wisconsin Quit Smoking: A Call for Clinical Action

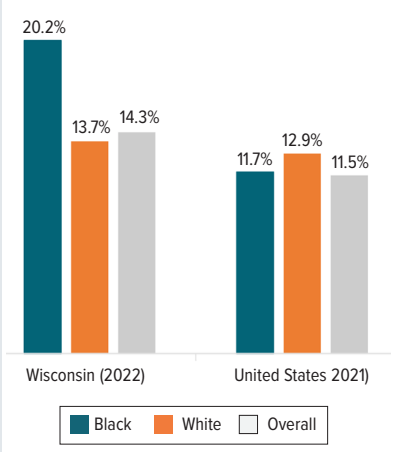
Michael C. Fiore, MD, MPH, MBA; Karen L. Conner, MPH; Lorraine S. Lathen, MA; Hasmeena Kathuria, MD; Megan E. Piper, PhD; Timothy B. Baker, PhD

Wisconsin faces a major health disparity that is negatively affecting the health of the state – Black adults have a smoking prevalence rate that has been consistently higher than the rate of White adults in Wisconsin. The 2021 National Health Interview Survey showed that the smoking rate of all adults (aged 18 and older) in the United States is 11.5%, and the rates of smoking are about equal among Black and White adults (11.7% and 12.9%, respectively).[1] However, according to the 2022 Wisconsin Behavioral Risk Factor Surveillance Survey, while approximately 14.3% of all Wisconsin adults smoked, an examination of smoking rates by race shows that 20.2% of Black adults smoked compared to about 13.7% of non-Hispanic White adults[2] (see Figure).

This disparity results in higher rates of smoking-caused morbidity and mortality in Black adults in Wisconsin. Specifically, Black adults who smoke are more likely to develop and die from a variety of tobacco-caused diseases, including cardiovascular diseases, chronic obstructive pulmonary disease, and cancer, than are White adults who smoke.[3] In 2019, Black adults had higher cancer mortality rates overall compared to other racial and ethnic groups.[4] Black males have especially high lung cancer incident rates, and they also have worse survival rates.[5] From 2001 to 2005, 22% of deaths among Black people in Wisconsin were attributable to cancer, 21% to heart disease, and 6% to stroke – all diseases caused by cigarette smoking.[6]

The high smoking prevalence rate among Black adults in Wisconsin and the resultant health risks warrants a renewed focus on clinical interventions to help Black individuals who smoke to quit. Such interventions should reflect an understanding of resources, challenges, smoking patterns, and quitting behaviors among Black individuals in Wisconsin. In this way, the medical community can be better positioned to support Black people to stop smoking.

Figure. Smoking Rates Among Blacks, Whites, and Overall Highlighting the Racial Disparity of Smoking in Wisconsin and the United States[1,2]



Smoking Among Black Adults in Wisconsin: Relevant Evidence

It is likely that numerous factors contribute to the higher rates of smoking among Black adults in Wisconsin. Below we describe critical issues that need to be understood and addressed through clinical interventions and public policy actions to provide the necessary support for Black adults who smoke.

Black adults who smoke are more likely to smoke menthol cigarettes and to smoke fewer cigarettes per day or intermittently compared to White individuals who smoke. The smoking patterns of Black adults overall in the United States differ from some other racial and ethnic groups. For instance, compared with White adults who smoke, Black adults are more likely to smoke menthol cigarettes and to smoke intermittently.[7,8] With regard to menthol smoking, in Wisconsin, nearly 90% of Black adults who smoke use menthol cigarettes compared to 41% of White adults who smoke.[9] Menthol cigarettes are as dangerous to an individual's health as nonmenthol cigarettes and may, in fact, be associated with higher rates of certain adverse health outcomes, such as lung

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cancer. Moreover, there is evidence that smoking menthol cigarettes makes it less likely that the individual can quit smoking successfully.[10,11] With respect to smoking heaviness, 50% of Black adults smoke 10 or fewer cigarettes per day (compared with 18% to 20% in the overall population), yet they experience a disproportionate share of tobacco-related disease and mortality.[12] Despite the fact that Black adults smoke fewer cigarettes than White adults, they still benefit from evidence-based interventions to help them quit.

Black adults who smoke are highly interested in quitting and try to quit at a higher rate than do White adults but are less successful. According to national data from 2015, 73% of Black adults want to quit smoking[13] and 63% make a quit attempt in a given year, whereas only 53% of White adults report making a quit attempt each year.[14] However, research shows that Black adults who smoke are, in fact, less likely to quit smoking successfully than White adults despite their making more quit attempts.[14]

Reduced success in quitting among Black adults may be related in part to their lower likelihood of receiving or using evidence-based smoking treatment. Less than 30% of Black adults who smoke use evidence-based smoking cessation treatment (eg, counseling, pharmacotherapy).[14] Black individuals' reduced use of evidence-based smoking treatment may be due to barriers to accessing these treatments, including reduced access to health care and a lower likelihood of receiving pharmacotherapy and/or clinical advice to quit.[15] In a nationally representative survey, only about 56% of Black adults who smoke reported that they received advice to quit smoking over the past year.[14] Other evidence shows that Black adults who smoke are especially unlikely to receive advice to quit if they are uninsured and their rate of receiving such advice is significantly less than it is for uninsured White individuals.[16]

Black adults' relative underuse of smoking cessation medications may be due, in part, to their concerns about the safety and addictiveness of cessation medications. A survey of people who currently smoke cigarettes found that compared with White adults, Black adults reported more concern about the potential to become addicted to smoking medications and were also less likely to endorse the need for such medications.[17,18] Such attitudes were predictive of less smoking cessation pharmacotherapy use. This may be due to a history of medical mistrust and negative experiences with the health care system. Clinicians should be sensitive to and explore patients' concerns, providing information to their patients in a sensitive and nonjudgmental manner.

A door-to-door survey done in inner-city Milwaukee found evidence that individuals living in areas of socioeconomic deprivation may benefit from additional information on smoking and quitting. The survey sample was recruited in an inner-city area of significant socioeconomic deprivation (ZIP code 53212). Of the residents sampled (79% of whom were Black), 42% reported smoking cigarettes. Of those who reported smoking, 83% believed quitting smoking was just a matter of will power, only 19% had used any medication to try to quit, and 56% had never heard of the Wisconsin Tobacco Quit Line.[19] These findings suggest that some of the disparities faced by Black individuals may reflect socioeconomic disadvantage in addition to race per se.[20]

Black individuals may respond differently to smoking cessation medications. Importantly, Black individuals who smoke may respond differently to evidence-based treatments than White individuals. For example, one large study found that varenicline is an effective smoking cessation medication for Black adults, but that nicotine replacement therapies and bupropion were not.[20] However, there are other studies that have shown that the nicotine patch and bupropion are effective.[21]

The tobacco industry targets Black individuals with marketing and other strategies to promote their addiction to tobacco products. For decades, the tobacco industry has targeted Black communities – including those in Wisconsin – in their marketing of tobacco products. This racial targeting is facilitated by the strong degree of racial segregation in cities like Milwaukee and has contributed to the high prevalence of tobacco use in these communities. A city of Milwaukee tobacco point-of-sale study compared the marketing of tobacco products in neighborhoods with different racial makeups. Relative to other locales, in neighborhoods with higher populations of Black persons, cigarettes were far more likely to be displayed near candy (42% vs 5%) and within 3 feet of the floor (35% vs 11%).[22] These tactics may enhance cigarette appeal and access in children and increase the perceived availability and accessibility of tobacco products among Black adults. Moreover, such product placement may encourage impulse purchases of tobacco products, cue cravings, and undermine quit attempts.[23] The Milwaukee point-of-sale study also found that outdoor marketing of menthol cigarette brands is twice as likely (68% vs 34%) in neighborhoods that had higher proportions of Black persons versus neighborhoods with higher proportions of White persons.[21] In addition, menthol price promotions were also much more common in the predominantly Black neighborhoods (69% vs 30%).[22]

> The high smoking prevalence rate among Black adults in Wisconsin and the resultant health risks warrants a renewed focus on clinical interventions to help Black individuals who smoke to quit.

The Pending Menthol Ban

There are important pending policy changes that have the potential to improve the health of Black adults who smoke. The US Food and Drug Administration (FDA) has indicated that in 2024, it will release a new product standard that prohibits menthol as a characterizing flavor in cigarettes. The result of this action will be the banning of all menthol cigarettes. This action has the potential to significantly reduce

disease and death from combusted tobacco product use, especially in Black populations (eg, 90% of Black adults in Wisconsin smoke menthol cigarettes). The pending FDA action will prompt many people who smoke menthol cigarettes to consider quitting combustible cigarettes. According to the Centers for Disease Control and Prevention (CDC), if menthol cigarettes are no longer available, an estimated 17 200 additional adults in Wisconsin who smoke will quit.[24] Many of these individuals will be Black. Wisconsin clinicians should prepare for this opportunity to help more Black individuals who smoke to quit. There are resources available to help patients who use menthol cigarettes to quit (eg, www.becomeanex.org/ex-resources/about-quitting/get-ready-to-quit/quitting-menthol-cigarettes/, www.cdc.gov/tobacco/basic_information/menthol/index.html).

Box. Clinical Strategies to Help Black Adults Who Smoke to Quita

- Urge Black patients who smoke to quit and to use evidence-based smoking cessation pharmacotherapy and counseling. When recommending pharmacotherapy for smoking cessation for Black adults, consider varenicline as the first-line medication as it has been shown in some research to be more effective than nicotine replacement therapy in Black adults. Varenicline treatment was effective even for light smokers (<10 cigarettes per day, see Cox et al.)
- Black patients who smoke may have concerns about the safety and addictiveness of cessation medications. When recommending pharmacotherapy for smoking cessation, clinicians should be sensitive to these concerns and answer questions and provide information to their patients in a sensitive and nonjudgmental manner.
- In Wisconsin, an estimated 90% of Black adults who smoke use menthol cigarettes. The pending menthol ban offers a valuable opportunity for Wisconsin clinicians to assist Black individuals and other menthol users to quit smoking because many of them will consider quitting when the menthol ban is implemented.
- Recognize that Black patients may be exposed to greater tobacco industry targeted advertisements and promotions that can challenge such individuals during quit attempts. Clinicians should offer recommendations on how to cope with triggers that Black patients may experience when exposed to this advertising.
- Consider using culturally tailored skills training when providing counseling to help Black patients who smoke to quit. The National Cancer Institute has made available materials that Black individuals can use to support their quit attempts (https://ebccp.cancercontrol.cancer.gov/programDetails.do?programId=312567)
- A cessation resource from the CDC called Pathways to Freedom can be recommended to Black patients who smoke. This evidence-based resource is available in brochure (https://www.cdc.gov/tobacco/quit_smoking/how_to_quit/pathways/index.htm) and video (https://www.youtube.com/watch?v=Ut5yRoJ5tKo)

[a]Based, in part, on *Helping African American Individuals Quit Smoking: Finally, Some Progress*[25]

The Challenge to Wisconsin Clinicians

This editorial has highlighted factors that challenge Wisconsin clinicians to address one of the critical issues damaging the health of Black persons living in the state. First, in Wisconsin, smoking prevalence is higher in Black adults than in White adults. Second, Black adults who smoke differ from White adults who smoke on numerous dimensions, and understanding these differences can aid in treating Black adults who smoke. Importantly, Black adults are more likely to want to quit and more likely to try to quit – so the goal for clinicians is to ensure that their Black patients have the necessary counseling and medication to increase their chances of success (see Box). For instance, clinicians should be sure to discuss the importance of using medication to aid in quit attempts and should encourage discussion about medication use and safety. Black individuals have been especially unlikely to use cessation medications. Clinicians should not only be prepared to strongly encourage their use but also should encourage the use of varenicline, which has been shown in some research to be more effective than other medications in helping Black adults stop smoking. Third, the pending menthol ban offers a valuable opportunity for Wisconsin clinicians to assist Black individuals and other menthol users to quit smoking. Both clinicians and health systems should prepare for this policy change. This could include making sure that clinicians are aware of the ban and knowledgeable about how to encourage their patients to quit smoking. Health systems should ensure that resources and training are available to offer, refer to, and deliver evidence-based smoking treatment. One step towards these goals is for clinicians to acquaint themselves with clinical strategies that can help Black adults quit smoking successfully as listed in the Box.

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REFERENCES

1. Cornelius ME, Loretan CG, Jamal A, et al. Tobacco product use among adults - United States, 2021. *MMWR Morb Mortal Wkly Rep*. 2023;72(18):475-483. doi:10.15585/mmwr.mm7218a1

2. BRFSS prevalence & trends data. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. July 19, 2023. Accessed January 16, 2024. https://www.cdc.gov/brfss/brfssprevalence/

3. Tobacco use among U.S. racial/ethnic minority groups – African Americans, American Indians and Alaska Natives, Asian Americans and Pacific Islanders, Hispanics. A Report of the Surgeon General. Executive summary. *MMWR Recomm Rep*. 1998;47(RR-18):v-16.

4. Lawrence WR, McGee-Avila JK, Vo JB, et al. Trends in cancer mortality among black individuals in the US from 1999 to 2019. *JAMA Oncol*. 2022;8(8):1184–1189. doi:10.1001/jamaoncol.2022.1472

5. American Cancer Society. Cancer facts and figures 2022. Accessed November 21, 2023. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2022/2022-cancer-facts-and-figures.pdf

6. Wisconsin Department of Health and Family Services. Wisconsin minority health report 2001-2005. January 2008. Accessed November 21, 2023. https://www.dhs.wisconsin.gov/publications/p4/p45716.pdf

7. Trinidad DR, Pérez-Stable EJ, Emery SL, et al. Intermittent and light daily smoking across racial/ethnic groups in the United States. *Nicotine Tob Res*. 2009;11(2):203-210. doi:10.1093/ntr/ntn018

8. Curtin GM, Sulsky SI, Van Landingham C, et al. Patterns of menthol cigarette use among current smokers, overall and within demographic strata, based on data from four U.S. government surveys. *Regul Toxicol Pharmacol*. 2014;70(1):189-196. doi:10.1016/j.yrtph.2014.06.018

9. Palmersheim KA. Center for Urban and Population Health, University of Wisconsin-Milwaukee. Wisconsin

tobacco facts: Menthol cigarette use among Wisconsin adults. March 2024. Accessed August 29, 2024. https://www.cuph.org/ uploads/2/5/8/5/25855930/tobacco_facts_menthol_use_ march_2024_final.pdf

10. Smith SS, Fiore MC, Baker TB. Smoking cessation in smokers who smoke menthol and non-menthol cigarettes. *Addiction*. 2014;109(12):2107-2117. doi:10.1111/add.12661

11. Cook S, Hirschtick JL, Patel A, et al. A longitudinal study of menthol cigarette use and smoking cessation among adult smokers in the US: assessing the roles of racial disparities and e-cigarette use. *Prev Med.* 2022;154:106882. doi:10.1016/j.ypmed.2021.106882

12. Nollen NL, Mayo MS, Sanderson Cox L, et al. Predictors of quitting among African American light smokers enrolled in a randomized, placebo-controlled trial. *J Gen Intern Med*. 2006;21(6):590-595. doi:10.1111/j.1525-1497.2006.00404.x

13. Gonzalez M, Sanders-Jackson A, Song AV, Cheng KW, Glantz SA. Strong smoke-free law coverage in the United States by race/ethnicity: 2000-2009. *Am J Public Health.* 2013;103(5):e62-e66. doi:10.2105/AJPH.2012.301045

14. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting smoking among adults - United States, 2000–2015. *MMWR Morb Mortal Wkly Rep*. 2017;65:1457–1464. doi:10.15585/mmwr.mm6552a1

15. Baker TB, Burris JL, Fiore MC. Helping African American individuals quit smoking: finally, some progress. *JAMA*. 2022;327(22):2192-2194. doi:10.1001/jama.2022.9161

16. Zhang L, Babb S, Schauer G, Asman K, Xu X, Malarcher A. Cessation behaviors and treatment use among U.S. smokers by insurance status, 2000-2015. *Am J Prev Med.* 2019;57(4):478-486. doi:10.1016/j.amepre.2019.06.010

17. Hendricks PS, Westmaas JL, Ta Park VM, et al. Smoking abstinence-related expectancies among American Indians, African Americans, and women: potential mechanisms of tobacco-related disparities. *Psychol Addict Behav.* 2014;28(1):193-205. doi:10.1037/a0031938

18. Yerger VB, Wertz M, McGruder C, Froelicher ES, Malone RE. Nicotine replacement therapy: perceptions of African-American smokers seeking to quit. *J Natl Med Assoc*. 2008;100(2):230-236. doi:10.1016/s0027-9684(15)31211-6

19. Christiansen B, Reeder K, Hill M, Baker TB, Fiore MC. Barriers to effective tobacco-dependence treatment for the very poor. *J Stud Alcohol Drugs*. 2012;73(6):874-884. doi:10.15288/jsad.2012.73.874

20. Nollen NL, Ahluwalia JS, Sanderson Cox L, et al. Assessment of racial differences in pharmacotherapy efficacy for smoking cessation: secondary analysis of the EAGLES randomized clinical trial. *JAMA Netw Open*. 2021;4(1):e2032053. doi:10.1001/jamanetworkopen.2020.32053

21. Ahluwalia JS, McNagny SE, Clark WS. Smoking cessation among inner-city African Americans using the nicotine transdermal patch. *J Gen Intern Med*. 1998 Jan;13(1):1-8. doi:10.1046/j.1525-1497.1998.00001.x.

22. Laestadius L, Sebero H, Myers A, et al. Identifying disparities and policy needs with the STARS surveillance tool. *Tob Regul Sci.* 2018;4(4):12-21(10). doi:10.18001/TRS.4.4.2

23. The war in the store. Counter Tools. Updated October 31, 2023. Accessed November 21, 2023. https://countertobacco.org/the-war-in-the-store/

24. Smoking and tobacco use: state menthol fact sheets-Wisconsin. Centers for Disease Control and Prevention. Updated February 23, 2024. Accessed January 21, 2024. https://www.cdc.gov/tobacco/basic_information/menthol/state-menthol-fact-sheets.html#WI

25. Baker TB, Burris JL, Fiore MC. Helping African American individuals quit smoking: finally, some progress. *JAMA*. 2022;327(22):2192-2194. doi:10.1001/jama.2022.9161.

Reflecting on the Past and Looking Toward the Future: A Brief History of University of Wisconsin Transplant Program

Isabel Breyer, MD; Didier Mandelbrot, MD; Sharon M. Bartosh, MD; Sandesh Parajuli, MD

The history of the University of Wisconsin (UW) solid organ transplant programs began with the first deceased donor kidney transplant in March 1966. Shortly after, pancreas and liver programs were started and began to grow as many influential individuals were recruited to the university.[1] In 2005 and 2006, the kidney program became the largest in the United States in terms of volume, and in November 2022, a program milestone was reached: 12 000 kidney transplants. Today, the University has 19 adult and 15 pediatric transplant programs, which together have performed over 17 216 adult and 574 pediatric transplants. In addition, major innovations to the field of solid organ transplantation, including the development of University of Wisconsin solution by Folkert Belzer, MD, and colleagues, took place at UW and are now used worldwide.[1]

This commentary reflects on the history and success of these programs with an eye toward the future.

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Early Days

The history of the UW Health Transplant Center was not without obstacles. Early programs experienced periods of slow growth as they worked to recruit faculty and improve operative techniques. The first two pancreas transplants at the center failed; programs such as the pediatric liver transplant program faced initial challenges in gaining support; and the first pediatric intestinal transplants were complicated by rejection and mortality.[1] These challenges, among others, helped push the center forward as faculty worked to remedy them.

Today, the University has 19 adult and 15 pediatric transplant programs, which together have performed over 17 216 adult and 574 pediatric transplants.

Adult Kidney Transplant Program

For over 800 000 adults living with end-stage kidney disease (ESKD) in the US,[2] kidney transplantation is life-altering and offers many advantages compared to dialysis: greater long-term (≥1 year) survival,[3] improved productivity and employment rates,[4] and better quality of life.[5] The most common conditions leading to ESKD in order of decreasing prevalence in the US are diabetes, hypertension, glomerulonephritis, and polycystic kidney disease.[6] Based on Organ Procurement and Transplantation Network (OPTN) data, almost 90 000 patients are currently on the kidney waiting list.[7]

In 1966, surgeons at UW began performing solid organ transplants with the first deceased donor and, later that year, the first living donor kidney transplant. At the end of 2022, 6477 deceased donor and 3875 living donor transplants had been performed at UW, with 3007 patients actively followed in the kidney transplant clinic (Table 1).

Pediatric Kidney Transplant Program

Among the US pediatric population, ESKD most often occurs secondary to congenital anomalies of the urinary tract, glomerular disease, or secondary glomerulonephritis.[6] Preemptive kidney transplantation is the preferred mode of renal replacement therapy (RRT), yet hemodialysis remains the most commonly used initial RRT (23% vs 43%, respectively),[2] likely reflecting the mismatch between the number of patients with ESKD and available organs. Amaral et al compared outcomes among pediatric patients with ESKD who underwent preemptive kidney transplantation versus those exposed to dialysis and

Table 1. Adult Transplant Programs Through December 31, 2022

Transplant Type	1st Year Performed	Total Transplants	Actively Following
Kidney, deceased donor	1966	6477[a]	3007[b]
Kidney, living donor	1966	3875	3007[b]
Heart	1973	893	291
Pancreas-kidney	1982	1454	537
Pancreas	1982	439	164
Liver, deceased donor	1984	2759	1095[b]
Heart-kidney	1987	34	16
Lung	1988	881	290
Liver-kidney	1989	173	85
Liver-intestine-pancreas	1989	1	2[c]
Heart-lung	1989	15	3
Heart-pancreas-kidney	1993	1	–
Intestine	1995	3	–
Lung-kidney	1996	3	2
Liver-living donor	1999	47	1095[b]
Intestine-liver-pancreas-kidney	2000	1	–
Kidney, autotransplant	2002	147	N/F
Liver-pancreas	2006	8	1
Heart-liver	2017	5	5

Abbreviation: N/F, not following.
[a]Includes dual and en-bloc kidneys.
[b]Includes both living and deceased organ recipients.
[c]Transplanted as pediatrics.

Table 2. Pediatric Transplant Programs Through December 31, 2022

Transplant Type	1st Year Performed	Total Transplants	Actively Following
Kidney-living donor	1967	88	99[a]
Kidney-deceased donor	1967	175	99[a]
Liver-deceased donor	1984	193	87[a]
Liver-intestine	1988	4	–
Liver-intestine-pancreas	1991	12	3
Intestine	1994	19	–
Heart	1994	3	1
Intestine-liver-pancreas-kidney	1999	1	1
Liver-kidney	2003	17	1
Pancreas-kidney	2005	20	–
Liver-living donor	2008	5	87[a]
Lung	2008	4	1
Kidney, autotransplant	2016	20	N/F
Pancreas	2017	13	1
Heart-kidney	Soon		

Abbreviation: N/F, not following.
[a]Includes both living and deceased organ recipients.

found dialysis exposure to be associated with a higher risk of both graft failure and death.[8]

In 1967, a year after the center's first adult kidney transplants, the first pediatric living and deceased donor kidney transplants were completed successfully. Since then, over 88 living donor and 175 deceased donor pediatric kidney transplants have been performed at the transplant center, with 99 patients actively followed in the clinic (Table 2).

Adult Simultaneous Pancreas-Kidney Transplants

For patients with ESKD secondary to type 1 diabetes or insulin-dependent type 2 diabetes, simultaneous pancreas-kidney transplant is a life-changing treatment that can significantly improve quality of life by replacing the need for daily insulin and regular dialysis. Currently, 83% of all pancreas transplants performed are simultaneous pancreas-kidney transplants, 12% are performed in patients who have previously received a kidney, and 5% of pancreas transplants alone are performed for patients with brittle type 1 diabetes without concurrent kidney disease.[9]

The first adult simultaneous pancreas-kidney transplant was performed at UW in 1982. This is one of the institution's larger programs, with 1454 transplants performed through 2022 and 537 patients actively followed in the clinic (Table 1).

Adult Liver Transplant Program

Among patients with end-stage liver disease (ESLD) listed for transplant, common primary diagnoses include alcohol-related liver disease, hepatocellular carcinoma, hepatitis C, and non-alcoholic steatohepatitis (NASH).[10] In recent years, NASH has become the most rapidly increasing indication for liver transplantation, reflecting the obesity epidemic in the US, while transplants due to chronic hepatitis C have declined due to the development of highly effective direct-acting antivirals.[11] Regardless of etiology, liver transplantation is the gold standard treatment for ESLD and can significantly improve life expectancy.

This is UW's third largest transplant program, surpassed only by the adult kidney programs. The program's first transplant was performed in 1984, and 2759 transplants had been performed by the end of 2022. At that time, 1095 patients, including some of the 47 living donor liver recipients, were followed in the transplant clinics (Table 1).

In 1999, 15 years after the first deceased donor adult liver transplant at UW, the first living donor adult liver transplant was performed at UW, marking the beginning of an exciting new era. For patients with liver failure, waiting for a deceased donor organ was no longer the only option. Instead, they could receive a partial liver from a living donor, and by the end of 2022, 47 living donor adult liver transplants had been performed at UW (Table 1).

Across the US, living donor liver programs have experienced slow growth due to challenges such as widespread media coverage of donor deaths in the 2000s and graft size issues leading to exclusion of potential living donor-recipient pairs.[12] Growth of these programs is needed to better serve over 10 000 patients currently waitlisted for a liver.[7] Increasing the donor pool via living donors is an important goal as nearly 20% of waitlisted patients either die or become too ill for transplant each year.[10]

Other Solid Organ Transplant Programs

Besides the aforementioned programs, there are various active thoracic and abdominal solid organ transplant programs at UW, including simultaneous multiorgan transplant programs (Tables 1 and 2). Most patients continue to follow up in the transplant clinic.

From 1966 to 2023, UW's solid organ transplant programs have affected thousands of lives, advanced the field of transplantation through research and innovation, and recruited teams of dedicated individuals. The large proportion of transplanted patients actively followed at our transplant clinics is one of the many strengths of these programs, as they ensure high quality care and provide extensive data for research. Some patients return to the clinics for decades of follow-up care, and we can gather invaluable longitudinal data from the successes and setbacks of their clinical courses.[13,14]

The successes of the UW Health Transplant Center would not be possible without its patients and the gifts of life from organ donors throughout Wisconsin and nationwide. It is only through their donations that the center has and will continue to serve patients for years to come.

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REFERENCES

1. Sollinger HW, Becker YT, Burlingham W, et al. The history of the University of Wisconsin transplant program. *Clin Transpl.* 2007;271-287.

2. The United States Renal Data System 2022 Annual Data Report. United States Renal Data System. Published 2022. Accessed date February 22, 2023. https://adr.usrds.org/2022

3. Chaudhry D, Chaudhry A, Peracha J, Sharif A. Survival for waitlisted kidney failure patients receiving transplantation versus remaining on waiting list: systematic review and meta-analysis. *BMJ*. 2022;376:e068769. doi:10.1136/bmj-2021-068769

4. Kirkeskov L, Carlsen RK, Lund T, Buus NH. Employment of patients with kidney failure treated with dialysis or kidney transplantation-a systematic review and meta-analysis. *BMC Nephrol.* 2021;22(1):348. doi:10.1186/s12882-021-02552-2

5. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant.* 2011;11(10):2093-2109. doi:10.1111/j.1600-6143.2011.03686.x

6. Gupta R, Woo K, Yi JA. Epidemiology of end-stage kidney disease. *Semin Vasc Surg.* 2021;34(1):71-78. doi:10.1053/j.semvascsurg.2021.02.010

7. Data and Trends. United Network for Organ Sharing. NOS. Accessed September 9, 2024. https://unos.org/data

8. Amaral S, Sayed BA, Kutner N, Patzer RE. Preemptive kidney transplantation is associated with survival benefits among pediatric patients with end-stage renal disease. *Kidney Int.* 2016;90(5):1100-1108. doi:10.1016/j.kint.2016.07.028

9. Jiang AT, BHSc, Rowe N, Sener A, Luke P. Simultaneous pancreas-kidney transplantation: the role in the treatment of type 1 diabetes and end-stage renal disease. *Can Urol Assoc J.* 2014;8(3-4):135-138. doi:10.5489/cuaj.1597

10. Kwong AJ, Ebel NH, Kim WR, et al. OPTN/SRTR 2021 annual data report: liver. *Am J Transplant*. 2023;23(2 Suppl 1):S178-S263. doi:10.1016/j.ajt.2023.02.006

11. Younossi ZM, Stepanova M, Ong J, et al. Nonalcoholic steatohepatitis is the most rapidly increasing indication for liver transplantation in the United States. *Clin Gastroenterol Hepatol.* 2021;19(3):580-589.e5. doi:10.1016/j.cgh.2020.05.064

12. Sturdevant M, Ganesh S, Samstein B, et al. Advances and innovations in living donor liver transplant techniques, matching and surgical training: meeting report from the living donor liver transplant consensus conference. *Clin Transplant.* 2023;37(7):e14968. doi:10.1111/ctr.14968

13. Parajuli S, Mandelbrot DA, Aziz F, et al. Characteristics and outcomes of kidney transplant recipients with a functioning graft for more than 25 years. *Kidney Dis (Basel).* 2018;4(4):255-261. doi:10.1159/000491575

14. Parajuli S, Bath NM, Aziz F, et al. More than 25 years of pancreas graft survival after simultaneous pancreas and kidney transplantation: experience from the world's largest series of long-term survivors. *Transplantation*. 2020;104(6):1287-1293. doi:10.1097/TP.0000000000002960

Identifying Local Facilitators and Barriers to Screening Mammography Within a Rural Acute Care Hospital Service Area

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ABSTRACT

Introduction: Women living in rural areas are more likely to be diagnosed with advanced-stage breast cancer than their urban counterparts. The advanced stage at diagnosis is potentially attributable to lower rates of mammogram screening. We aimed to elucidate factors affecting women in decision-making about mammogram screening in a rural area in Wisconsin served by a critical access hospital.

Methods: We conducted an observational cross-sectional mixed-methods study, collecting data from various sources using 3 methods. Virtual interviews with hospital staff, virtual focus groups with community members, and a survey of women 40 years and older occurred from September 2021 through February 2022. Qualitative data were organized into themes of facilitators and barriers to mammogram screening. Survey responses were reported descriptively.

Findings: Eleven hospital staff interviewed and 21 community members who joined 1 of 3 virtual focus groups voiced similar perceptions of facilitators and barriers to mammogram screening. Clinician recommendation was among facilitators, while insurance concerns were the primary barrier. Among survey respondents (N = 282), mean age was 58.7, 98% self-identified as White, and 91% saw a health care provider in the past year. Top reasons for having their first mammogram were doctor recommendation (70%), family history (19%), and personal decision (18%). Top reasons they did not have a mammogram screening at least every year were putting it off (23%), lack of problems (17%), and pandemic-related reasons (15%).

Conclusions: Improving patient education and supporting clinicians to deliver screening recommendations may increase appropriate screening. Future studies should focus on reaching women not engaged with the health system.

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INTRODUCTION

More than 20 million adult US women live in rural areas.[1] Mortality rates for all cancers, including breast cancer, are higher in rural than in urban areas.2 Multiple factors contribute to this increased mortality.[2-9] Residents in rural areas may face socioeconomic disadvantages, such as lower levels of education,[2-4] lower income,[2-4] and increased distance to health care facilities.[2,5-7] Moreover, up to 14% of women in rural areas do not have health insurance, which further limits access to care.[1] A study with data from the Pregnancy Risk Assessment Monitoring System reported that, between 2016 and 2019, during pregnancy, rural residents were more likely to be uninsured compared to urban residents (15.4% vs 12.1%; adjusted odds ratio 1.19; 95% CI, 1.11–1.28).[10] Many rural women have decreased access to preventive health care due to the shortage of rural primary care clinicians,[7] obstetrician/gynecologists,[7] and care facilities in rural areas.[5] In addition, effects of inclement weather—particularly winter—in many US rural areas can interfere with the ability to seek preventive care.[6]

Women residing in rural areas are more likely to be diagnosed with advanced stage breast cancer (disease stage III and IV) than women in urban areas,[1,5,6,8]—potentially attributable to lower rates of screening mammography[1,4-6,8,9]—although there are conflicting results in the literature. A study of women in 11 states found disparate screening rates for colorectal cancer but similar rates for mammogram screening between rural and urban women.[11] However, less access to medical treatment for breast cancer and decreased

treatment with chemotherapy have been described for rural women, which may impact mortality.[9] Importantly, advanced stage at diagnosis is a prognostic factor affecting relative 5-year survival rates (99% for women with localized breast cancer, 86% for women with regional disease, and 30% for women with distant disease).[12] Presenting with advanced stage at diagnosis also decreases the possibility of receiving breast-conserving surgery.[13] Thus, early detection of breast cancer is important to increase the probability of achieving better outcomes.

Columbia County, located in south central Wisconsin,[14] is the primary site for this research. Approximately 60% of the nearly 58000 residents are considered rural,[15] 48% are women, and 94.5% are White.[16] Breast cancer is the most common cancer diagnosed among women in Columbia County.[15] However, data from the Behavioral Risk Factor Surveillance System 2020 survey show that the estimated age-adjusted prevalence of mammogram screening for women ages 50-74 in the county is lower compared with the state (71.9% vs 80.9%).[17] Prairie Ridge Health Hospital (PRHH) is a critical access hospital in Columbus, Wisconsin, with a service area that includes rural ZIP codes from neighboring counties (Figure 1).[14,18,19] Two other facilities offer mammogram screening in the area and are located approximately 13 and 30 miles from Columbus. Prairie Ridge Health partnered with researchers at the University of Wisconsin–Madison Carbone Cancer Center to evaluate barriers and facilitators to mammogram screening among eligible women residing in the service area, aiming to elucidate specific factors that affected women's decision-making about mammogram screening.

Figure. Wisconsin County Map With Rural-Urban Continuum Codes County Classification

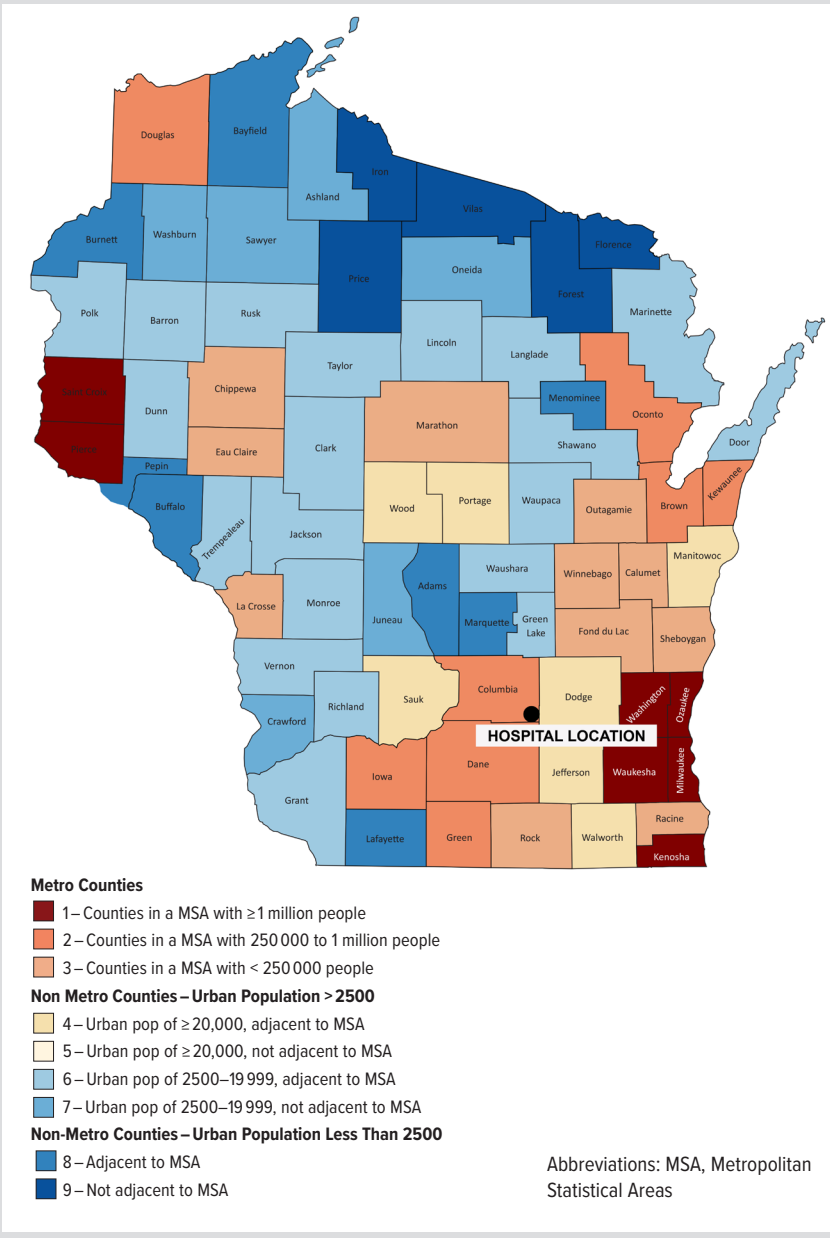

Figure adapted with permission from the University of Wisconsin-Madison, Division of Extension.[14]

METHODS

Study Design

We conducted an observational cross-sectional mixed-methods study. Our multidisciplinary team is comprised of researchers from Prairie Ridge Health, the University of Wisconsin–Madison Carbone Cancer Center, and the Wisconsin Research and Education Network (WREN). Implied consent was obtained and the project was deemed exempt by Institution A's Institutional Review Board, which reviewed and approved all study procedures.

Setting

In the 2013 Rural-Urban Continuum Codes (RUCC) classification, counties are assigned codes from 1 to 9, and those with codes 1 through 3 are considered metropolitan, while those with codes 4 through 9 are rural (Figure 1).[14] Columbia County is classified as metropolitan 2 based on the 2013 RUCC,[14] and the hospital catchment area includes neighboring nonmetropolitan counties classified as RUCC 4, 6, and 8. In addition, many ZIP codes within Columbia County have rural characteristics based on land utilization and local culture.[18,19] The Area Health Education Center System's Wisconsin Urban-Rural Classification system[18] was utilized to better characterize rural locations within metro-

politan counties and allowed our team to identify rural ZIP codes served by PRHH.[18]

The hospital performed approximately 1780 screening mammograms in 2022. It utilizes several strategies to improve mammogram screening utilization in the service area. Besides regular scheduled screening mammography, a "walk-in" option is offered without referral or appointment scheduled. The "walk-in" occurs every week in October and on the last week of the remaining months. Walk-in days had an average of 15 exams per day in 2022 and 19 per day in the first 2 months of 2023. In addition, an oncology nurse navigator follows up with patients regarding mammogram screening results. If results are abnormal, the oncology nurse navigator facilitates referrals to additional imaging, breast biopsy, and medical appointments.

Recruitment and Data Collection

Recruitment approaches are discussed below, with attention to each data collection method. Data were collected from various sources (which aided in data triangulation) and through different methods (methodological triangulation).[20,21] Given concerns about the COVID-19 pandemic, all interviews and focus groups were conducted virtually.

Interviews With Hospital Staff

Hospital research team members recruited staff involved in mammogram screening services, including primary care clinicians, mammography technicians, and schedulers/registration staff. A snowball approach[20] among staff also was utilized to generate potential participants. Virtual structured interviews occurred from September 2021 through February 2022. Participants were compensated for their time.

Focus Groups With Community Members and Hospital Patients

Multiple approaches were used to encourage diverse participation. Study advertisements were posted on the hospital website and Facebook page. In addition, focus group invitations were mailed with the survey to 1800 women aged 40 to 75 years who resided in the 9 rural ZIP codes[18,20] within the hospital's service area. The mailing list was purchased from Madison Media Partners, which facilitated the printing and mailing of the survey, and had a list of 10705 women ages 40 to 75 residing in the 9 rural ZIP codes within the hospital's service area. Among these women, 1800 were selected randomly for the mailing as weighted by the percentage of Hospital market share for each community (proportionally to the number of patients from each location seen at the hospital). Potential participants who contacted the research team were screened for eligibility criteria (40 years of age or older, female sex at birth, and residing within the hospital's service area). Participants did not need to receive medical care at the hospital to be eligible. Three 60-minute virtual focus groups were conducted between November 2021 and February 2022.

Survey for Women Within the Hospital's Service Area

A 28-question survey, including 3 questions on exclusion criteria, was developed to examine community members' attitudes, perceived barriers, and facilitators to mammogram screening. An additional field was provided for open comments. The survey link was available online on the hospital's website from September 2021 through February 2022. Printed surveys were mailed with the focus group advertisements. Women were eligible to complete the survey if they were 40 years or older, did not have a personal history of breast cancer, and did not participate in the interview or focus groups for this project.

Data Analysis

Interviews and focus groups were recorded and transcribed. Content analysis was conducted.[20] After removing identifiers, transcripts were coded inductively by 3 independent coders. The coders met to resolve discrepancies and create a final codebook. The codes that emerged were thematically organized as barriers, facilitators, or neutral comments. Data from online and paper surveys were combined, and descriptive statistics were calculated.

The research team used triangulation – a combination of multiple data sources or methods – to provide robust data, whereby different sampling methods can complement each other in understanding a particular phenomenon.[20] In addition, complex health issues may require consideration of multidimensional perspectives.[21]

RESULTS

Interviews With Hospital Staff

Eleven hospital staff participated in interviews, including 4 physicians (specialized in family medicine, internal medicine, or obstetrics and gynecology), 3 mammography technicians, 2 schedulers/registration staff, 1 medical assistant, and 1 advanced practice nurse. Thirty-two codes were created and organized into themes of facilitators (n = 12), barriers (n = 13), neutral (n = 5), not within the scope of position or not applicable (n=1), or no code (response could not be coded). A total of 257 responses were recorded, and a total of 349 codes were assigned. Each response could have been assigned up to 4 codes. Overall, 45% (158/349) of codes were for facilitators to mammogram screening, 21% (75/349) were barriers, 17% (61/349) were neutral, and 16% (55/349) were either not coded, not applicable (N/A), or not within scope of the staff member's position. Some questions and responses were considered neutral, such as probes on which guidelines were followed for mammogram recommendations.

Among codes reported by hospital staff, the scheduling process was the top facilitator of mammogram screening (23%; 37/158), followed by marketing and advertising strategies utilized by the hospital (15%; 23/158). Clinician communication/recommendations (12%; 19/158) was another mammogram screening facilitator reported by hospital staff. Of the codes determined to be

Table 1. A Sample of Facilitators and Barriers Reported by Interview and Focus Group Participants

	Interview With Hospital Staff	Focus Group With Community Members
FACILITATORS		
Scheduling	"I would say that as far as screening (mammography), yes, I would say that's straightforward. It gets a little more complicated when there are issues and we do need to do the diagnostic mammograms. So, I would say that is a little bit more confusing and, in some cases, frustrating for the patients, because they don't quite understand it."	"Yeah, I had all my mammograms recently at Hospital C, and they have so many different times, including there were weekends where you could go in on the weekend and have it done too. So it was really, really easy to get it scheduled."
Marketing/ advertising	"I think the hospital does a good job of marketing advertising I know now. The next 4 or 5 months, they're going to have walk-in [screening mammography without scheduling or referral] Wednesdays all day on the last Wednesday of the month. So, things like that, and getting the word out for that, where people seem to really respond to those types of things."	
Clinician communication/ recommendations	"Well, in the 50 and up, I talk to them, and I say, you know, we don't know the right answer. Like, it's reasonable to get mammograms every 2 years. If you want to get an annual mammogram, insurance pays for it, is usually [how] I'll bring it up. And then in the 40s, it's an even longer conversation for me…I tried to do shared decision-making with the patient, in the 40s especially."	"I would say I have discussed it with my health care provider… I've now gotten myself in a rhythm where I have my mammogram before my annual."
Family history		"You know, my mom had breast cancer, and at 35, it never would have occurred to me to get a mammogram. But her doctor was the one who advocated to both my sister and I because of the type of cancer she had."
Knowing somebody with breast cancer		"It seems like everyone I know who has died, who's older and who's died has died from some kind of cancer. And so, like at age 50, I went right away for my colonoscopy, and that's why every year I go for my mammogram. Even though there isn't any family history or anything, the earlier you catch cancer, the better your chances are of surviving from cancer. So as soon as I know I can go get a screening of one cancer or another, I'm going."
BARRIERS		
Insurance	"I feel like sometimes women might avoid a mammogram, even if they have insurance, because they don't believe that it would be fully covered or maybe they would have some kind of a copay that they can't afford. …I feel like that comes up quite frequently: 'Will my mammogram be covered?'"	"…people that don't have health insurance, they probably aren't going to pay for it if they don't need it, if they don't think that they're sick or have any symptoms."
Transportation	"Sometimes there's some transportation issues. They don't have a way to get in. There's one car in the family. And that's used during the day, and …they can't get in. There's no public transportation for that."	
Scheduling	"The hours that we offer the mammograms. With people's work schedules. Probably about 15 years ago, I worked just the weekend program so then we did do mammograms on Saturday mornings, which helped a lot of women, but we don't offer that any more because we're just too busy with ER/urgent care. But that worked out really nice for a lot of the working women."	"I was just going to say maybe it's hard to schedule, you know. If it's a working woman who works, you know, 8 to 4 or 9 to 5, maybe she needs some alternative hours to be able to schedule that."
Fear of procedure	"Maybe some women think they should wait for their age to get mammograms. Maybe that of personal fear, like, they don't want to get it done."	"Well, I think sometimes it's a woman's fear, or maybe for whatever reason, I don't have the experience, but maybe for whatever reason, they've had one before, it was very uncomfortable, so they don't want to go back."

barriers to mammogram (n=75), the top barriers were insurance (19%), lack of appointments or convenient appointment times (15%), transportation (12%), COVID-19 (11%), and discomfort/pain from the procedure (9%).

Focus Groups With Community Members and Hospital Patients

The first focus group had 1 participant due to cancellation and dropouts. There were 12 potential participants initially; however, 3 declined and 8 did not attend. As a result, the first session was conducted as a one-on-one interview, using the focus group guide to maintain consistency. The following 2 focus groups had 9 and 11 participants (for total of 21 unique community members). Twenty-four codes were created and organized into themes of facilitators (n = 14), barriers (n = 9), or no code (response could not be coded). A total of 162 (80%) codes assigned were facilitators and 41 (20%) were barriers to mammogram screening. Clinician recommendation/patient education (23%; 37/162) was the top facilitator of mammogram screening. Having a family history

of breast cancer (11%; 18/162) was also a facilitator. Insurance/financial issues (39%; 16/41) were the most frequently reported barrier. Issues with scheduling a mammogram (17%; 7/41), such as lack of convenient times for appointments, were reported as a barrier to getting screened, as was fear of the procedure (pain, discomfort; 15%; 6/41). Excerpts presented in Table 1 exemplify some of the facilitators and barriers reported by hospital staff and focus group participants.

Survey for Women Within the Hospital's Service Area

A total of 307 women responded to the survey (140 online, 167 paper copy). While the online survey response rate cannot be calculated, the mailed survey had a response rate of 9.2% (167/1800). Of the 307 respondents, 25 women were ineligible (4 were younger than 40 years of age, 9 were part of the focus groups, and 12 were diagnosed previously with breast cancer); these data are not included in analysis. Among survey respondents (N = 282), the mean age was 58.7 years (40-82 years), 98% (266/272) self-identified as White, and 62% (165/265) as menopausal (Table 2).

Family history of breast cancer was reported by 42% (114/270) of women surveyed, 93% (250/270) knew someone with breast cancer, and 91% (246/270) reported seeing a health care provider in the past year. Awareness of mammogram was high, as 99% (267/268) of women indicated that they know what a mammogram is and 90% (240/268) had seen or heard an advertisement encouraging them to get a mammogram. A total of 85% (227/268) of women indicated that a clinician had recommend that they get screened for breast cancer. A majority of respondents (88%; 197/225) indicated that the recommendation for screening was communicated to them in-person. Conversely, 15% (41/268) of women responded that a clinician had never recommended screening mammography. Half of respondents (50%; 129/259) wrote that they thought the age at which starting mammograms is recommended was 40 years old. Survey respondents' answers regarding mammogram screening are represented in Tables 3 and 4.

Two open-ended questions and 1 free-text comments field were included at the end of the survey. A sample of the write-in responses and comments are presented in Supplemental Table 5 (Appendix) and include mention of walk-in appointments, challenges with insurance, and beliefs about the need for a physician referral for mammography.

Table 2. Demographic Data for Survey Respondents

	No. Respondents	Results n (%)
Mean age, y (Range)	266	58.7 (40-82)
Race[a]	272	
White		266 (98)
African American or Black		3 (1)
Native American or Alaska Native		2 (<1)
Prefer not to answer		2 (<1)
Education	270	
Less than high school		1 (<1)
High school graduate		66 (24)
Some college		72 (27)
College graduate and above		128 (47)
Prefer not to answer		3 (1)
Past pregnancy	272	
Yes		229 (84)
No		41 (15)
Prefer not to answer		2 (1)
Mean age at birth of first child, years (range)	224[b]	25.5 (16-44)
Menopausal	265	
Yes		165 (62)
No		95 (36)
Prefer not to answer		5 (2)
Family history of breast cancer	270	
Yes		114 (42)
No		155 (57)
Prefer not to answer		1 (0.5)
Knows someone with breast cancer	270	
Yes		250 (93)
No		19 (6.5)
Prefer not to answer		1 (0.5)

[a]Could select more than 1 response.
[b]Includes 2 respondents who indicated "Prefer not to answer." Nonresponses (blanks) were excluded from this analysis.

DISCUSSION

Our study represents a community-based mixed-methods approach to elucidate facilitators and barriers affecting decision-making on mammogram screening by women in a critical access hospital serving a high proportion of rural women. Acknowledging that rural health disparities have their roots in multilevel interdependent factors,[2] capturing perspectives of different stakeholders is a crucial step to developing community-engaged multilevel interventions to improve rural women's access and adherence to screening mammography recommendations.

The utilization of data and methodological triangulation is a strength of this study.[20,21] Clinicians, hospital staff, patients, and community members—vassessed via varying data collection methods—voiced similar perceptions of barriers and facilitators. Hospital staff identified insurance, lack of convenient appointment times, and transportation as potential barriers to mammography. Focus group participants also identified insurance/financial issues and appointment scheduling as barriers. Fears about the procedure (pain, discomfort) were noted as barriers by both focus group participants and hospital staff, suggesting that interviewed staff recognize community's perceptions. Among survey participants, the top reasons for not having a mammogram at least every year were "put it off," "haven't had any problems," "pandemic/COVID-related reasons," the perception that mammography is "not needed/necessary," and "don't have a family history of breast cancer." Previous research showed that positive family history for breast cancer affects the perception of being at risk of developing breast cancer and the decision for getting screened.[22] These

Table 3. Survey Respondents' Answers to Questions Regarding Mammogram Screening

	Results n (%)
Multiple-choice question "At what age did you have your first mammogram?" (n = 256)	
≤ 29 years old	27 (11)
30-39 years old	70 (27)
40-49 years old	133 (52)
50-59 years old	19 (7)
60-69 years old	1 (< 1)
70-74 years old	0
≥ 75 years old	0
Don't remember	2 (< 1)
Prefer not to answer	4 (2)
Multiple-answer question "Why did you have your first mammogram?" (n = 257)	
Doctor told me to/referred me	181 (70)
Family history	50 (19)
Personal decision	47 (18)
Found a lump or something concerning	32 (12)
Know someone with breast cancer	14 (5)
Family/friend referral	4 (2)
Other[a]	3 (1)
Heard an advertisement	1 (< 1)
Prefer not to answer	1 (< 1)
Multiple-choice question "How often are you having a mammogram?" (n = 256)	
Once a year	172 (67)
Twice a year	3 (1)
Every other year	43 (17)
Once every 5-10 years	31 (12)
Prefer not to answer	7 (3)
Write-in answers to the question "At what age do you think it is recommended that women should start having mammograms?" (In years) (n = 259)	
16	2 (1)
18	5 (2)
20	9 (3)
21	6 (2)
24	1 (< 1)
25	12 (5)
30	31 (12)
35	22 (8)
40	129 (50)
45	11 (4)
50	12 (5)
Prefer not to answer	6 (2)
Other[b]	13 (5)
Multiple-choice question "How often do you think it is recommended that a woman should get a mammogram?" (n = 268)	
Once a year	195 (73)
Twice a year	6 (2)
Every other year	47 (18)
Once every 5-10 years	9 (3)
I do not know	9 (3)
Prefer not to answer	2 (< 1)

Multiple-answer question: multiple responses could be selected.

[a]Three participants selected Other, although only one specified with the write-in answer " Health."

[b]Other represents responses such as ranges of numbers, question marks, and text regarding family history.

Table 4. Responses to the Multiple-Answer Question "If you do not have a mammogram at least every year, what are some reasons why?" (N = 184)

Reasons	n (% respondents)
Not applicable, I have a mammogram every year	73 (40)
Put it off	43 (23)
Haven't had any problems	31 (17)
Pandemic/COVID related reason	28 (15)
Not needed/necessary	21 (11)
Don't have a family history of breast cancer	19 (10)
Not recommended by my doctor/PA/NP	17 (9)
Painful procedure	14 (8)
Didn't know that I should	11 (6)
Fear of finding cancer	10 (5)
Too busy	8 (4)
Couldn't get an appointment that fit my schedule	7 (4)
Problem with insurance coverage	6 (3)
Don't know	6 (3)
Too embarrassing	5 (3)
Other	5 (3)
I am not old enough to need yearly mammograms	4 (2)
I don't have health insurance	3 (2)
Have emotional health concern(s) (depression or anxiety)	3 (2)
Prefer not to answer	3 (2)
Didn't know how to schedule	2 (< 1)
Too far away	1 (< 1)
Couldn't get an appointment (full)	0 (0)
No childcare	0 (0)
Results take too long to came back	0 (0)

Multiple-answer question: multiple responses could be selected. Other represents write-in options and includes concerns with radiation exposure (n = 3, 1.6%), "lack of doctor" (n = 1, < 1%), and the statement "too old and no more sex" (n = 1, < 1%).

findings are important to inform the development of strategies to address educational gaps and misperceptions regarding the role of screening mammography.

Clinician recommendation/patient education were reported as the top mammography facilitator among those reported by focus group participants (23%). Clinicians' recommendation triggered the first mammography of 70% of surveyed women, followed by family history of breast cancer (19%), and personal decision (18%). Previous research demonstrated that cancer screening advice from a clinician is a strong modifiable factor influencing patients' behaviors.[23,24] The quality of patient-clinician communication is important, as patients have a positive response when the cancer screening recommendation involves an explanation of procedures and addresses patient-specific barriers.[23] High-quality patient-clinician communication involves clinicians' time and willingness,[25] which are affected by multiple factors such as the time available for patient encounter, number of clinicians in the practice, and clinician workload, contextualized by the persistent low density of primary care clinicians in rural settings.[7,26] Clinicians may inspire patients' personal decisions, as patients often rely

on recommendations from their physician to guide their health behavior.[23,27] Clinician recommendation is particularly important among women 40 to 49 years, for whom starting screening mammography practices was based on shared-decision-making as suggested by the United States Preventive Services Task Force (USPSTF) until recently.[25,28]

The USPSTF and the American Cancer Society (ACS) mammogram screening guidelines are the most commonly utilized among Wisconsin's primary care clinicians.[29] Per ACS recommendations, women ages 40 to 44 years should be offered annual mammogram screening, and women 45 to 54 years should get screened annually.[29] Women 55 years and older can maintain annual screening or get screened every other year. ACS suggests mammogram screening may continue while the woman is healthy, with life expectancy of at least 10 more years.[29] USPSTF recommends all women should get screened every other year between the ages 40 and 75 years,[28] and evidence is insufficient to evaluate benefits and harms of mammogram screening among women 75 years and older.[28] Evaluating guideline adherence and standard of care procedures is challenging in the face of multiple guidelines recommendation.[29]

Among survey participants, the majority are getting screened annually (67%) or biennially (17%), corresponding to ACS and USPSTF guidelines recommendations. Beliefs regarding how often a mammogram screening should occur followed a corresponding pattern (73% annually, 18% biennially), similar to a previous study on barriers to mammogram between rural and urban women.[24] Beliefs regarding the starting age to get screened had more variability. Approximately 33% of survey participants wrote that they think the recommended age to start getting screened is before 40 years. Although this result exposes the misconceptions regarding mammogram screening, it may represent an improvement compared to previous research that reported 72% of rural participants answering that screening should start before 40 years.[24]

Scheduling can be a barrier and a facilitator of mammogram screening. A straightforward scheduling process was reported as a main facilitator, while lack of convenient appointment times was reported as a barrier. Appointments outside of business hours may facilitate mammography for women with competing commitments and busy schedules. Pairing cancer screening as a "walk-in" option with an appointment for other reasons has been well received by patients and increases screening utilization in urban areas.[30-32] Same day clinical breast exam with mammography referral and cervical cancer screening following an acute care visit for nongynecological concerns have been shown to have high acceptance among patients (55%).[32] Walk-in mammogram screening following a scheduled visit[31,32] seems to be particularly beneficial for women at risk of not being screened (unemployed,[31] with fewer mammograms in the past,[31] non-White,[32] Medicaid-insured).[32] Thus, mammography as a walk-in appointment has the potential to engage women who face a variety of barriers to get screened.

Limitations

A study limitation is that focus groups and survey participants tended to be highly engaged with the health care system, as evidenced by the high percentage of survey respondents who had seen a health care provider in the past year. In addition, focus group participants were supportive of mammography, which may suggest participation and social desirability biases. Thus, our outreach did not recruit participants who never had mammogram screening or who face significant barriers to mammography. Conducting the first focus group meeting as an individual interview may have limited the discussion on barriers and facilitators for mammogram screening for that particular subject. A limitation of the qualitative assessment by codes alone is that the interview questions specifically probed for facilitators and barriers to mammography and used primarily deductive coding and analysis. The survey was developed by the research team, and the wording utilized in survey questions may have influenced participants' responses, which may limit reliability. We cannot estimate the online survey response rate because the survey link was available for all individuals who landed on the hospital's website. Ninety-seven percent of the survey participants were White (consistent with the demographics of this county);[15,16] 74% had at least some college education; and we did not register participants place of residence, limiting the ability to generalize our results to other non-White, more rural, groups with little formal education, who may face different challenges in obtaining a mammogram screening.

CONCLUSIONS

Understanding factors involved in women's decision-making regarding mammogram screening is important for improving screening utilization in rural areas. Our study suggests hospitals could focus on supporting health care professionals to deliver mammogram screening recommendations more efficiently to patients in rural communities. Health care teams should prioritize identifying and addressing patient education gaps[24] and improving mammogram screening scheduling options, because these are modifiable factors that have the potential to increase screening adherence. Future studies should focus on reaching and increasing awareness among women who are not engaged with the health system, as well as racial and ethnic minority women and migrant workers in rural communities. Other potential strategies for future work are addressing gaps in patient education on the benefits of preventive care (including screening mammography), increasing education and awareness that breast cancer can occur in the absence of family history, and providing clinician education on engaging women in shared decision-making regarding mammogram screening.

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Previous Presentations: Data from this research were presented as posters at the following events: the 2023 Wisconsin Hospital Association Advocacy Day, April 18-19, 2023; the 2022 NAPCRG Practice-based Research Network (PBRN) Conference, June 2-3, 2022, in Bethesda, Maryland; the UW Women's Health Equity and Health Equity Research Lecture and Symposium, October 20, 2022, in Madison, Wisconsin.

REFERENCES

1. Bennett KJ, Lopes JE, Spencer K, van Hecke S. National Rural Health Association policy brief: Rural Women's Health. Approved January 2013. Accessed July 29, 2022. https://www.ruralhealth.us/getmedia/59200550-91c7-48c9-bd64-83621a7d93b6/RuralWomensHealth-(1).pdf

2. Yabroff KR, Han X, Zhao J, Nogueira L, Jemal A. Rural cancer disparities in the United States: a multilevel framework to improve access to care and patient outcomes. *JCO Oncol Pract*. 2020;16(7):409-413. doi:10.1200/OP.20.00352

3. Obeng-Gyasi S, Obeng-Gyasi B, Tarver W. Breast Cancer disparities and the impact of geography. *Surg Oncol Clin N Am*. 2022;31(1):81-90. doi:10.1016/j.soc.2021.08.002

4. Thompson JA, Chollet-Hinton L, Keighley J, et al. The need to study rural cancer outcome disparities at the local level: a retrospective cohort study in Kansas and Missouri. *BMC Public Health*. 2021;21(1):2154. doi:10.1186/s12889-021-12190-w

5. Chandak A, Nayar P, Lin G. Rural-urban disparities in access to breast cancer screening: a spatial clustering analysis. J Rural Health. 2019;35(2):229-235. doi:10.1111/jrh.12308

6. Onitilo AA, Liang H, Stankowski RV, et al. Geographical and seasonal barriers to mammography services and breast cancer stage at diagnosis. *Rural Remote Health*. 2014;14(3):2738.

7. Barry J. The Relationship between the supply of primary care physicians and measures of breast health service use. *J Womens Health (Larchmt*). 2017;26(5):511-519. doi:10.1089/jwh.2016.5830

8. Nguyen-Pham S, Leung J, McLaughlin D. Disparities in breast cancer stage at diagnosis in urban and rural adult women: a systematic review and meta-analysis. *Ann Epidemiol*. 2014;24(3):228-235. doi:10.1016/j.annepidem.2013.12.002

9. Andreason M, Zhang C, Onitilo AA, et al. Treatment differences between urban and rural women with hormone receptor-positive early-stage breast cancer based on 21-gene assay recurrence score result. *J Community Support Oncol*. 2015;13(5):195-201. doi:10.12788/jcso.0135

10. Admon LK, Daw JR, Interrante JD, Ibrahim BB, Millette MJ, Kozhimannil KB. Rural and urban differences in insurance coverage at prepregnancy, birth, and postpartum. *Obstet Gynecol.* 2023;141(3):570-581. doi:10.1097/AOG.0000000000005081

11. Shete S, Deng Y, Shannon J, et al; Rural Workgroup of the Population Health Assessment in Cancer Center Catchment Areas Initiative. Differences in breast and colorectal cancer screening adherence among women residing in urban and rural communities in the United States. *JAMA Netw Open*. 2021;4(10):e2128000. doi:10.1001/jamanetworkopen.2021.28000

12. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin.* 2023;73(1):17-48. doi:10.3322/caac.21763

13. Giaquinto AN, Sung H, Miller KD, et al. Breast cancer statistics, 2022. *CA Cancer J Clin.* 2022;72(6):524-541. doi:10.3322/caac.21754

14. UW Extension. A Snapshot of Rural Wisconsin. Accessed October 17, 2022. https://www.rwhc.com//mediasite/5-App-Kures,%20Matt_%20Plenary_am_Demographics.pdf

15. Wisconsin Cancer Collaborative. Interactive County Cancer Data Dashboard. Accessed October 17, 2022. https://wicancer.org/resources/12148-2/county-cancer-profiles/county-cancer-data-dashboard/

16. QuickFacts: Columbia County, Wisconsin; United States. United States Census Bureau. Accessed October 22, 2022. https://www.census.gov/quickfacts/fact/table/columbiacountywisconsin,US/SEX255221

17. U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute. Released November 2022. Updated June 2024. Accessed April 4, 2023. https://gis.cdc.gov/Cancer/USCS/#/CancerScreening/

18. Wisconsin Urban-Rural Classification (WURC) System. Area Health Education Centers System – Wisconsin. Revised July 2014. Accessed November 10, 2022. https://ahec.wisc.edu/wp-content/uploads/sites/99/2017/02/Wisconsin-Urban-Rural-Codes-July2014.pdf

19. Putting Rural Wisconsin on the Map. WisCONTEXT. Accessed November 10, 2022. https://www.wiscontext.org/putting-rural-wisconsin-map

20. Patton MQ. *Qualitative Research and Evaluation Methods.* 3rd ed. Sage; 2002.

21. Farmer T, Robinson K, Elliott SJ, Eyles J. Developing and implementing a triangulation protocol for qualitative health research. *Qual Health Res*. 2006;16(3):377-394. doi:10.1177/1049732305285708

22. Haber G, Ahmed NU, Pekovic V. Family history of cancer and its association with breast cancer risk perception and repeat mammography. *Am J Public Health*. 2012;102(12):2322-2329. doi:10.2105/AJPH.2012.300786

23. Peterson EB, Ostroff JS, DuHamel KN, et al. Impact of provider-patient communication on cancer screening adherence: A systematic review. *Prev Med*. 2016;93:96-105. doi:10.1016/j.ypmed.2016.09.034

24. Davis TC, Arnold CL, Rademaker A, et al. Differences in barriers to mammography between rural and urban women. *J Womens Health (Larchmt).* 2012;21(7):748-755. doi:10.1089/jwh.2011.3397

25. Martinez KA, Deshpande A, Ruff AL, Bolen SD, Teng K, Rothberg MB. Are providers prepared to engage younger women in shared decision-making for mammography? *J Womens Health (Larchmt).* 2018;27(1):24-31. doi:10.1089/jwh.2016.6047

26. Zhang D, Son H, Shen Y, et al. Assessment of changes in rural and urban primary care workforce in the United States from 2009 to 2017. *JAMA Netw Open*. 2020;3(10):e2022914. doi:10.1001/jamanetworkopen.2020.22914

27. Blanch-Hartigan D, Viswanath K. Socioeconomic and sociodemographic predictors of cancer-related information sources used by cancer survivors. *J Health Commun.* 2015;20(2):204-210. doi:10.1080/10810730.2014.921742

28. US Preventive Services Task Force. Final Recommendation Statement - Breast Cancer: Screening. April 30, 2024. Accessed August 26, 2024. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/breast-cancer-screening#bcei-recommendation-title-area

29. Nachtigal E, LoConte NK, Kerch S, Zhang X, Parkes A. Variation in breast cancer screening recommendations by primary care providers surveyed in Wisconsin. *J Gen Intern Med.* 2020;35(9):2553-2559. doi:10.1007/s11606-020-05922-y

30. Doyle JP, Parker RM, Jacobson TA, McNagny SE. Breast and cervical cancer screening in an inner-city medical walk-in clinic: taking advantage of an often missed opportunity. *Am J Prev Med.* 1996;12(5):345-350.

31. Dolan NC, McDermott MM, Morrow M, Venta L, Martin GJ. Impact of same-day screening mammography availability: results of a controlled clinical trial. *Arch Intern Med*. 1999;159(4):393-398. doi:10.1001/archinte.159.4.393

32. Wang GX, Pizzi BT, Miles RC, et al. Implementation and utilization of a "pink card" walk-in screening mammography program integrated with physician visits. *J Am Coll Radiol*. 2020;17(12):1602-1608. doi:10.1016/j.jacr.2020.07.007

Lead Poisoning in Milwaukee: A Medical and Public Health Update

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ABSTRACT

Introduction: Every year, children are poisoned with lead with irreversible effects. This exposure most often occurs in older housing built before 1978 with chipping paint from windowsills where children play and ingest the lead particulates. Exposure to lead can cause neurological and psychological dysfunction, among other health issues.

Objective: This quality improvement study aims to evaluate our knowledge of at-risk children through a public health approach by analyzing the current public health data and possible barriers to lead screening, testing follow-up, and identifying at-risk children.

Methods: We received data on lead-poisoned children and inspected properties from the City of Milwaukee Health Department. We analyzed each child's initial blood lead level, as well as follow-up tests recorded, ZIP code of residence, and family renter versus home ownership.

Results: Over 90% of children in the database had recorded follow-up blood lead testing following an initial elevated blood lead level. There was no difference in initial recorded blood lead levels between children with recorded follow-up blood lead levels and children without (21.40, SD = 11.26); t[1.17], *P* = 0.24). Most affected children were from economically disadvantaged ZIP codes (53206, 53208, 53215), and 94% lived in rented properties.

Conclusions: More work is needed to reduce lead in the environment and improve follow-up in affected children. ZIP code and rental data may indicate at-risk children. Although follow-up testing rates are high, the study revealed a wide range in lead levels with follow-up. Identifying at-risk children and reducing lead levels in children is vital to support health equity.

INTRODUCTION

Lead poisoning affects children across the United States and is especially prevalent in communities with older housing stock. Although lead poisoning and exposure have decreased in recent years, it remains a public health issue.[1-5] Lead exposure through ingestion typically is caused by chipping paint from windowsills where children play, as well as dust and lead in the soil and water.[2] Lead poisoning can present as neurologic dysfunction, psychological disorders, speech and language delay, anemia, or no symptoms. It can cause long-term problems for exposed children, such as kidney dysfunction, gout, peripheral neuropathy, neurocognitive defects, and developmental delay.[2,3] Levels over 3.5 µg/dl are described by the Centers for Disease Control and Prevention (CDC) as the current reference level for risk.[6] Despite the CDC reference level, no level of lead in the body is safe.[4,6,7]

With some of the state's highest lead poisoning rates, lead remains a severe problem in the city of Milwaukee. In 2021, nearly 6% of tested children under age 6 had levels greater than 3.5 µg/dL.[8] In Wisconsin, 4.3% of children have a detectable (>1.0 µg/dL) blood lead level (BLL) compared to the 1.9% national average.[9] Advancements towards less lead poisoning are underway, and some improvements of the environmental conditions already have been made.[10] Despite the advances, the need to bring lead exposures and levels down further provides a sense of urgency.[3,8,11]

The Wisconsin Department of Health Services (DHS), as of January 2024, recommends universal testing and that all children

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should obtain 2 lead tests by age 2. Children between ages 3 and 5 also should receive testing without a prior record.[11] Per Wis. Stat 254.11, children who have 2 venous levels between 15 mg/dl and 19.9 mg/dl more than 90 days apart or 1 venous BLL > 20 mg/dl qualify for a public health nurse referral for case management and monitoring as well as environmental investigations.[12,13] Additional measures are in place for all children with BLLs >5 mg/dl, including mailed educational materials and reminders about the importance of venous follow-up BLLs.[12] DHS also recommends local health department actions for any children with a BLL of 3.5 mg/dl.or above.[3] Local health departments rely heavily on local clinicians to perform screening and BLL testing on young children.[3]

The Medical College of Wisconsin (MCW) collaborates on a lead prevention project funded by Advancing a Healthier Wisconsin with City of Milwaukee Health Department (MHD), Children's Wisconsin, Children's Health Alliance of Wisconsin, and the Social Development Commission. This project prioritizes children and communities experiencing poverty, housing with lead hazards, challenges accessing health care, and environmental mitigation, racism, and discrimination. The goal of this project is to identify children with elevated BLLs and increase the connectedness between the clinical enterprise, MHD, community responses, and parental engagement following a positive lead test to mitigate ongoing lead exposures and decrease lead poisoning. Objectives include identifying children affected by lead in Milwaukee and the type of housing that families live in when exposed to lead.

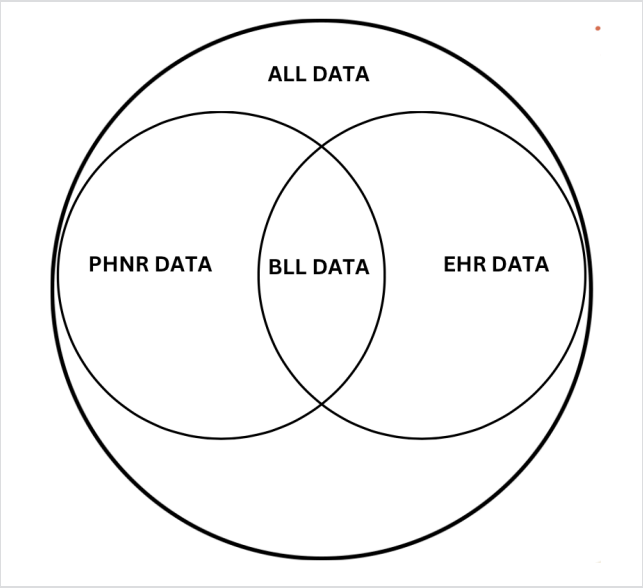
The project allows us to employ a quality improvement (QI) process to determine how to increase the number of children tested for lead within primary care clinics, improve follow-up, and support physicians' practices through a public health approach.

METHODS

A data use agreement was established between MHD and MCW to share data for research purposes. The data included: (1) blood lead test results, (2) nursing case management and monitoring encounters, and (3) home lead risk assessments. The data included a subset of children with elevated BLLs and who qualified for public health nurse referral case management and monitoring by having 2 levels between 15 μg/dl and 19.9 μg/dl more than 90 days apart or 1 level > 20 μg/dl (and some special cases where they accepted children with only 1 value >15 μg/dl) from January 2018 through December 2020. These dates apply to all data. The MCW Human Research Review Board approved the protocol.

The data received comprised 3 separate datasets: BLL data, public health nurse referrals, and environmental health referrals. Public health nurse referrals provide affected families with a public health nurse advocate for care coordination and resources. The environmental health referral dataset included children who had cases requiring home investigation. There was not necessarily exact overlap between the 3 datasets (Figure 1). The sample consisted of 367 children: the BLL dataset consisted of 281 children and included all BLLs recorded; the public health nurse referral dataset consisted of 205 children; and the environmental health referral dataset consisted of 285 children. Because data were extracted from an internal MHD database used during its transition from paper to electronic tracking, there was not direct overlap between demographic data found in the public health nurse referral dataset and BLL data. For this reason, we did not analyze descriptive statistics of the children within the datasets.

Figure 1. Venn Diagram of Data Overlaps



Abbreviations: PHNR, public health nurse referral; BLL, blood lead level; EHR, environmental health referral.

Some children were included in BLL data only (n = 56), PHNR plus BLL (n = 24), EHR plus BLL (n = 222), and some were included in all 3 datasets (n = 179). There was total BLL data for 281 children. The PHNR dataset consisted of 205 children and the EHR dataset consisted of 285 children.

Follow-up testing from the BLL dataset was analyzed in Excel. Mean first-recorded (initial) BLLs for each child with multiple recorded BLLs and those with only 1 BLL were analyzed and compared using an unpaired *t* test. ZIP code data from the environmental health referral dataset for each child's address was analyzed. Some children had multiple environmental home inspections performed at the same property. Some families had inspections completed at the same property for multiple children, such as siblings. Additionally, some children moved to a different address where an inspection was completed and then moved back to the original address where further inspections were completed. To be consistent, each child was analyzed individually regardless of relationship to different children. The first inspection performed at an address was counted. If multiple inspections were performed at the same address—even if they moved back to the original address after having moved away—they were not counted. Moving to a new address was counted as a new inspection. Per DHS, environmental home inspections continue at a new address if BLL is still elevated.[13] Property

Table. Comparison of Initial Blood Lead Levels (BLL) in Children (N = 281) Who Had Multiple Recorded BLLs and Children With Only One Recorded BLL

	Children With Multiple Recorded BLLs (N = 257)	Children With 1 Recorded BLL (n = 24)
Mean Initial BLL	25.3 µg/dL	21.4 µg/dL
Median Initial BLL	21.2 µg/dL	17.2 µg/dL
Maximum BLL	184.0 µg/dL	70.0 µg/dL
Minimum BLL	1.0 µg/dL	15.0 µg/dL 70.0 µg/dL
Total Children n (%)	257 (91.5)	24 (8.5)

ownership was determined by comparing the affected child's last name to the owner's name and came from the environmental health referral dataset. Child last names that were the same as the property owner's name were counted as ownership, whereas property owner names that were a limited liability company (LLC) or different from child names were counted as rented property. Although this novel method has limitations, without more detailed property ownership data and with the LLCs in the Milwaukee area owning many properties included in the dataset, comparing last names was used as a surrogate for home ownership information. A chi-square test was done to compare owned versus rented properties.

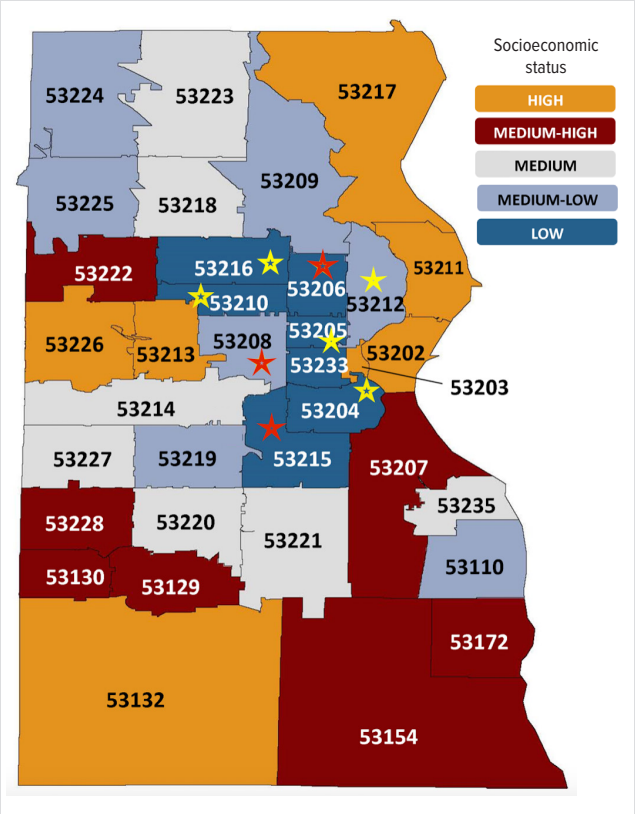
RESULTS

The dataset included 367 individual children. Out of 281 children with BLL data, 8.5% of had only 1recorded BLL (Table). There was no significant difference in initial BLL between the children who had multiple BLLs (25.33, SD = 16.06) and the children who only had 1 BLL in the dataset (21.40, SD = 11.26); t[1.17], $P = 0.24$). ZIP codes most affected were 53208 and 53206, making up just over 28% of the case-managed children (Figure 2). Out of 316 home inspection referrals in the dataset, 19 cases (6%) were individually owned, with the remaining 297 cases appearing to be rented (chi-square = 244, 1 degrees of freedom [DF]; 2-tailed P value ≤ 0.0001) based on previously described criteria.

DISCUSSION

Lead poisoning disproportionately affects historically marginalized and vulnerable populations. Previous studies suggest minority populations are disproportionately affected by lead—even beginning in utero.[14,15] Additionally, in this study, most children with an elevated BLLs are from historically underserved and economically disadvantaged ZIP codes (53208, 53206, 53215), consistent with previous data.[16-18] Being Black or African American has been shown to be the most important risk factor, second only to living in a pre-1950s house – even when controlling for all other factors, such as housing quality, poverty, and education.[14] Identifying as Black or African American and experiencing such a disproportionate amount of lead poisoning is likely a result of environmental racism, where Black and African American people in Milwaukee were forced into poor quality housing as the result

Figure 2. ZIP Codes of Public Health Lead Case Managed Children Categorized by Socioeconomic Status Using Education and Income Criteria per ZIP Code



ZIP code data was analyzed from 389 opened electronic health referral cases. Red stars indicate the highest numbers of public health lead case managed children (53208, 64 children total; 53206, 49 children total; 53215, 48 children total). Yellow stars indicate other high rates of case managed children (53210, 44 children total; 53204, 34 children total; 53212, 39 children total; 53216, 22 children total; 53205, 20 children total). Remaining children were from ZIP codes across Milwaukee County (from greatest to least number of cases: 53209, 53218, 53223, 53224, 53207, 53225, 53202, 53221, 53222, 53233, 53219). Map used with permission, courtesy of Health Compass Milwaukee.

of redlining in the 1930s and later, making Milwaukee one of the most segregated cities in the United States.[19,20] Our findings may reflect the enduring negative effects of segregation and redlining, as has been demonstrated in other disease states.[21-23] This puts Black or African American individuals in Milwaukee at continuous risk for and suffering from lead poisoning by living in the poor-quality housing in these ZIP codes.

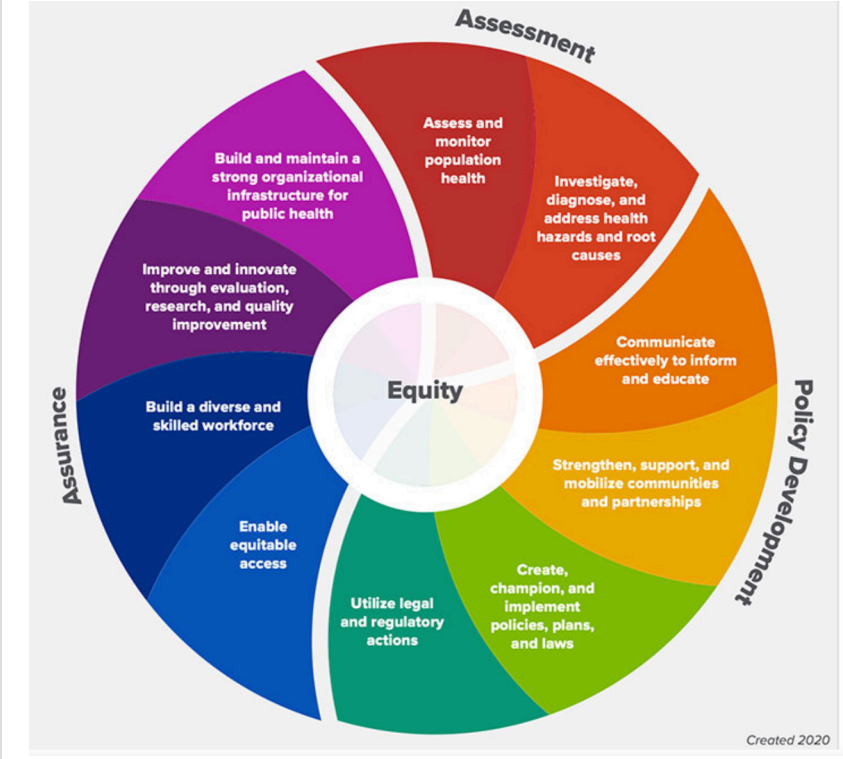
Multiple efforts are being made to monitor children exposed to lead. Over 90% of eligible children with an elevated BLL who received a public health nurse referral participated in public health nurse case management and monitoring care. Despite these successes, future efforts should seek to understand more about families who do not engage in public health intervention after referral.

Even with successful local public health follow-up and engagement, there continues to be a need to move towards primary prevention through home lead abatement. Evidence suggests that

social circumstances may be a barrier to care for the individuals who do not have medical follow-up, such as lack of cell phones or regularly changing phone numbers, eviction, needing to move, and lack of transportation.[24,25] More collaborative engagement strategies are needed to connect clinicians, families, and public health. One possible strategy could be equipping clinicians to provide public health mitigation measures, such as cleaning supply kits.[26,27] Clinicians can provide education on cleaning to parents, such as dusting windowsills, mopping floors, and eliminating carpets, which can help reinforce public health teaching.

To improve access to lead testing, we must better support the community by bringing lead safety materials and screening to community events. A combination of clinical focus, community response including landlord participation, and public health leadership to ensure safe environments could bring levels down more for the entire community. Although we have succeeded in trending towards lower BLLs and maintaining follow-up in most patients, there is room for improvement.

Figure 3. Essential Public Health Services per American Public Health Association[29]



A more equitable and socially just housing environment also is needed to protect future children from lead poisoning. Federal law mandates tenants in rented properties and those who buy a home need to be informed of lead hazards in any pre-1978 home.[28] However, almost all children with an elevated BLL live in rented properties, likely because they are the most affordable options. This is a key finding for clinicians. If most affected children are in rented homes, that may be a valuable demographic question to discuss with families to determine if they should be lead tested. Inquiring about rented versus owned properties is yet to be included on lead intake forms to determine lead screening in children.[11] A better understanding of living situations may provide further insight into lead poisoning risk.

More work is needed to achieve equity regarding housing stock, health care, and lead poisoning screening and treatment. The American Public Health Association has identified 10 essential services necessary to strengthen the public health system (Figure 3).[29] To achieve the goal of a lead-free Milwaukee, we first must assess the problem of lead poisoning. This includes continuing research into root causes, such as ZIP code data, property ownership data, and other risk factors. Second, policy development must support the goal of eliminating lead and its effects. This includes strengthening partnerships between local health departments, health care professionals, and property owners, ensuring funds are available for remodeling and infrastructure to house families who are removed from housing for abatement to take place, and requiring that all apartment complexes are lead-free. Lastly, researchers and public health officials must continue to assess and reevaluate lead and its effect in the community for new or persistent inequities.

Of course, these processes are not without unintended consequences and limitations. Funding for lead abatement, often paid by government grants, is inadequate. Residents may be evicted or need to find other housing while abatement occurs, which may not be affordable. Landlords may be unwilling or unable to renovate their complexes without significant supportive funding. Additionally, cleaning products and time spent on cleaning education in the clinical setting requires resources and takes up valuable and constrained clinician time. Thus, lead education and abatement require a significant increase in multimodal funding to eliminate the problem.

Limitations

A major limitation of this study is that the dataset comprised 3 individual datasets without exact overlap between the children, making it difficult to extrapolate which children received which services.

An additional limitation was determining rented versus owned properties. Because these data were not recorded, we used the child's last name and compared it to the owner's last name to determine property ownership. Most properties determined to be

rented were LLCs or names that repeated on multiple properties, but it is possible that the child's last name and parent/guardian's last name did not match and were counted in rented properties. However, because 93% of Blacks/African American residents in the city of Milwaukee reside in rented homes, the assessments are likely fairly accurate.[30]

Furthermore, the data set only included those who were referred for public health nurse case management and monitoring services, rather than all children who tested positive for lead. Similarly, blood lead tests from previous or future years may have been included in the dataset if they were related to a child referred for case management and monitoring during 2018-2020.

Lastly, public health relies on clinicians to order and perform blood lead testing, for which clinical practices differ. It is unknown what additional clinical follow-up children received and if differences in BLLs were a result of clinical protocols. This study examined only public health data.

CONCLUSIONS

A partnership of clinicians, public health, and community leaders is needed to decrease BLL more quickly and effectively in children. Understanding the community at-risk, eg, renters in particular ZIP codes, may help clinicians to understand risk and target lead screening to children most likely to be affected. Continued efforts should promote collaboration between clinical, community, and public health sectors. Lead poisoning is 100% preventable, and no measurable BLL is safe. We must advance our efforts to create a more just and equitable environment.

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REFERENCES

1. Hanna-Attisha M, Lanphear B, Landrigan P. Lead poisoning in the 21st century: the silent epidemic continues. *Am J Public Health*. 2018;108(11):1430. doi:10.2105/AJPH.2018.304725

2. Sachdeva C, Thakur K, Sharma A, Sharma KK. Lead: tiny but mighty poison. *Indian J Clin Biochem*. 2018;33(2):132-146. doi:10.1007/s12291-017-0680-3

3. Lead-safe Wisconsin: prevention and intervention for childhood lead exposure. Wisconsin Department of Health Services. Updated July 3, 2024. Accessed March 2, 2023. https://www.dhs.wisconsin.gov/lead/prevention.htm

4. Naranjo VI, Hendricks M, Jones KS. Lead toxicity in children: an unremitting public health problem. *Pediatr Neurol.* 2020;113:51-55. doi:10.1016/j.pediatrneurol.2020.08.005

5. Needleman H. Lead poisoning. *Annu Rev Med.* 2004;55:209-222. doi:10.1146/annurev.med.55.091902.103653

6. Childhood lead poisoning prevention: about the data: blood lead surveillance. Centers for Disease Control and Prevention. Updated April 17, 2024. Accessed March 2, 2023. https://www.cdc.gov/nceh/lead/data/blood-lead-reference-value.htm#:~:text=The%20%20Federal%20%20Advisory%20Committee%2C%20%20called,based%20on%20the%20NHANES%20data

7. Needleman H. Low level lead exposure: history and discovery. *Ann Epidemiol.* 2009;19(4):235-238. doi:10.1016/j.annepidem.2009.01.022

8. Lead-safe Wisconsin: childhood lead poisoning data and data analysis. Wisconsin Department of Health Services. Updated March 14, 2024. Accessed March 2, 2023. https://dhs.wisconsin.gov/lead/data.htm

9. Hauptman M, Niles JK, Gudin J, Kaufman HW. Individual- and community-level factors associated with detectable and elevated blood lead levels in US Children: results from a national clinical laboratory. *JAMA Pediatr.* 2021;175(12):1252-1260. doi:10.1001/jamapediatrics.2021.3518

10. Lead and water. Milwaukee Water Works. Accessed March 2, 2023. https://city.milwaukee.gov/water/News/Water-Main-Projects

11. Lead-safe Wisconsin: pediatric lead testing and reporting. Wisconsin Department of Health Services. Updated February 2, 2024. Accessed September 5, 2024. https://www.dhs.wisconsin.gov/lead/universal-testing.htm.

12. Chidhood lead poisoning prevention: intervention schedule. City of Milwaukee Health Department. November 1, 2018. Accessed March 2, 2023. https://city.milwaukee.gov/ImageLibrary/Groups/healthAuthors/HEH/PDFs/InterventionScheduleforweb.pdf

13. Childhood blood lead level case management guidelines. Wisconsin Department of Health Services. March 2, 2023. https://www.dhs.wisconsin.gov/publications/p03474.pdf

14. Yeter D, Banks EC, Aschner M. Disparity in risk factor severity for early childhood blood lead among predominantly African-American Black children: the 1999 to 2010 US NHANES. *Int J Environ Res Public Health*. 2020;17(5):1552. doi:10.3390/ijerph17051552

15. Cassidy-Bushrow AE, Sitarik AR, Havstad S, et al. Burden of higher lead exposure in African-Americans starts in utero and persists into childhood. *Environ Int.* 2017;108:221-227. doi:10.1016/j.envint.2017.08.021

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

17. Socioeconomic status and health. Health Compass Milwaukee. Accessed March 16, 2023. https://metopio.blob.core.windows.net/lalage/insights/2024-06-27/CHNA_Appendix_A_Demographics_Report_DRAFT_2022.04.26_yicmofgk.pdf

18. City of Milwaukee lead poisoning prevention data & reports. Milwaukee Health Department. Accessed March 16, 2023. https://city.milwaukee.gov/Health/Reports-and-Publications/Lead-Poisoning-Prevention-Data

19. Frey WH. Black-white segregation edges downward since 2000, census shows. Brookings Institution. December 17, 2018. Accessed March 16, 2023. https://www.brookings.edu/blog/the-avenue/2018/12/17/black-white-segregation-edges-downward-since-2000-census-shows/

20. Dang D, Lively M, Jalan A. Lead poisoning and racism in the time of COVID-19. *WMJ*. 2021;120(S1):S59-S60.

21. Nguyen KH, Buckle-Rashid R, Thorsness R, Agbai CO, Crews DC, Trivedi AN. Structural racism, historical redlining, and incidence of kidney failure in US cities, 2012-2019. *J Am Soc Nephrol*. 2023;34(9):1493-1503. doi:10.1681/ASN.0000000000000165

22. Linde S, Walker RJ, Campbell JA, Egede LE. Historic residential redlining and present-day diabetes mortality and years of life lost: the persistence of structural racism. *Diabetes Care*. 2022;45(8):1772-1778. doi:10.2337/dc21-2563

23. Wing JJ, Lynch EE, Laurent SE, Mitchell B, Richardson J, Meier HCS. Historic redlining in Columbus, Ohio associated with stroke prevalence. *J Stroke Cerebrovasc Dis*. 2022;31(12):106853. doi:10.1016/j.jstrokecerebrovasdis.2022.106853

24. Yoon H, Jang Y, Vaughan PW, Garcia M. Older adults' internet use for health information: digital divide by race/ethnicity and socioeconomic status. *J Appl Gerontol*. 2020;39(1):105-110. doi:10.1177/0733464818770772

25. Wolfe MK, McDonald NC, Holmes GM. Transportation barriers to health care in the United States: findings from the National Health Interview Survey, 1997-2017. *Am J Public Health*. 2020;110(6):815-822. doi:10.2105/AJPH.2020.305579

26. For home renovators. Milwaukee Health Department. Accessed March 30, 2023. https://city.milwaukee.gov/Health/Services-and-Programs/HomeEnvironmentalHealth/Lead-Safe-Procedures

27. Lead safe kits. Milwaukee Health Department. Accessed March 30, 2023. https://city.milwaukee.gov/Health/Services-and-Programs/HomeEnvironmentalHealth/Lead-Safe-Homes

28. Protect your family from lead in your home. US Environmental Protection Agency; September 2001. Accessed March 30, 2023. https://www.fsa.usda.gov/Internet/FSA_File/pfflinyhbrochure.pdf.

29. 10 Essential Public Health Services Futures Initiative Task Force. 10 essential public health services. September 9, 2020. Accessed March 30, 2023. https://www.apha.org/what-is-public-health/10-essential-public-health-services

30. Hess C. Milwaukee ranks 3rd worst in US for Black Home ownership. *Wisconsin Public Radio*. June 6, 2019. Accessed March 30, 2023. https://www.wpr.org/milwaukee-ranks-3rd-worst-us-black-home-ownership

Multiple *Lactobacillus* Infections Caused by Probiotics at Pediatric and Adult Academic Medical Centers

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ABSTRACT

Background: Probiotics are synthetic oral supplements containing live bacterial and fungal species hypothesized to help with various gastrointestinal conditions. However, they can cause infection if the organism spreads outside of the gastrointestinal tract. The aim of this study was to identify and describe patients who experienced systemic infections caused by probiotic use.

Methods: This study was a retrospective chart review of pediatric and adult patients at academic medical centers who received probiotics and subsequently developed positive cultures from a sterile site for probiotic-related species. Two individuals completed the chart reviews to determine if the probiotic was the true cause of the infection.

Results: *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces* cultures were reviewed, with a total of 71, 8, and 2 cultures isolated from sterile sites for each organism, respectively. Further review revealed 23 *Lactobacillus* cultures from 13 unique patients who were taking *Lactobacillus*-containing probiotics. Four patients without gastrointestinal tract compromise were included in the final analysis, including 1 patient whose culture was confirmed as identical to the probiotic. Types of infections included meningitis and bacteremia. Targeted antimicrobial therapy included ampicillin, ampicillin-sulbactam, and piperacillin-tazobactam, with total durations of therapy ranging from 10 to 22 days. No patients had mortality attributed to *Lactobacillus* infection.

Conclusions: Probiotics are not harmless supplements as they come with risk of serious infection as demonstrated in this review. Before use, the risks of probiotics should be considered carefully for each individual patient. Clinicians should consider avoiding probiotics in hospitalized patients, especially those with vascular or extra-ventricular access devices.

INTRODUCTION

Probiotics are synthetic oral supplements containing live microorganisms that have questionable efficacy and safety to consumers. A common species contained in probiotics is *Lactobacillus* – a gram-positive, anaerobic rod commonly found in the gastrointestinal (GI) tract of humans – in addition to *Bifidobacterium* and *Saccharomyces*.[1] Studies suggest that intestinal colonization with *Lactobacillus* may be protective against intraabdominal infections.[2,3] Numerous clinical trials have shown probiotics to be ineffective for GI tract disorders, and the American Gastroenterological Association (AGA) describes a lack of high-quality evidence to suggest efficacy of probiotics; the organization either does not provide a recommendation for probiotic use or provides a conditional recommendation for use based on low levels of evidence in the pediatric and adult populations.[4] Despite these guidelines, consumers and health care providers often think of probiotics as benign supplements. Currently, the US Food and Drug Administration (FDA) recognizes probiotics as generally safe dietary supplements or live microbial food supplements, but they are not approved by the FDA as a medication and, therefore, are not formally evaluated for safety and efficacy prior to release for consumer consumption.[5]

The organisms within probiotics have the ability to become opportunistic pathogens and cause significant infection.[6] There are several proposed mechanisms for probiotic-mediated alter ations to the GI tract that allow for increased infection risk,

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including changes to the composition of the microbiome, modification of the immune system, and adherence to the GI mucosa.[3] When *Lactobacillus* is present in the GI tract – whether from a probiotic or as a naturally occurring microorganism – there is opportunity for spread elsewhere in the body if the GI tract is leaking, inflamed, or immature.[7] As methods of probiotic administration and delivery have continued to advance to produce sustained organism survival within the GI tract, longer organism lifespans may lead to increased opportunity for infection.[8] Published literature has documented a range of probiotic-related systemic infections and other harms, including transmissible antibiotic resistance, metabolic disturbance, allergic response, bowel ischemia, and mortality.[5-6,9-12]

The objective of this single-center retrospective cohort study was to identify and describe multiple patients who experienced clinically significant systemic infections associated with the use of *Lactobacillus* probiotic products.

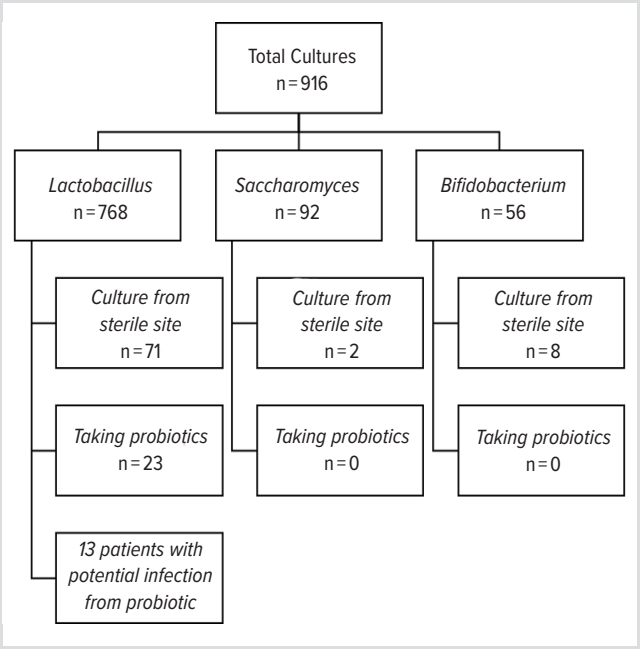
METHODS

This retrospective review is 1 part of a multidisciplinary, Institutional Review Boards-exempt quality improvement project at a health system containing 1 adult and 1 pediatric academic medical center. All adult and pediatric patients admitted to the institutions with a positive culture for *Lactobacillus*, *Bifidobacterium*, or *Saccharomyces* from a sterile site were included in the retrospective review. Patients were excluded if the culture was drawn at an outside hospital or clinic and sent to the academic medical center for laboratory processing. Sterile sites including blood, peritoneal fluid, ascites fluid, pleural fluid, and cerebral spinal fluid were reviewed. Urine cultures were not considered universally sterile and were excluded from analysis.

Positive culture results were obtained from the institution's laboratory database. All positive cultures obtained from January 1, 2019, to July 31, 2022, were eligible for inclusion. Data available from the laboratory, including patient medical record number, culture date, culture type, culture source, and organism, were automatically collected while all other data were collected by manual chart review. Additional variables collected included but are not limited to patient demographics, medical history, hospitalization information, antibiotic choice, treatment duration, mortality, and probiotic exposure. Probiotic exposure was characterized as any probiotic administration within 1 week of obtaining the positive culture, either inpatient or prior to admission. Patients were considered immunocompromised if they had a primary immunodeficiency, acquired immunodeficiency, or drug-induced immunodeficiency, which was defined as receipt of monoclonal antibodies, chemotherapy, anti-rejection medications, or steroid use equivalent to prednisone 20 milligrams per day or more for at least 2 weeks within the past month.[13]

Chart review by 2 authors (MGL and JAM) was performed on all patients with both positive cultures for probiotic-associated species and preceding probiotic exposure to determine if the infection was attributed to probiotic use. Cases were not definitively attributed to probiotic use in patients with clinical improvement in the absence of appropriate antimicrobial therapy, low suspicion for true infection by the treating medical team, or an anatomically or functionally compromised GI tract, such as perforated bowel or cirrhosis. An infection was attributed to probiotic use if the case did not meet any of the above exclusion criteria and had no other identifiable source.

Figure 1. Patient Inclusion and Exclusion Summary



Depiction of number of patients initially acquired from laboratory database from and final included patients for analysis.

Table 1. Patient Demographics

Patient	Age (Years)	Sex	Race	Ethnicity	Immune Deficient	365-Day Mortality
1	70	Female	White	Not Hispanic	No	Yes
2	1	Male	White	Not Hispanic	No	No
3	33	Male	White	Hispanic	No	No
4	33	Female	Black	Not Hispanic	No	Yes

RESULTS

A total of 768 *Lactobacillus*, 56 *Bifidobacterium*, and 92 *Saccharomyces* positive cultures were obtained during the specified time frame (Figure 1). There were 71 *Lactobacillus*, 8 *Bifidobacterium*, and 2 *Saccharomyces* positive cultures obtained from sterile sites. Of these sterile cultures, there were 39 blood cultures, 14 peritoneal fluid cultures, 7 pleural fluid cultures, 6 cerebral spinal fluid cultures, and 15 other miscellaneous sterile body fluid cultures. None of the patients with positive

Bifidobacterium or *Saccharomyces* cultures were confirmed to be taking probiotics with the associated organism. However, 23 positive *Lactobacillus* cultures were obtained from 13 unique patients who were taking probiotics. After independent chart review, 4 patients were excluded due to low suspicion for true infection by the treating medical team, and 5 patients were excluded due to presence of a compromised GI tract. Four patients were considered to have an invasive *Lactobacillus* infection from probiotic use and were included in the complete analysis.

Of the 4 patients with probiotic-mediated infections, 2 were male and 2 were female, with an average age of 34.2 years (Table 1). Patient ages ranged from 1 year to 70 years old and included only 1 pediatric patient. Primary admitting services included neurosurgery intensive care and hematology/oncology. None of the patients received probiotics prior to admission; all probiotic exposure was due to *Lactobacillus* consumption during the admission. Of note, in addition to administration of a probiotic to the pediatric patient, the mother of the patient was breastfeeding and taking a *Lactobacillus*-based probiotic as well.

Three patients had *Lactobacillus* bacteremia and 1 patient had *Lactobacillus* meningitis (Table 2). All patients received the probiotic product via opening the capsule formulation and administering the powder through a nasogastric tube (Table 3). Bacterial identification revealed *Lactobacillus rhamnosus* in all patients. Each patient received the same probiotic product from the institution's formulary containing a monomicrobial strain of *Lactobacillus rhamnosus*. Time to positivity for blood cultures ranged from 24 to 82 hours, with only 1 culture growing after 48 hours. One patient had *Lactobacillus* recovered on multiple cultures. All cultures were monomicrobial without growth of other organisms. None of the patients had a known immunodeficiency. All 3 patients with bacteremia had an indwelling peripherally inserted central catheter (PICC) line, while the patient with meningitis had an external ventriculostomy drain (EVD). Given the presence of indwelling hardware at the site of infection for all patients and probiotics being administered via opening of capsules, nosocomial transmission through contamination of indwelling lines and drains from capsule opening was the presumed cause of infection.

The institution's infectious diseases team was consulted for 3 of the 4 patients to assist with management of the infections. Definitive antimicrobial therapy included ampicillin, ampicillin-sulbactam, or piperacillin-tazobactam (Table 3). Of note, ceftriaxone, cefepime, and vancomycin were not considered appropriate targeted therapy based on lack of expected activity against the isolated organism. Duration of therapy ranged from 10 to 22 days, which included all days of antibacterial treatment regardless of expected activity against *Lactobacillus*. The average length of hospital stay was 43.0 days, with a range of 18 to 74 days. One patient required intensive care unit (ICU) admission related to hemodynamic instability, which may have been attributed to sepsis from *Lactobacillus*. All-cause mortality was 50% within 1 year of infection, including 25% within 30 days. No patients had mortality attributed directly to the *Lactobacillus* infection, although the possibility of infection as a contributing factor cannot be excluded.

The case of *Lactobacillus rhamnosus* meningitis warrants special consideration given the persistent growth on cerebrospinal fluid samples despite targeted antibiotic therapy. The patient was

Table 2. Infection Description

Patient	Infection	Culture Source	Species	No. of Positive Cultures	Time to Positivity (Hours)	Hardware or Central Access
1	Meningitis	Ventricular fluid	*Lactobacillus rhamnosus*	6	Not specified	Yes
2	Bacteremia	Upper extremity, left	*Lactobacillus rhamnosus*	1	23.7	Yes
3	Bacteremia	Forearm, right	*Lactobacillus rhamnosus*	1	37.0	Yes
4	Bacteremia	Foot, right	*Lactobacillus rhamnosus*	1	81.8	Yes

Table 3. Description of Probiotic and Antibiotic Use

Patient	Indication for Probiotic Use[a]	Duration of Probiotic Use (Days)	Dose, Route, Frequency of Probiotic Administration	Infection Type Associated With Probiotic Use	Antibiotic Treatment for Probiotic Infection[b]	Duration of Antibiotic Therapy (Days)[c]
1	Prevention of AAD	33	1 capsule, nasogastric tube, 2x/daily	Meningitis	Ampicillin	22
2	AAD	7	1 capsule, nasogastric tube, 1x/daily	Bacteremia	Ampicillin	12
3	Prevention of AAD	10	1 capsule, nasogastric tube, 2x/daily	Bacteremia	Ampicillin-sulbactam	10
4	Prevention of AAD	14	1 capsule, nasogastric tube, 2x/daily	Bacteremia	Piperacillin-tazobactam	11

Abbreviations: AAD, antibiotic-associated diarrhea.

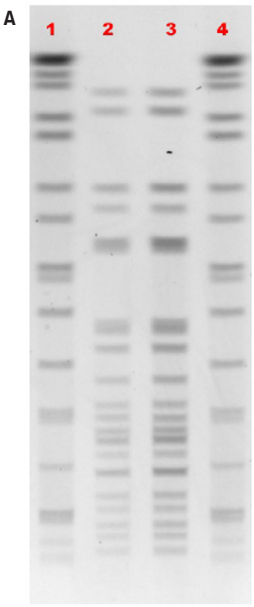
[a]The 3 patients with the probiotic indication of "prevention of AAD" were initiated on probiotics because the probiotic was automatically ordered on admission as part of the admission order sets.

[b]Definitive treatment for completion of antibiotic course after narrowing to targeted therapy for treatment of *Lactobacillus*.

[c]Total duration of antibiotic therapy including all days of antibacterial treatment regardless of expected activity against *Lactobacillus*.

a 70-year-old female admitted following subarachnoid hemorrhage status-post decompression with EVD placement. The cerebrospinal fluid grew *Lactobacillus rhamnosus* on 6 separate days. No probiotics were taken prior to admission, but she was exposed to a *Lactobacillus*-containing probiotic during the hospitalization–including during the first 4 days of positive cultures–before discontinuation due to concern for contamination of the EVD from opening the capsules prior to administration via nasogastric tube. Pulsed field gel electrophoresis confirmed the infecting *Lactobacillus rhamnosus* strain and the administered probiotic as indistinguishable (Figure 2). She remained hospitalized for 62 days, including 2 days requiring continued ICU-level care for hemodynamic instability and an additional 20 days receiving intravenous antimicrobials. She was treated with a variety of antibiotics prior to consolidating to ampicillin monotherapy after speciation and initial clinical improvement. The EVD was exchanged on day 6 of infection with 1 subsequent positive culture prior to clearing. Final duration of antimicrobial therapy was 22 days with no subsequent recurrence of *Lactobacillus* infection. Unfortunately, the patient died within 1 year of admission related to a brain abscess caused by a different infectious organism.

Figure 2. Pulsed Field Gel Electrophoresis Summary



A) Pulsed field gel electrophoresis image. Lanes 1 and 4 are Salmonella enterica ser. Braenderup H9812 Standard controls, Lane 2 is the cerebrospinal fluid sample, and Lane 3 is the probiotic capsule.[a]

B) Pulsed field gel electrophoresis dendrogram.

[a]Results of the pulsed field gel electrophoresis indicated that the patient isolate and probiotic capsule were indistinguishable using the Tenover criteria for pattern interpretation. The Tenover criteria defines "indistinguishable" as patterns that were identical; "closely related" as 1-3 band(s) different between patterns, which could be achieved by a single mutation; "possibly related" as 4-6 bands different between patterns, which requires a minimum of 2 mutations; and "unrelated" as ≥7 bands different between patterns, which requires a minimum of 3 mutations.

DISCUSSION

In this retrospective review, 4 cases of serious bacterial infections with concern for probiotic use as a causative factor are described. This study adds to the existing literature regarding the risk of nosocomial probiotic use and suggests that infectious risks of probiotics may be higher in patients with an indwelling central line or EVD. Each case demonstrates the route of transmission was likely via probiotic contamination of the central line or EVD rather than through GI tract translocation given the absence of gastrointestinal pathology, although the latter cannot be excluded. Regardless, nosocomial transmission is confirmed for each patient due to lack of receipt of probiotics prior to the hospitalization. For the patients who experienced *Lactobacillus* infection in the absence of probiotic consumption, nosocomial transmission from neighboring patient rooms sharing the same clinicians cannot be excluded.

As described, these infections were not benign. All patients required initiation of broad-spectrum antimicrobials, extended durations of therapy, and increased hospital length of stay. Although none of the patients had mortality directly caused by overwhelming infection, there remained a high 1-year mortality rate amongst patients with probiotic-associated *Lactobacillus* infections, which highlights the weakened protoplasm of infected individuals and importance of reconsidering the use of probiotics–especially in the inpatient setting–to prevent morbidity. At the time these infections occurred, there were no restrictions associated with inpatient probiotic use at the institutions and clinicians did not require input from the infectious diseases team prior to initiating these products. Some order sets in the adult academic medical center included probiotics by default upon admission, which is where the probiotic orders for the 3 adult patients admitted to neurosurgery intensive care originated. Due to numerous probiotic-associated infections in the neurosurgical ICU, probiotics have since been removed from all admission order sets at the institution due to institutional safety concerns with probiotic use.

This retrospective study uniquely aimed to identify infections caused not only by *Lactobacillus*-containing probiotics but also *Bifidobacterium*- and *Saccharomyces*-containing probiotics, although there were no patients who qualified for the latter 2 infection types. However, multiple previous large studies have described infections due to bacterial species associated with such products.[14-18] Fungemia due to ingestion of *Saccharomyces*-containing probiotics is heavily documented, and *Bifidobacterium* bacteremia due to probiotic supplementation has been widely reported--most frequently in neonates.[19,20] *Lactobacillus* bacteremia and other severe infections caused by consumption of probiotics also have been published.[10] Although *Lactobacillus*

meningitis has been described previously, no previous studies have described meningitis confirmed to be caused by probiotics through techniques such as pulsed field gel electrophoresis sequencing.[15,21-24]

In patients with reduced gut integrity or weakened immune systems, probiotics pose a greater risk of infection as the organism in the probiotic can translocate and cause infection.[2,7] This risk is highest in patients who have perforated, leaky, inflamed, or immature GI tracts. The organisms also have unique hemolysis, adhesin, and enzymatic properties that can increase risk of translocation and subsequent infection, biofilm formation, and colonization within the GI tract. Moreover, the organisms in probiotics are synthetically modified and consequentially have enhanced duration of action within the GI tract.[3] Due to the unique properties and mechanism of action of probiotics to survive the normal defenses of the GI tract, probiotics can become pathogenic in a susceptible host. Multiple patients with cultures positive for *Lactobacillus* were excluded due to the presence of GI compromise resulting in inherent uncertainty of the cause of infection and the clinical significance of the isolate; however, the possibility remains that GI leakage of the consumed probiotic may have caused a clinically significant infection.

Antibiotic resistance remains a large risk with use of probiotics. A recently published study demonstrated high rates of drug resistance amongst *Lactobacillus* isolates from probiotics.[25] *Lactobacillus* in the supplements was found to be universally resistant to vancomycin, amikacin, and fluoroquinolones and occasionally resistant to tetracyclines and cephalosporins. The strains remained susceptible to penicillins, carbapenems, and linezolid. Previous studies found similar resistance patterns but identified less resistance to clindamycin.[6,15,16] Resistance to currently available broad-spectrum antibiotics is alarming and raises the possibility of high rates of treatment failure with limited treatment options, particularly if isolates have developed resistance to beta lactams. Furthermore, antibiotic resistance genes from probiotics can undergo horizontal gene transfer to other organisms naturally residing in the GI tract, which can lead to multidrug-resistant organisms.[7]

The AGA published a clinical practice guideline in 2020 summarizing its recommendations surrounding the use of probiotics for various GI conditions.[4] There is acknowledgement within the guideline that there is a lack of foundational research in this area to make any strong recommendations and, therefore, advises clinicians to consider avoiding probiotic use to prevent harm. Specifically, for patients with *Clostridioides difficile* infection, inflammatory bowel disease, and irritable bowel syndrome, the AGA advises against routine use of probiotics. Similar to other over-the-counter supplements, probiotics are not approved by the FDA and their production and marketing are not evaluated for safety and efficacy in the same manner as medications.

There are many patient and institutional costs attributed to probiotic-induced invasive infections including but not limited to the costs of the probiotic product, antimicrobial treatment, prolonged hospitalization, and additional resultant nosocomial-associated events from prolonged hospitalizations. These extensive costs are avoidable by ceasing unnecessary probiotic use. In addition, the impact of culture contamination from a probiotic-related organism also should be included as an indirect cost as each isolation of *Lactobacillus* of unclear clinical significance results in diagnostic uncertainty requiring subsequent testing, clinical burdens, and antimicrobial exposure. Probiotics must be used with caution, or avoided entirely, to minimize causing unintended patient harm and excess costs.

As all data in this review are descriptive and retrospective in nature, this study is unable to establish true causation of infection or mortality, although suspicion is high due to extensive nature of the chart review and removing as many confounding factors as possible. Confounding factors include the presence of infections at multiple sites, prolonged length of broad-spectrum antibiotic use for empiric versus targeted coverage, critically ill status of patients, timeline of probiotic use, and inability to identify the status of GI tract integrity. Attributing the infection to probiotic exposure required clinical review, which introduces the risk for bias; however, this risk was mitigated using 2 independent reviewers. A strength of this study was the detailed chart review utilized to determine the cause of infection and the description of subsequent therapies received for treatment. In addition, this is the first known publication to confirm a probiotic strain as the cause of *Lactobacillus rhamnosus* meningitis and includes the pulsed field gel electrophoresis analysis. Previously published case reports of *Lactobacillus* meningitis do not include methods to provide definitive confirmation of a probiotic causing the infection, so the inclusion of sequencing makes this study a unique, significant addition to currently existing literature.[15,21-24]

CONCLUSIONS

This retrospective study of pediatric and adult patients who developed serious infections caused by probiotic consumption demonstrates that probiotics are not benign, harmless supplements that can be used in all patients. Initiation of probiotic therapy should be considered carefully and individualized to each patient within the context of risk versus benefit analysis. Hospitalized patients appear to be an already at-risk population—especially those with vascular or extra-ventricular catheters—and clinicians should avoid probiotic use in these patients. Due to the lack of data surrounding any indication for probiotic use, patients should be advised to not consume probiotics in the inpatient or outpatient setting due to the serious, albeit rare, risk of systemic infection leading to potential morbidity and mortality.

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REFERENCES

1. Auwaerter P. Lactobacillus. In: Auwaerter P, ed. *The Johns Hopkins POC-IT ABX Guide*. Unbound Medicine. Updated April 8, 2023. Accessed December 16, 2022. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540304/all/Lactobacillus

2. Yu Y, Zong M, Lao L, Wen J, Pan D, Wu Z. Adhesion properties of cell surface proteins in Lactobacillus strains in the GIT environment. *Food Funct.* 2022;13(6):3098-3109. doi:10.1039/d1fo04328e

3. Bermudez-Brito M, Plaza-Díaz J, Muñoz-Quezada S, Gómez-Llorente C, Gil A. Probiotic mechanisms of action. *Ann Nutr Metab*. 2012;61(2):160-174. doi:10.1159/000342079

4. Su GL, Ko CW, Bercik P, et al. AGA clinical practice guidelines on the role of probiotics in the management of gastrointestinal disorders. *Gastroenterology*. 2020;159(2):697-705. doi:10.1053/j.gastro.2020.05.059

5. Statement from FDA Commissioner Scott Gottlieb, M.D., on advancing the science and regulation of live microbiome-based products used to prevent, treat, or cure diseases in humans. News release. US Food and Drug Administration. August 16, 2018. Accessed June 20, 2023. https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-advancing-science-and-regulation-live-microbiome-based

6. Goldstein EJC, Tyrrell KL, Citron DM. Lactobacillus species: taxonomic complexity and controversial susceptibilities. *Clin Infect Dis*. 2015;60:S98-S107. doi:10.1093/cid/civ072

7. Kothari D, Patel S, Kim S-K. Probiotic supplements might not be universally-effective and safe: a review. *Biomed Pharmacother.* 2019;111:537-547. doi:10.1016/j.biopha.2018.12.104

8. Govender M, Choonara YE, Kumar P, du Toit LC, van Vuuren S, Pillay V. A review of the advancements in probiotic delivery: conventional vs. non-conventional formulations for intestinal flora supplementation. *AAPS PharmSciTech*. 2014;15(1):29-43. doi:10.1208/s12249-013-0027-1

9. Sherid M, Samo S, Sulaiman S, Husein H, Sifuentes H, Sridhar S. Liver abscess and bacteremia caused by Lactobacillus: role of probiotics? Case report and review of the literature. *BMC Gastroenterol*. 2016;16(1):138. doi:10.1186/s12876-016-0552-y

10. Mikucka A, Deptula A, Bogiel T, Chmielarczyk A, Nurczynska E, Gospodarek-Komkowska E. Bacteraemia caused by probiotic strains of Lacticaseibacillus rhamnosus - case studies highlighting the need for careful thought before using microbes for health benefits. *Pathogens*. 2022;11(9):977. doi:10.3390/pathogens11090977

11. Besselink MG, van Santvoort HC, Buskens E, et al. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2008;371(9613):651-659. doi:10.1016/S0140-6736(08)60207-X

12. Joint Food and Agriculture Organization/World Health Organization Working Group. Guidelines for the Evaluation of Probiotics in Food: Report of a joint FAO/WHO working group on drafting guidelines for the evaluation of probiotics in food. Food and Agriculture Organization and World Health Organization; 2002. Accessed Sept. 5. 2023. https://isappscience.org/wp-content/uploads/2019/04/probiotic_guidelines.pdf

13. Altered immunocompetence: general best practice guidelines for immunization. Centers for Disease Control and Prevention. Updated August 1, 2023. Accessed June 20, 2023. https://cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html#

14. Salminen MK, Rautelin H, Tynkkynen S, et al. Lactobacillus bacteremia, clinical signficance, and patient outcome, with special focus on probiotic L. rhamnosus GG. *Clin Infect Dis*. 2004;38(1):62-69. doi:10.1086/380455

15. Cannon JP, Lee TA, Bolanos JT, Danziger LH. Pathogenic relevance of Lactobacillus: a retrospective review of over 200 cases. *Eur J Clin Microbiol Infect Dis*. 2005;24(1):31-40. doi:10.1007/s10096-004-1253-y

16. Salminen MK, Rautelin H, Tynkkynen S, et al. Lactobacillus bacteremia, species identification, and antimicrobial susceptibility of 85 blood isolates. *Clin Infect Dis.* 2006;42(5):e35-44. doi:10.1086/500214

17. Honeycutt TCB, El Khashab M, Wardrop RM, et al. Probiotic administration and the incidence of nosocomial infection in pediatric intensive care: a randomized placebo-controlled trial. *Pediatr Crit Care Med*. 2007;8(5):452-458. doi:10.1097/01.PCC.0000282176.41134.E6

18. Gouriet F, Million M, Henri M, Fournier P-E, Raoult D. Lactobacillus rhamnosus bacteremia: an emerging clinical entity. *Eur J Clin Microbiol Infect Dis*. 2012;31(9):2469-2480. doi:10.1007/s10096-012-1599-5

19. Doron S, Snydman DR. Risk and safety of probiotics. *Clin Infect Dis.* 2015;60(2):S129-134. doi:10.1093/cid/civ085

20. Pillai A, Tan J, Paquette V, Panczuk J. Does probiotic bacteremia in premature infants impact clinically relevant outcomes? A case report and updated review of literature. *Clin Nutr ESPEN*. 2020;39:255-259. doi:10.1016/j.clnesp.2020.05.020

21. Broughton RA, Gruber WC, Haffar AA, Baker CJ. Neonatal meningitis due to Lactobacillus. *Pediatr Infect Dis*. 1983;2(5):382-384. doi:10.1097/00006454-198309000-00012

22. Robin F, Paillard C, Marchandin H, et al. Lactobacillus rhamnosus meningitis following recurrent episodes of bacteremia in a child undergoing allogeneic hematopoietic stem cell transplantation. *J Clin Microbiol.* 2010;48(11):4317-4319. doi:10.1128/JCM.00250-10

23. Schmidt M, Maxime V, Pareire F, et al. A lethal case of meningitis due to Lactobacillus rhamnosus as a late complication of anterior cervical spine surgery. *J Infect*. 2011;62(4):309-310. doi:10.1016/j.jinf.2011.02.006

24. Biesiada G, Krycinska R, Czepiel J, et al. Meningoencephalitis caused by Lactobacillus plantarum – case report. *Int J Neurosci.* 2019;129(7):715-718. doi:10.1080/00207454.2018.1482293

25. Anisimova E, Gorokhova I, Karimullina G, Yarullina D. Alarming antibiotic resistance of Lactobacilli isolated from probiotic preparations and dietary supplements. *Antibiotics (Basel).* 2022;11(11):1557. doi:10.3390/antibiotics11111557

Scrotal Trauma Treatment and Outcomes

Moshe Wald, MD

ABSTRACT

Introduction: Genitourinary tract injuries have been reported to account for 3% to 10% of trauma patients, and scrotal injuries have been reported to comprise 71% of male genital trauma. Scrotal trauma is particularly prevalent in males 10 to 30 years of age, thus posing a potential threat to fertility. Scrotal trauma can be blunt or penetrating in nature, and the mechanism of trauma can have an impact on the management and outcomes of this type of injury.

Methods: A retrospective chart review of adult patients who presented with scrotal trauma to a single large level I trauma center from January 1, 2000, to June 1, 2022, was conducted to assess the relative occurrence and type of trauma (blunt vs penetrating), as well as differences in the management, duration of hospital stay, and need for orchiectomy between these 2 types of injury.

Results: There were 102 patients included in this study, with an average age of 39.5 years (18.7-77.2 years). Fifty-six patients had blunt scrotal trauma, and 46 had penetrating scrotal injury. There was not a statistically significant difference in the percentages of blunt versus penetrating trauma ($P=0.3729$). Patients with penetrating trauma were more likely to be inpatient than those with blunt trauma (69.6% vs 42.9%; $P=0.013$; 95% CI, 0.062-0.473). A total of 61 patients were treated conservatively (44 and 17 patients in the blunt and penetrating trauma groups, respectively). Overall, 41 patients required surgical intervention: 12 who had blunt trauma and 29 who suffered penetrating injury. Surgical treatment was more common for penetrating trauma than for blunt trauma (63.0% vs 21.4%; $P<0.0001$; 95% CI, 0.220-0.612). Eleven patients underwent orchiectomy – 4 from the blunt trauma group and 7 from the penetrating trauma group; the rate of orchiectomy was not significantly different between the 2 groups.

Conclusions: In this study, blunt scrotal trauma was slightly more common than penetrating injury, but the difference did not reach statistical significance. Blunt scrotal trauma was associated with a higher rate of conservative treatment. Further study is needed to better understand the impact of scrotal trauma on future fertility.

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INTRODUCTION

Genitourinary tract injuries were reported to be present in approximately 10% of cases of abdominal trauma, with up to 67% of genitourinary injuries involving the external genitalia.[1] The increased incidence of genital trauma in males has been attributed to both the more exposed location of the male genitalia and men's increased participation in contact sports and violent and combat activities.[1]

The incidence of scrotal or testicular injury in the setting of trauma generally has been considered less than 1%, presumably due to the protective effects of testicular mobility within the scrotum, the cremasteric reflex, and the tunica albuginea.[1] However, the scrotum was reported to be the main site of injury in 71% of men who sustained genital trauma.[2] Furthermore, the potential fertility impairment and psychological effects associated with scrotal trauma may amplify the importance of these injuries, in terms of both subsequent patient morbidity and health care costs.[1,3-4] Scrotal trauma can cause direct acute injury to the reproductive organs, and obstruction of the vas deferens and epididymis can develop later on secondary to fibrotic changes involved in the posttraumatic healing process. Additionally, scrotal trauma can violate the blood-testis barrier, with subsequent formation of antisperm antibodies, potentially leading to immunologic infertility.

Scrotal trauma can be blunt or penetrating in nature. The type

Table. Characteristics of Patients with Scrotal Trauma

	No. of Patients	Age (Range)	Outpatients	Inpatients LOS (Days)	Avg Hospital Management	Conservative Intervention	Surgical	Orchiectomy
Overall	102	39.5 (18.7-77.2)	46	56	15.6	61	41	11
Blunt Trauma	56	37.7 (18.8-77.2)	32	24	11.1	44	12	4
Penetrating Trauma	46	41.4 (18.5-69.9)	14	32	19.6	17	29	7

Abbreviations: No., number; Avg, average; LOS, length of stay.

and mechanism of scrotal trauma may be of clinical significance, in terms of the extent of injury to the testicles, epididymi, and the scrotal portion of the vasa deferentia; the need for immediate surgical intervention; and long-term sequel of this type of injury. In a study of adult men with injuries of the genitals (including the scrotum as well as the penis and the urethra), blunt trauma was more common than penetrating injuries (61% vs 39%, respectively). In that study, surgical intervention was more common after penetrating injury than blunt trauma (89% vs 64%, $P<0.01$).[2]

The current study focused on scrotal trauma cases and involved an extensive retrospective chart review of such cases at a large tertiary care center over 2 decades. The goal was to assess the relative occurrence of blunt and penetrating scrotal trauma, as well as differences in the management, duration of hospital stay, and need for orchiectomy between these 2 types of scrotal injury.

This study provides a particular view of scrotal trauma in the rural Midwest of the United States, which could be helpful to clinicians practicing in this area, and also adds to the general knowledge of the topic by delineating characteristics of scrotal trauma that are typical to this geographical area.

METHODS

After obtaining Institutional Review Board approval, a retrospective chart review was conducted involving charts of adult patients who presented to the University of Iowa Hospitals and Clinics for scrotal trauma from January 1, 2000, to June 1, 2022. Charts were identified by the biomedical informatics team at the University of Iowa's Institute for Clinical and Translational Science (based on *Current Procedural Terminology* [CPT] codes pertaining to scrotal trauma) and subsequently reviewed by research team members. Data extracted from each chart included the type of scrotal injury (blunt or penetrating, determined by review of clinical notes), duration of hospital stay, whether any surgical intervention regarding scrotal injury was performed in the operating room, and if an orchiectomy was required. Charts with missing data were excluded.

Descriptive statistics were provided for study variables, with median and interquartile range (IQR) reported for continuous variables and frequencies for categorical variables. Chi-square tests were used for 1 sample proportion and 2-sample tests with a continuity correction. Due to low expected counts, Fisher exact testing was used to assess differences in rates of orchiectomy. All statistical analyses were performed in R, version 4.2.1 (R Core Team, 2022).

RESULTS

A total of 102 charts were reviewed. The average age of patients was 39.5 years (18.7-77.2 years). The majority (54.9%) were treated as inpatient, and average hospital length of stay (LOS) was 15.6 days (11.1 and 19.6 days for the blunt and penetrating trauma groups, respectively). More than half of the patients received conservative management (59.8%). Fifty-six patients (54.9%) had blunt trauma and 46 (45.1%) had a penetrating trauma (Table). There was insufficient evidence to suggest a difference in the percentage of blunt trauma versus penetrating trauma ($P=0.3729$, 95% CI for patients with blunt trauma, 44.7%-64.7%).

Patients with penetrating trauma were more likely to be inpatient than those with blunt trauma (69.6% vs 42.9%; $P=0.013$; 95% CI, 0.062-0.473). Surgical treatment was also more common for penetrating trauma than for blunt trauma (63.0% vs 21.4%, $P<0.0001$; 95% CI, 0.220-0.612). There was not sufficient evidence to suggest a difference in rate of orchiectomy for penetrating trauma versus blunt trauma (15.2% vs 7.1%, $P=0.2159$).

Among those patients who required surgical intervention, the rate of orchiectomy for those with penetrating trauma versus blunt trauma was not significantly different (24.1% vs 33.3%, $P=0.7195$). There were no differences in orchiectomy complications (eg, wound healing issues, infections) between patients who had penetrating trauma and those who sustained blunt trauma.

DISCUSSION

Scrotal trauma has been reported to comprise 71% of male genital trauma.[2] While typically not life-threatening, scrotal trauma has the potential to impair future fertility as it is particularly prevalent in males who are 10 to 30 years old. The type of scrotal trauma—specifically whether it is blunt or penetrating in nature—scan affect injury management and outcomes.

The management of scrotal trauma begins with obtaining detailed history to learn about the circumstances and timing of injury. This should be followed by physical examination to assess for other injuries, such as associated abdominal or pelvic injuries that require general or orthopedic surgery consultation and also may require immediate attention. Scrotal examination may reveal obvious findings of penetrating trauma, such as open lacerations

with or without visualized exposed testicular tissue. In the absence of the such findings, however, imaging in the form of a scrotal ultrasound is be helpful in assessing testicular integrity and blood flow and guiding decisions regarding the need for surgical intervention (see Figure).

Surgical intervention in the setting of scrotal trauma is indicated in cases of disruption of the tunica albuginea with extrusion of testicular tissue[5-7] and when doppler study suggests testicular devascularization. While milder cases of tunica albuginea disruption may be repaired surgically with salvage of the testicle, more severe cases of such disruption and cases of testicular devascularization would require an orchiectomy.

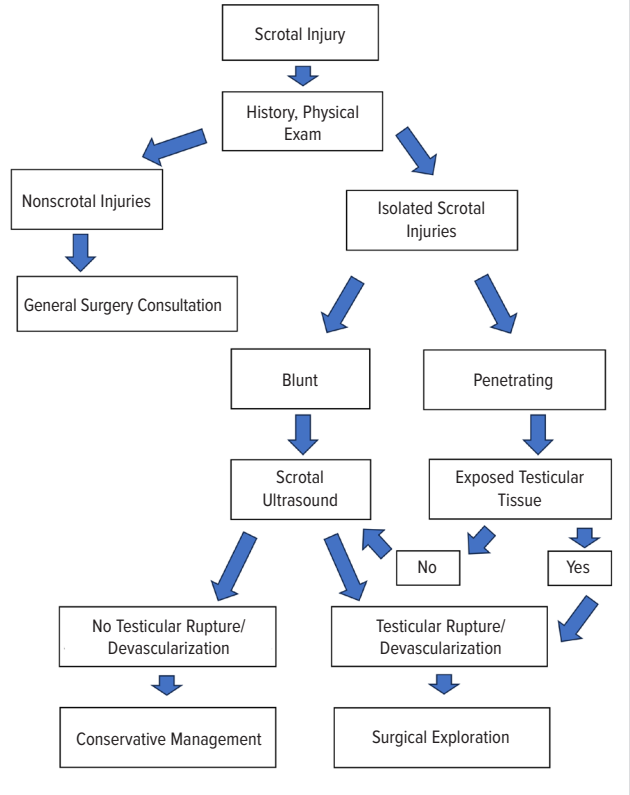
Antibiotic prophylaxis has been recommended for scrotal trauma due to animal bites.[8] For other types of penetrating scrotal trauma, the decision about antibiotic prophylaxis depends on the circumstances of injury and assessment of the wound upon presentation. Early exploration and repair of a testicular injury has been associated with increased testicular salvage compared to delayed intervention. Orchiectomy was reported to be required in 9% of patients who underwent early scrotal exploration and repair versus 45% in cases of delayed exploration.[9]

Scrotal trauma can impair male fertility by different mechanisms involving the testicles, epididymis, and vas deferens or a combination of these organs.[10-11] Testicular injury can result in loss of seminiferous tubules at varying extent, even up to loss of an entire testicle. Additionally, scrotal trauma can violate the blood-testis barrier, which can lead to the development of antisperm antibodies and subsequent immunologic infertility. Scrotal injury also can disrupt the epididymis and/or the vas deferens, causing interference in sperm transport.

The effect of testicular trauma on hormonal parameters also has been studied. Theoretically, changes in serum levels of reproductive hormones in patients with scrotal trauma could suggest possible mechanisms by which scrotal trauma could impact future fertility. In a study of patients who sustained a gunshot wound to the external genitalia (scrotum and/or penis), rapid return of endocrine function was noted on short-term follow-up when testicular parenchyma was preserved.[12] However, Nolten et al reported that testicular trauma was associated with permanent hormonal changes. In this study, estradiol levels were found to be higher in infertile men who suffered testicular trauma compared to either infertile men without such trauma or to a control group of fertile men without testicular trauma. There were no differences in follicle-stimulating and luteinizing hormone levels between infertile men with and without testicular trauma or in prolactin and testosterone levels among infertile men with or without testicular trauma and the control group.[13]

In the current study, blunt scrotal trauma was slightly more common than penetrating injury (56 and 46 patients, respectively). As suggested by our findings, blunt scrotal trauma was associated with a higher rate of conservative management (44 and 17 patients in the blunt and penetrating trauma groups, respectively) and with a lower number of orchiectomies. Both findings may offer a better future fertility prognosis for blunt scrotal trauma, given the presumed testicular tissue-sparing nature of such injury, which also is less likely to cause transection or physical disruption of the epididymis and vas deferens. While these findings may offer some reassurance to patients with blunt scrotal trauma who are interested in future fertility, further study is needed to better understand the impact of scrotal trauma on postinjury fertility.

Figure. Approach to Acute Scrotal Injury



Interestingly, in a large study by Grigorian et al, a higher rate of penetrating scrotal injury (50.5% of cases) was reported, with gunshot injury (75.8%) being the most common cause.[3] The latter might suggest varying injury patterns in different geographical areas, as our center typically serves more rural communities. Further, Grigorian et al reported that 48.3% of patients with scrotal or testicular trauma required scrotal or testicular operation[3] but did not assess rates of surgical intervention separately for cases of blunt versus penetrating scrotal trauma, as performed in our study. Thus, our study offers a higher resolution assessment of scrotal trauma based on type of injury – specifically, if the injury was penetrating or blunt in nature.

The average hospital LOS in our study was 15.6 days (11.1 and 19.6 days in the blunt and penetrating trauma groups, respectively), which is longer than the median hospital stay of 3 days reported by Grigorian et al.[3] This discrepancy could be explained

by the fact that most patients enrolled in the latter study (74.5%) sustained isolated scrotal injuries.

Limitations

This study has several limitations. It is based on cases from a single institution that has a large volume but serves mostly mid-size towns and rural communities, rather than large metropolitan areas. This may have an impact on the type and mechanisms of trauma sustained by patients. Additionally, this study categorized scrotal trauma as either blunt or penetrating injuries, without further subgrouping (eg, gunshot vs stab injuries). Subgroup analysis was not performed as the initial chart review suggested that some subgroups would include a very small number of patients that, in turn, could compromise statistical analysis. Finally, some patients sustained nonscrotal injuries that could impact the hospital LOS but were unlikely to affect the actual management of scrotal injuries.

CONCLUSIONS

This study provides focused insight on scrotal trauma based on information gathered over more than 2 decades at a level I trauma center whose location allows assessment of the type of scrotal trauma sustained in a more rural area of the United States. Blunt scrotal trauma was slightly more common than penetrating injury, but the difference did not reach statistical significance. Blunt scrotal trauma also was associated with a higher rate of conservative management. Further study is needed to better understand the impact of scrotal trauma on future fertility.

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REFERENCES

1. Randhawa H, Blankstein U, Davies T. Scrotal trauma: a case report and review of the literature. *Can Urol Assoc J.* 2019;13(6 Suppl4):S67-S71. doi:10.5489/cuaj.5981

2. McCormick CS, Dumais MG, Johnsen NV, Voelzke BB, Hagedorn JC. Male genital trauma at a level 1 trauma center. *World J Urol.* 2020;38(12):3283-3289. doi:10.1007/s00345-020-03115-0

3. Grigorian A, Livingston JK, Schubl SD, et al. National analysis of testicular and scrotal trauma in the USA. *Res Rep Urol.* 2018;10:51-56. doi:10.2147/RRU.S172848

4. McGeady JB, Breyer BN. Current epidemiology of genitourinary trauma. *Urol Clin North Am.* 2013;40(3):323-334. doi:10.1016/j.ucl.2013.04.001

5. Wang Z, Yang JR, Huang YM, et al. Diagnosis and management of testicular rupture after blunt scrotal trauma: a literature review. *Int Urol Nephrol*. 2016;48(12):1967-1976. doi:10.1007/s11255-016-1402-0

6. Ballestero R, Correas Gomez MA, Lastra Garcia-Baron P, et al. Testicular reconstruction after testicular rupture and review of the literature. *Arch Esp Urol.* 2013;66(4):372-376.

7. Freehill MT, Gorbachinsky I, Lavender JD, Davis RL 3rd, Mannava S. Presumed testicular rupture during a college baseball game: a case report and review of the literature for on-field recognition and management. *Sports Health.* 2015;7(2):177-180. doi:10.1177/1941738114537786

8. Gomes CM, Ribeiro-Filho L, Giron AM, Mitre AI, Figueira ER, Arap S. Genital trauma due to animal bites. *J Urol.* 2001;165(1):80-83. doi:10.1097/00005392-200101000-00020

9. Cass AS. Testicular trauma. *J Urol*. 1983;129(2):299-300. doi:10.1016/s0022-5347(17)52062-5

10. Starmer BZ, Baird A, Lucky MA. Considerations in fertility preservation in cases of testicular trauma. *BJU Int.* 2018;121(3):466-471. doi:10.1111/bju.14084

11. Kukadia AN, Ercole CJ, Gleich P, Hensleigh H, Pryor JL. Testicular trauma: potential impact on reproductive function. *J Urol.* 1996;156(5):1643-1646. doi:10.1016/s0022-5347(01)65472-7

12. Gomez RG, Castanheira AC, McAninch JW. Gunshot wounds to the male external genitalia. *J Urol.* 1993;150(4):1147-1149. doi:10.1016/s0022-5347(17)35710-5

13. Nolten WE, Viosca SP, Korenman SG, Mardi R, Shapiro SS. Association of elevated estradiol with remote testicular trauma in young infertile men. *Fertil Steril.* 1994;62(1):143-149. doi:10.1016/s0015-0282(16)56830-7

Exploring Expressive Writing with Patients With Chronic Pain During Primary Care Visits

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ABSTRACT

Background: Patients living with chronic pain may feel frustrated with and neglected by clinicians who care for them, leading to negative health care experiences. Clinicians may struggle to find new ways to engage and connect with patients experiencing chronic pain. Both patients and clinicians may benefit from expressive writing by potentially improving communication and creating a deeper sense of connection within medical visits.

Methods: An expressive writing activity, the Three-Minute Mental Makeover (3MMM), was conducted with 15 patients living with chronic pain during primary care visits with 5 UW Health family medicine physicians. Patient and physician experience using the 3MMM was measured using pre- and post-visit surveys and individual interviews.

Results: Both physicians and patients viewed the experience of doing the 3MMM together positively. We identified 8 key themes from individual follow-up interviews with patients and physicians: (1) opening the door, (2) insight into the doctor/patient as a person, (3) peer-to-peer communication, (4) closeness and connection, (5) comfort and relaxation, (6) unexpected learning, (7) unexpected value to patients, and (8) vulnerability and self-disclosure. The most commonly reported barriers to physicians using the activity in practice were lack of time and persuading other physicians to do the activity.

Discussion: Patients with chronic pain and the clinicians who care for them may benefit from an expressive writing exercise, such as the 3MMM, in the key realms of building relationships, communication, and trust.

BACKGROUND

Chronic pain affects 50 million adults in the United States and, along with intense physical symptoms, is associated with burdensome psychosocial comorbidities, including anxiety and depression.[1] Open communication and confidence in their clinicians may help patients with chronic pain feel better supported in coping with pain.[2] Increased use of interventions that promote empathy and understanding between the patient and clinician has been recommended to benefit both patients who have chronic pain and the clinicians who care for them.[3] We chose to study a guided expressive writing activity—the Three-Minute Mental Makeover (3MMM—based on work demonstrating that it both reduced stress and improved communication among patients, parents, and clinicians in a pediatric setting.[4,5] Although it has not been used in adult patients or patients with chronic pain, we hypothesized that the 3MMM could be used with adults with chronic pain during family medicine clinic appointments and may reduce stress and improve communication between physicians and patients.

The goal of this study was to evaluate the feasibility of using the 3MMM writing exercise for patients with chronic pain and to measure the effect and experience of the activity on patients and clinicians, with focus on the clinician-patient relationship.

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METHODS

All study materials and recruitment methods for both physicians and patients were approved by the University of Wisconsin-Madison Institutional Review Board.

Five family medicine physicians practicing at UW Health in Madison, Wisconisn, were recruited via a recruitment email that invited recipients to participate in a research study about expressive writing with patients with chronic pain. All physicians were affili-

ated with the Department of Family Medicine and Community Health at the University of Wisconsin School of Medicine and Public Health. Physicians were trained in the use of the activity through a 1-time, 1-hour virtual workshop, following the protocol used by the 3MMM developer (author DGT) and received an optional script to use with patients.[4] They were instructed to write at the same time as their patients and to share and discuss their answers to the following prompts afterwards:

1) Write 3 things you are grateful for (be specific).
2) Write the story of your life in 6 words.
3) Write 3 wishes you have.

Physicians identified 10 to 15 potentially eligible patients under their care. Patients were to have a diagnosis of chronic pain and were excluded if future appointments included specific urgent medical concerns unrelated to chronic pain. Patients with an upcoming appointment within the enrollment period (the subsequent 6 months) were sent a letter inviting them to participate in the study along with a study information sheet. Follow-up calls were conducted by the study team to gauge patient interest and complete enrollment. After patients were enrolled, a research coordinator met with each patient before an upcoming primary care visit during which they agreed to do the activity. Pre- and post-visit surveys were administered to both patients and physicians.

Follow-up interviews were conducted with patients after their visit and with study physicians at the end of the study period. Interviews were conducted over the phone, recorded, transcribed, and deidentified.

Results were analyzed using mixed methods. Interview transcripts were evaluated using qualitative methods based on a phenomenology framework. Two coders (SH, CS) reviewed the transcripts from both patients and physicians, and each coder independently developed a codebook. The coders met and finalized the codebook, which was used by a third coder (MFH). Coded data were reviewed by all 3 coders for thematic analysis. Descriptive statistics (n, %) or mean (SD) were reported for patient and physician characteristics and survey responses. On patient surveys, 4 Likert outcomes were coded from 1 through 5 and current pain used a scale of 0 to 10 (0 = no pain and 10 = the worst pain you can imagine). Changes were assessed using paired Mann-Whitney-Wilcoxon tests. Analysis was conducted using R, version 4.1.3 (R Core Team, 2022).

RESULTS

Recruitment materials were sent to 44 potential participants. Of those contacted, 26 were excluded (declined, did not have chronic pain, or could not be reached and/or had no appointment during the study period). The remaining 18 were enrolled in the study, and 15 of 18 participants completed the activity with their primary care clinician. The majority of patient participants who completed the activity identified as female and White (Table 1). Most patients were older than 45 years and had experienced pain for more than a decade. Slightly more patient participants currently were not taking prescribed opioid medication for treatment of their chronic pain, and half of them had used journaling before to cope with stress or pain in their lives. Types of chronic pain varied, with half of the patient participants identifying multiple areas of chronic pain. The other pain sites listed were marked as the only site of pain (eg, back pain only, cancer-related pain only).

Table 1. Patient Characteristics[a]

Characteristic	n (%)
Age	
Age < 45	5 (33)
Age 46-65	4 (27)
Age > 65	6 (40)
Please describe the gender identity or identities with which you best identify	
Female	13 (87)
Male	2 (13)
How would you describe your ethnicity?	
Not Hispanic or Latino	15 (100)
How would you describe the race(s) you best identify with? (Please select ALL that apply)[a]	
White	14 (93)
Black or African American	2 (13)
American Indian or Alaska Native	2 (13)
What type of chronic pain do you have? (Please select ALL that apply)a	
Back pain	10 (67)
Neck pain	5 (33)
Cancer-related pain	1 (7)
Trauma-related pain	1 (7)
Headache	6 (40)
Other	10 (67)
How long have you lived with chronic pain?	
10 years or less	5 (33)
> 10 years	10 (67)
Are you currently taking any opioid medication (such as morphine, oxycodone, hydrocodone, or others) for your chronic pain?	
Yes	6 (40)
Have you used journaling or expressive writing to cope with stress or pain in your life?	
Yes	7 (47)

[a]Options with no responses are not shown. Categories may add to more than 100% when patients selected more than 1 option. "Other" categories for type of chronic pain included the following responses: stomach pain, leg pain, hand pain, arthritis, underarm pain, whole-body pain, shoulder pain, fibromyalgia.

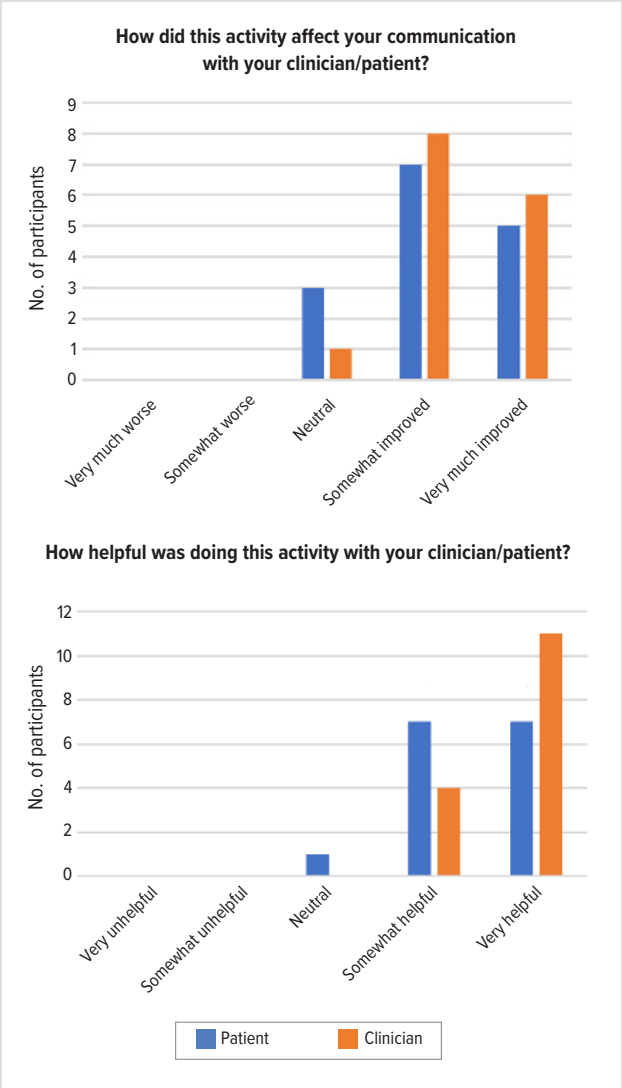
Of the 5 physicians who participated in the study, 3 were male and 2 were female. Three were 5 to 10 years post-residency, and 2 were over 10 years post-residency. Almost all physicians estimated 10% to 30% of their patients had chronic pain, with 1 reporting 70% to 90% of their patients having chronic pain. Most physicians also had prior experience with journaling.

Although results for pre- and post-visit survey questions on experience, empathy, and communication were not significantly different, descriptive statistics showed that most patients reported that there was improvement in communication (responded "excel-

lent," n = 11 pre-visit (73.3%), 13 post-visit (86.7%); $P = 0.157$), increased agreement that their clinician behaved with empathy toward them (responded "strongly agree," n = 12 pre-visit (80%), 15 post-visit (100%); $P = 0.083$), increased agreement that their clinician listened to them immediately (responded "strongly agree," n = 13 pre-visit (86.7%), 15 post-visit (100%); $P = 0.157$), and increased agreement that their clinician understands their health issues (responded "strongly agree," n = 10 pre-visit (66.7%), 13 post-visit (86.7%); $P = 0.102$). Most clinicians reported that the activity took 10 minutes or less (11/13, 85%) and that it was an appropriate amount of time (14/15, 93%), with only 1 response indicating that it took too long to complete the activity (1/15, 7%). The most common barriers identified by physicians to making this activity part of a regular practice were lack of time and persuading other physicians to do this activity.

We identified 4 common key themes from individual follow-up interviews with patients and physicians: (1) opening the door to communication, (2) insight into the doctor/patient as a person, (3) peer-to-peer communication, and (4) closeness and connection (Table 2). We observed 1 theme unique to patient experience—comfort and relaxation—and 3 themes unique to clinician experience: (1) unexpected learning, (2) unexpected value to patients, and (3) vulnerability and self-disclosure.

Figure. Number of Patient and Physician Responses Corresponding to Each Likert-type Response Choice



DISCUSSION

People coping with chronic pain may experience serious physical symptoms but are also more likely to experience mental health comorbidities than patients without chronic pain.[6] The complex nature of chronic pain means that many patients may feel frustrated, stigmatized, and neglected by clinicians due to a perceived lack of empathy, listening, and understanding.[3,4] Patients are not the only ones who feel disappointed during health care visits; stress and burnout symptoms are common in pain physicians and other clinicians who care for patients living with chronic pain, including primary care physicians.[7-9]

Our pilot study demonstrated the feasibility of an expressive writing exercise within a primary care visit with patients with chronic pain. Physicians maintained that the activity took a reasonable amount of time to complete within a standard, 25-minute family medicine outpatient clinic appointment. The themes identified from qualitative interviews with both patients and physicians, as well as the positive responses from survey questions, suggest that potential benefits of the exercise include improved communication and connection within the clinician-patient relationship, perhaps leading to observed increased patient perceptions of empathy shown by physicians. The theme of increased comfort/relaxation was unique to patients and may be a result of shifting focus to the activity from other stressors. Physicians reported unexpected learning and value to patients, which could be considered in context of whether the exercise is worth the time within a clinic visit. We believe the theme of insight into the doctor/patient as a person and the theme of vulnerability/self-disclosure, which was unique to physician experience, may be closely related. Patients seemed to appreciate getting to know their doctor as a person—and although the exercise may have pressed physicians towards greater self-disclosure than usual, this self-disclosure also may be a reason that patients perceived their doctors as more empathetic.

This activity could be useful in settings outside of chronic pain management, as physicians observed unexpected value to and learning about patients, and patients expressed wanting to know their doctors as people. Use of the 3MMM could offer a relatively short way for patients to get to know doctors with whom they do not have as close a relationship and for doctors to better understand new patients. Barriers to the use of the 3MMM identified by physicians include lack of time and persuading other clinicians to do the activity.

Table 2. Themes Identified Through Individual Follow-up Interviews With Patients and Physicians

CATEGORY/Themes	Quotes
UNIQUE TO PATIENT EXPERIENCES	
Comfort and relaxation Several patients talked about feelings of comfort or relaxation while doing the activity. Two spoke about how time pressures or worries about being ill can increase anxiety during a visit, but they did not feel that while doing the activity.	"It just felt more comfortable. It felt like it eased my anxieties of just being scared of what was going on, it took me out of that…whole doctor – you know – sickness thing, and it was just something else."
UNIQUE TO PHYSICIAN EXPERIENCES	
Unexpected learning All physicians reported that they learned something new about their patients through the activity and that what they learned would be helpful in further care of their patients.	"I didn't realize too that one of my patients –how close they were to their parents – and…definitely because it's always like a jumping off point in the future – things like parents or cats – a jumping off point to have a conversation, because I always feel like it opens the door, and then after we chat about that we can move on to other things, but it's…definitely something to warm things up and get the juices flowing for them to talk."
Unexpected perceived value to patients Physicians valued the activity more than they thought they would and enjoyed doing the activity with their patients, with potential positive impacts on relationships.	"I initially went into this thinking that [it] is just really manipulative and people are going to look through it and roll their eyes, but they didn't. People really appreciated that. So I was a little not surprised, but like, wow and maybe it was because I was genuine. I mean, it's true. I was hoping things for them. And I did say one of the things I was thankful for, I tried to make at least one about them. So I feel like, I don't know, that it helps communication, but it certainly helps the relationship."
Vulnerability and self-disclosure Physicians talked about a sense of vulnerability in doing the exercise together with the patients and the concept of self-disclosure as a tool to express caring within the visit.	"But in this sort of a very limited exercise, I felt like the self disclosure actually helped the therapeutic relationship, as opposed to sometimes self disclosure can actually take the attention away from the patient and sort of bring it to you and that's a danger for people who don't know kind of how to use it. I feel like in this exercise, it was just enough so that it really helped with the therapeutic relationship. I also felt like it provided me a way to express caring and concern that wasn't over the top. One patient was like, oh, that was so nice that one of your wishes was about me."
COMMON TO BOTH PATIENT AND PHYSICIAN EXPERIENCES	
Opening the door to communication Narratives of doing the expressive writing activity together allowed a sense of opening the door to communication as a means of deeper sharing for both patients and physicians.	***Patient:*** "I guess for the moments that we were doing the activity, I just felt a little bit less like a patient…I mean, I like my provider, I feel like [they are] very compassionate, very personable, and yet I'm always there with [them] because I am a patient. And participating in this exercise was not about me being a patient…I think the other thing that this brought is it allowed maybe my provider to see me in a different way too, to see a little glimpse of me, of who I was before, and what my hopes are after." ***Clinician:*** "My sense is that they had an appreciation of the vulnerability of it as well. And my sense was that while maybe uncomfortable to a certain extent, there is sort of a doorway that opened between us that hadn't been opened before, I guess, is how I envisioned that. And I think because of that…my sense is that there is an appreciation for that opportunity."
Insight into my doctor/patient Many patients expressed gratitude for the opportunity to learn about their doctors as people, not just as physicians taking care of patients. Deep engagement and being present together with their doctor through this activity seemed important. Several patients noted that they believe this insight might help further develop the relationship they already have with their doctor. Physicians indicated they felt able to learn new and valuable information about patients – even patients with whom they already had a longstanding relationship.	***Patient:*** "I think it actually freed [my doctor] up a lot, to be able to be a person and not a doctor for 10 minutes, if you know what I mean. And so I felt like that increased the warmth of the interaction… Yeah, not be problem-solving so much as like here we are in this moment together, you know?" ***Clinician:*** "I felt like not only did it help me sort of glean a little, a few new things about patients, I also think it helped them learn a little bit about me that maybe they didn't know before and that's like a whole other thing."
Peer-to-peer communication Through doing this activity, many of the patients indicated that the nature of the expressive writing prompts and the sharing and discussing of the writing prompts allowed them to connect on a more equal footing with their doctor. In the moments of doing the activity, patients and physicians both mentioned feeling a shift in the relationship.	***Patient:*** "I think learning a little bit more about [my doctor] as far as [they've] got kids, [they've] got family,…just being able to hear what [they're] grateful for…I think it kind of brings your doctor down to standard human level, I guess. At least that's how I feel about it. ***Clinician:*** "I think [they] appreciated knowing that I am a human being. I think [they] always know that, but just kind of being reminded of that. And I think the nice thing about the exercise is it sort of puts you on…the same level for a little bit."
Closeness and connection Many patients talked about how the activity made them feel in regard to the relationship they have with their doctor. For many, it seemed to deepen a sense of closeness—that they shared something personal with their doctor and, importantly, that their doctor listened and expressed compassion. Physicians spoke about how the activity could further develop elements of the relationship, like building trust.	***Patient:*** "Some of my provider's responses…said positive things about me or included positive things about me and that felt good." ***Clinician:***"So I feel like it's sped things along for establishing care.. I feel like it helped [them] feel connected to me or trust me in a way that maybe would have taken longer. And I feel like I care about [them] and, I'll remember this activity with [them] forever. …You know, sometimes – even in primary care where we get to know our patients really well – having some type of extra connection, I think – I feel like, while [they] and I may have gotten there over years working together, I feel connected to [them] in a way that certainly would not have happened so quickly without that activity, and maybe it wouldn't have happened at all."

This pilot study had limitations, including small physician and patient sample size and use of convenience sampling for patient recruitment. The study did not evaluate the impact of the use of the 3MMM over time, which could include lessening impact or fatigue for clinicians with repeated use. Larger studies are needed to demonstrate the potential benefits of 3MMM and determine which patients and clinicians might get the most benefit from this exercise. Despite these limitations, this study demonstrates that offering an expressive writing activity during a regular primary care appointment is feasible.

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REFERENCES

1. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2018;67(36):1001-1006. doi:10.15585/mmwr.mm6736a2

2. St Marie B. Primary care experiences of people who live with chronic pain and receive opioids to manage pain: a qualitative methodology. *J Am Assoc Nurse Pract.* 2016;28(8):429-435. doi:10.1002/2327-6924.12342

3. Kress HG, Aldington D, Alon E, et al. A holistic approach to chronic pain management that involves all stakeholders: change is needed. *Curr Med Res Opin.* 2015;31(9):1743-1754. doi:10.1185/03007995.2015.1072088

4. Thoele DG, Gunalp C, Baran D, et al. Health care practitioners and families writing together: the three-minute mental makeover. *Perm J.* 2020;24:19.056. doi:10.7812/TPP/19.056

5. Schaufel M, Moss D, Donovan R, Li Y, Thoele DG. Better together: long-term behaviors and perspectives after a practitioner-family writing intervention in clinical practice. *Perm J.* 2021;25:20.250. doi:10.7812/TPP/20.250

6. Foley HE, Knight JC, Ploughman M, Asghari S, Audas R. Association of chronic pain with comorbidities and health care utilization: a retrospective cohort study using health administrative data. *Pain*. 2021;162(11):2737-2749. doi:10.1097/j.pain.0000000000002264

7. Kroll HR, Macaulay T, Jesse M. A preliminary survey examining predictors of burnout in pain medicine physicians in the United States. *Pain Physician*. 2016;19(5):E689-E696.

8. Riquelme I, Chacón JI, Gándara AV, et al. Prevalence of burnout among pain medicine physicians and its potential effect upon clinical outcomes in patients with oncologic pain or chronic pain of nononcologic origin. *Pain Med*. 2018;19(12):2398-2407. doi:10.1093/pm/pnx335

9. Webster F, Rice K, Katz J, Bhattacharyya O, Dale C, Upshur R. An ethnography of chronic pain management in primary care: the social organization of physicians' work in the midst of the opioid crisis. *PLoS One*. 2019;14(5):e0215148. doi:10.1371/journal.pone.0215148

Use of a PHQ-9 Heat Map to Facilitate Management Decisions in Patients with Depression

Steven L. Rosas, MD; Mark E. Deyo-Svendsen, MD; Robert A. Taylor, DO; Rachael R. Taylor, PA-C; Michael R. Phillips, MD; Austin Fowler, MD; Lauren Casey

ABSTRACT

Background: Depression is a common concern for patients seeking medical care. The Patient Health Questionnaire-9 (PHQ-9) is a tool used to diagnose and manage depression. Tracking individual symptom scores rather than the sum of multiple symptom scores has been found to be more predictive of depression treatment response.

Methods: The records of 30 patients who had a follow-up visit in primary care were reviewed. We discuss 3 patient scenarios and present their PHQ-9 data as individual symptom scores, in the form of a color-coded heat map.

Results: In the cases presented, medication side effects, anxiety, a thyroid disorder, and fibromyalgia were identified as possible influencers of the PHQ-9 survey scores.

Discussion: A heat map helped clinicians understand the patient's clinical status in an efficient manner. We encourage the development of a PHQ-9 heat map in electronic medical record systems.

INTRODUCTION

Depression is a common concern among primary care patients. The Patient Health Questionnaire-9 (PHQ-9)[1-4] is a clinical tool frequently used to diagnose and manage depression. However, the authors have experienced some dissatisfaction with the use of the PHQ-9 total score as the primary means to follow patients with depression. We developed this project to evaluate other methods to review data from serial PHQ-9 surveys.

The PHQ-9 questionnaire consists of 9 depression-related questions that patients score from 0 (no symptoms) to 3 (daily symptoms). Individual responses to those 9 questions are tabulated to give a total score, ranging from 0 to 27. Use of the PHQ-9 tool has been validated to diagnose depression; however, use of the PHQ-9 survey total score to track depression over time has not been studied extensively.

Previous studies have identified limitations of the tool.[5-9] For example, one limitation is that the total score includes both somatic symptoms, such as sleep and appetite changes, and nonsomatic symptoms, such as depressed mood.[5-9] Questions 1, 2, 6, and 9 (dealing with loss of appetite, depressed mood, thought of being a failure, and suicide) generally are considered cognitive/affective in nature. Questions 3, 4, 5, and 7 (dealing with sleep, energy, appetite, concentration, and moving slowly) are generally considered somatic-related. Nonsomatic symptoms are more closely aligned with depression status, whereas somatic symptoms are more easily influenced by medication side effects or unrelated medical conditions.[5] Some sources recommend tracking these 2 subsets separately.[6-9] Previously, tracking of individual symptom scores rather than a sum of scores has been found to be more predictive of depression treatment response.[10]

This report presents 3 patient's scenarios that depict the benefit of reviewing PHQ-9 answers independently. We also demonstrate the use of a heat map to depict PHQ-9 data over time. A heat map assigns colors to different responses to highlight answers of a higher intensity and draw clinicians' attention to those answers.

METHODS

This project occurred in 2 phases. During phase 1, we used data

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from responses to PHQ-9 surveys to evaluate the course of a patient's depression at the time of a follow-up visit. We utilized the functionality of our current electronic medical record (EMR) to review PHQ-9 data for 30 patients who had a follow-up visit for depression. During the patient's visit, the clinician reviewed changes in the total PHQ-9 score and patient interview to arrive at a clinical impression and treatment recommendations. Then, while still in the room with the patient, responses to individual PHQ-9 questions were reviewed utilizing EMR functionality. The clinician then determined if the additional review resulted in further conversation with the patient that led to additional or different treatment recommendations.

During phase 2 of the project, our group evaluated several methods of depicting data from the PHQ-9 responses of the 3 patients who were identified during phase 1. Although responses to individual questions over time can be visualized with our current EMR functionality, users are limited to reviewing a maximum of 4 responses at any given time. These responses are presented in multicolored graphs and can be difficult to interpret. Among several options depicting this data, our group preferred a heat map, which was created by assigning a color to each of the possible answers to the PHQ-9 questions. A score of 3 (most or all of days) was designated by the color red. Orange was designated for answer 2 (half of the days), yellow for 1 (1-2 days) and green for zero (no days).

Figure 1. Heat Map for Patient 1 PHQ-9 Survey

PHQ-9 Question	10/23/20	3/13/21	8/19/21	10/14/21	12/27/21	2/10/22
1. Little interest or pleasure in doing things	3	1	1	1	3	1
2. Feeling down, depressed or hopeless	2	1	2	1	3	1
3. Trouble falling asleep, staying asleep or sleeping too much	1	0	3	3	3	3
4. Feeling tired or having little energy	3	2	1	1	3	2
5. Poor appetite or overeating	1	2	3	3	2	1
6. Feeling bad about yourself or that you are a failure	2	1	1	1	3	0
7. Trouble concentrating on things	2	2	2	1	2	1
8. Moving or speaking slowly or being fidgety or restless	1	2	2	3	2	0
9. Thoughts that you would be better off dead or of hurting yourself	1	0	0	0	2	0
Total PHQ-9 Score	16	11	15	14	23	9
Fluoxetine 30 mg daily						
Venlafaxine XR 37.5 mg daily						

Blue indicates start and stop dates of medication.

Figure 2. Heat Map for Patient 2 PHQ-9 Survey

PHQ-9 Question	6/10/20	9/11/20	11/19/20
1. Little interest or pleasure in doing things	2	1	2
2. Feeling down, depressed or hopeless	0	1	1
3. Trouble falling asleep, staying asleep or sleeping too much	1	2	3
4. Feeling tired or having little energy	1	1	1
5. Poor appetite or overeating	0	0	0
6. Feeling bad about yourself or that you are a failure	0	2	0
7. Trouble concentrating on things	0	2	2
8. Moving or speaking slowly or being fidgety or restless	0	0	0
9. Thoughts that you would be better off dead or of hurting yourself	0	0	0
Total PHQ-9 Score	4	9	7
Sertraline 100 mg daily			
Trazodone 100 mg daily			
Duloxetine 60 mg daily			

Blue indicates start and stop dates of medication.

RESULTS

In each of the 3 cases studied, a heat map depicts data at the decision point described in the clinical scenario. We provide further patient follow-up information, including PHQ 9 scores, but do not depict this follow-up data in the heat maps.

The first patient had been taking fluoxetine 30 mg daily for depression for over a year. They stopped the medication due to emotional blunting in November 2021. When they presented to their physician in December 2021, the emotional blunting had improved, but the depression was much worse. This was demonstrated by worsening of the PHQ-9 score from 14 to 23. Venlafaxine XR 37.5 mg was initiated. In subsequent follow-up on February 10, 2022, their total PHQ-9 score decreased from 23 to 9. However, the patient was interested in further improvement in the depression symptoms and a dose increase was considered. Individual scores were reviewed and it was noted that responses to all 9 questions either improved or remained low except the sleep score (question 3). "Trouble falling asleep, staying asleep, or sleeping too much" was still occurring "nearly every day." The response to medication changes is depicted in a heat map (Figure 1).

At the time of the visit, trouble with sleep was the only question that still had a score of 3 (the color red). The patient indicated that this was related to insomnia. Since insomnia is a possible side effect of venlafaxine XR, a recommendation was made

to continue the low dose (37.5 mg) of venlafaxine XR and focus on sleep hygiene. Several nonpharmacologic recommendations to improve sleep hygiene were made. Three months later, the sleep question score decreased from 3 to 0, resulting in a decrease in total PHQ-9 score from 9 to 6, and the patient indicated that depression symptoms were under adequate control at this point.

The second patient had a history of depression, anxiety, and fibromyalgia. Sertraline 100 mg daily and trazodone 100 mg at bedtime had been prescribed by her primary care clinician. Unbeknownst to this clinician, a specialist at an outside facility prescribed duloxetine 60 mg twice daily for fibromyalgia. The primary clinician saw the patient in June, September, and November, and her PHQ-9 total score went up slightly from 4 to 9 and then to 7. On November 19, 2020, the primary care clinician became aware that the patient was taking duloxetine in addition to the trazodone and sertraline and they reviewed with her the PHQ-9 total and individual question scores. These data are depicted in Figure 2.

Figure 3. Heat Map for Patient 3 PHQ-9 Survey

PHQ-9 Question	2/5/21	2/6/21	3/22/21	4/22/21
1. Little interest or pleasure in doing things	1	1	2	2
2. Feeling down, depressed or hopeless	3	2	2	3
3. Trouble falling asleep, staying asleep or sleeping too much	1	2	3	1
4. Feeling tired or having little energy	2	2	2	1
5. Poor appetite or overeating	3	3	3	3
6. Feeling bad about yourself or that you are a failure	3	2	2	2
7. Trouble concentrating on things	2	2	1	3
8. Moving or speaking slowly or being fidgety or restless	2	1	1	1
9. Thoughts that you would be better off dead or of hurting yourself	1	1	1	1
Total PHQ-9 Score	18	15	17	17
Venlafaxine XR 37.5 mg daily				
Venlafaxine XR 75 mg daily				
Levothyroxine 25 mcg				

Blue indicates start and stop dates of medication.

Although total PHQ-9 sores remained low, review of individual answers indicated that sleep—specifically insomnia—had become more of an issue for her. Review of individual data guided the clinician toward a recommendation to taper and discontinue the sertraline and continue the duloxetine and trazodone. When seen for follow-up 3 months later, sleep had improved. The score for the sleep-related question (no. 3) improved from 3 to 1, and the total PHQ-9 score improved from 7 to 5. Although this was a small change in numeric score, the patient reported that her quality of life was much better, and she was satisfied with her depression management.

The third patient had depression and Hashimoto's thyroiditis. Over time, this individual progressed from a hyperthyroid to a hypothyroid state. Their depression was treated initially with venlafaxine XR 37.5 mg daily and subsequently increased to 75 mg daily without significant change in PHQ-9 total sore. When seen on April 22, 2021, the individual PHQ-9 scores were assessed with responses demonstrated in the heat map (Figure 3). In this instance, the sleep issue was not insomnia but excessive sleeping and fatigue. Thyroid studies at that time revealed progression to the hypothyroid state. Levothyroxine was started; venlafaxine XR and counseling were continued. The patient's PHQ-9 total score improved from 17 to 9.

DISCUSSION

Depression frequently coexists and shares symptoms with other psychiatric and physical conditions. In these examples, medication side effects, thyroid disease, and fibromyalgia were identified as possible influences to the PHQ-9 survey. Although the review of individual scores was helpful in only 3 of the 30 patients we reviewed, in those 3 situations, the review led the clinician to consider alternative interventions not contemplated when looking only at the total PHQ-9 scores. We encourage further study of the effect that patients' coexisting medical conditions and medications may have on individual PHQ-9 survey responses and believe that presentation of the individual responses over time can be clinically helpful in some scenarios.

When following patients with depression, clinicians have multiple decisions to consider, including dose increase or decrease, change of medication, addition of adjuvant medication, referral for cognitive behavior therapy or other counseling, sleep hygiene recommendations, and consideration of other medical issues. We found that a heat map matched to individual PHQ-9 responses helped clinicians appreciate details about the patient's current clinical status in an efficient manner. We encourage development of the PHQ-9 heat map within EMR systems so this tool would be available to clinicians as they see patients in follow-up for depression.

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REFERENCES

1. Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatr Ann*. 2013;32(9):509-151. doi:10.3928/0048-5713-20020901-06

2. Bianchi R, Verkuilen J, Toker S, et al. Is the PHQ-9 a unidimensional measure of depression? A 58,272-participant study. *Psychol Assess*. 2022;34(6):595-603. doi:10.1037/pas0001124

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

4. Martin A, Rief W, Klaiberg A, Braehler E. Validity of the Brief Patient Health Questionnaire Mood Scale (PHQ-9) in the general population. *Gen Hosp Psychiatry.* 2006;28(1):71-77. doi:10.1016/j.genhosppsych.2005.07.003

5. Harrison P, Walton S, Fennema D, et al. Development and validation of the Maudsley Modified Patient Health Questionnaire (MM-PHQ-9). *BJPsych Open.* 2021;7(4):e123. doi:10.1192/bjo.2021.953

6. Krause JS, Reed KS, McArdle JJ. Factor structure and predictive validity of somatic and nonsomatic symptoms from the Patient Health Questionnaire-9: a longitudinal study after spinal cord injury. *Arch Phys Med Rehabil.* 2010;91(8):1218-1224. doi:10.1016/j.apmr.2010.04.015

7. Beard C, Hsu KJ, Rifkin LS, Busch AB, Björgvinsson T. Validation of the PHQ-9 in a psychiatric sample. *J Affect Disord*. 2016;193:267-273. doi:10.1016/j.jad.2015.12.075

8. Ong CW, Pierce BG, Klein KP, Hudson CC, Beard C, Björgvinsson T. Longitudinal measurement invariance of the PHQ-9 and GAD-7. *Assessment*. 2022;29(8):1901-1916. doi:10.1177/10731911211035833

9. González-Blanch C, Medrano LA, Muñoz-Navarro R, et al. Factor structure and measurement invariance across various demographic groups and over time for the PHQ-9 in primary care patients in Spain. *PLoS One*. 2018;13(2):e0193356. doi:10.1371/journal.pone.0193356

10. Sakurai H, Uchida H, Abe T, et al. Trajectories of individual symptoms in remitters versus non-remitters with depression. *J Affect Disord*. 2013;151(2):506-513. doi:10.1016/j.jad.2013.06.035

Community Agency Preferences for and Perceptions of Disseminating and Implementing a Continence Promotion Program

Madeline K. Moureau, BS; Nicholas B. Schmuhl, PhD; Zoey B. Shultz, BA; Cathryn P. Phouybanhdyt, BS; Heidi W. Brown, MD, MAS

ABSTRACT

Background: This study sought to assess the perceived value of in-person and online implementation of a community-based continence promotion program among Wisconsin community agencies serving older adults.

Methods: Electronic surveys were administered to representatives of organizations that serve older adults and assessed their preferences and perceptions of disseminating and implementing a continence promotion program to members of their organization.

Results: Among 101 participants, most (68%) reported an online program would appeal to their organization, while fewer noted the appeal of an in-person program. Many considered technology a barrier but indicated the online format could improve program reach and provide privacy to women with incontinence.

Conclusions: Community organizations perceived incontinence as a prevalent and important issue and see advantages of in-person and online program implementation.

BACKGROUND

More than 60% of older adult women experience incontinence, but few seek care.[1,2] "Mind Over Matter; Healthy Bowels, Healthy Bladder" (MOM) is a small-group, evidence-based continence promotion program hosted by community agencies and delivered by trained lay facilitators to prevent or improve urinary or bowel incontinence. Over 3 sessions, women 50 and older build skills to perform pelvic floor muscle exercises, avoid bladder irritants, improve toileting habits, optimize fiber and fluid intake, and learn how to seek care with a clinician if symptoms persist.

In 2017, six Wisconsin community agencies recruited members from their organizations to test MOM in a randomized, controlled trial. The participants in the in-person MOM program reported an 8-fold improvement in bladder symptoms and a 3-fold improvement in bowel symptoms compared to controls.[3] While half of the community agencies continued to provide MOM after the trial, demonstrating the potential for sustainability, most statewide community agencies reported that they did not have the resources or scope of services to offer MOM regularly.[4] Furthermore, women with incontinence have reported previously that they would not attend an in-person continence promotion program; however, they would be willing to participate in an online program because of the convenience and privacy.[5] Thus, we thus sought to understand whether community organizations, similar to those offering the in-person MOM program, would be interested in disseminating or implementing an online version.

The objectives of this study were to (1) assess the perceived value of in-person and online continence promotion programs for community agencies that serve older women, (2) gauge willingness to disseminate information about continence promotion programs, (3) understand the perceived advantages and disadvantages of continence promotion, and (4) understand community organization representatives' preferences on program delivery format (in-person vs online).

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METHODS

With input from community organization partners, we assembled a contact list of agency representatives serving older adults in Wisconsin. The list was compiled using a combination of sources, including Aging and Disability Resource Center and Aging Unit websites and email addresses supplied by community partners engaged in developing and pilot-testing the in-person MOM program. The roles of invited agency representatives varied and included specialists, coordinators, managers, and directors. In May 2019, we invited representatives via email to participate in a brief, 16-item electronic survey assembled with guidance from community organization partners. We sent email reminders to nonresponders at 2 and 4 weeks. No incentives were offered for participation.

The survey ascertained representatives' perspectives on a bladder and bowel health promotion program. Representatives could look through the MOM pilot website (https://www.healthybowelandbladder.org) before answering questions. In the survey, representatives provided information regarding their (1) perceived value of an online bladder and bowel health program to their members, (2) interest in providing members with information about such an in-person or online program, (3) perceived value of the in-person or online program to their members, (4) reservations about promoting such an in-person or online program, and (5) preference on program delivery format (online, in-person with partner organization, in-person with own organization).

Descriptive statistics characterized representatives' preferences and perceptions of a bladder and bowel health program. Two study team members independently analyzed free-text responses for emerging themes and sorted responses into thematic groups, which 2 additional study team members reviewed. The team refined thematic groupings and resolved discrepancies through iterative discussions.

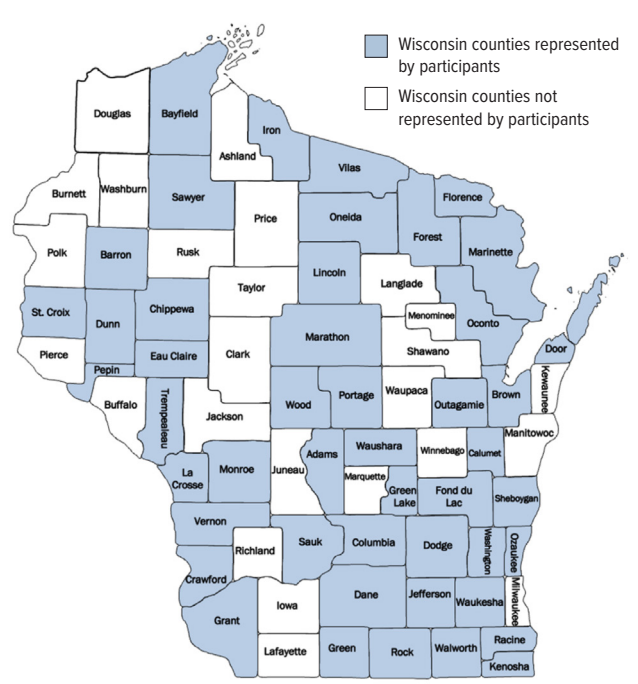
RESULTS

Of 582 email addresses, 39 bounced back, and 543 were valid. We received responses from 101 (19%) community agency representatives. Participants represented Aging and Disability Resource Centers (42%), senior centers (22%), aging units (14%), and other similar organizations (21%) across 47 (65%) Wisconsin counties (Figure). Among those who could estimate the age distribution of their members, almost all (98%) reported that more than half were 65 years or older. The number of members served varied, ranging from less than 100 to more than 5000.

Perceived Value of Continence Promotion Programs

Half of the participants reported their organization's members would find an online continence promotion program "very valuable," followed by 44% and 6% endorsing "somewhat valuable" and "not at all valuable," respectively (Table 1). When asked to indicate all continence promotion program formats that would appeal to their community organization, most participants reported that an online program would be appealing (80%), followed by an in-person program hosted by a partner agency (65%) and an in-person program offered by their organization (38%).

Figure. Geographical Characterization of the Wisconsin Counties Survey Participants Represented



Willingness to Disseminate Information About Continence Promotion Programs

Most participants (87%) reported that their organization is currently engaged in electronic or online outreach, and almost all participants (95%) were interested in providing their members with information about an online bladder and bowel health program (Table 2). Participants reported they would be most likely to disseminate information about an online program through paper flyers or brochures, announcements in written newsletters, and promotions on their organizations' websites and social media platforms.

A third of the participants reported reservations about promoting an online bladder and bowel health program, including concerns about the lack of computer or Internet access among members, lack of familiarity with the program and its results, and concerns that organization staff could not effectively field questions. A few participants reported perceptions that the program or related messaging would be unpopular, cause embarrassment, increase stigma, or generate complaints.

Perceived Advantages and Disadvantages of Community-based Continence Promotion

Table 3 outlines the advantages and disadvantages of commu-

nity-based continence promotion programs as recognized by representatives for their organization and members. The need for education about bladder and bowel health among older adults was a common sentiment, because many participants recognized incontinence as a prevalent health condition among the population served by their organizations. Participants also opined that community-based continence promotion programs may help overcome the stigma surrounding incontinence, as they can aid in initiating the discussion.

Many representatives interested in offering in-person programs noted that health promotion aligned with their organization's mission and scope of services. Others said an in-person program would be well-suited for their members but preferred that the program be offered by a partner organization due to resource limitations. Some participants who said offering health promotion programs did not fall within their organization's scope of services still expressed willingness to promote the program.

Preferences on Program Delivery Format

Some participants expressed concerns that an online platform could present barriers for older women, as they may not have access to computers or the Internet, while simultaneously recognizing the potential for online resources to reach a broad audience (Table 4). Furthermore, despite the potential advantages of an online program, the perception that many older adults prefer in-person activities persisted. Several comments indicated that in-person activities would appeal to older adults' desire to learn while reducing social isolation.

Table 1. Perceived Value of and Format Preferences for a Bladder and Bowel Health Program

Perceptions of a Bladder and Bowel Health Program Questions	n	%
Do you believe an online bladder and bowel health program would be valuable to your members? (N = 94)		
No, not at all	6	6
Yes, somewhat valuable	41	44
Yes, very valuable	47	50
Which of the following bladder and bowel health program options would appeal to your organization? (N = 84) (Select all that apply)[a]		
An in-person program offered by my organization	32	38
An in-person program offered by a partner organization	55	65
An online program that does not require maintenance from my organization	68	80
None of these programs would appeal to my organization	4	5
Which bladder and bowel health program option would be most appealing to your organization? (N = 81)		
An in-person program offered by my organization	7	9
An in-person program offered by a partner organization	22	27
An online program that does not require maintenance from my organization	33	41
Both online and in-person programs appeal equally to my organization	19	23

[a]The percentages do not sum to 100%, as community organization representatives were able to select more than 1 response.

Table 2. Willingness to Disseminate Information About Bladder and Bowel Health Programs

Bladder and Bowel Health Program Outreach Questions	n	%
Does your organization currently offer any electronic outreach? (N = 76)		
Yes	66	87
No	9	12
Not sure	1	1
Would your organization be interested in providing your members with information about an online bladder and bowel health program? (N = 89)		
No, not at all interested	5	6
Yes, somewhat interested	30	34
Yes, definitely interested	54	61
Which would your organization use to share information about an online bladder and bowel health program with your members?[a] (N = 95)		
Paper flyers or brochures	65	68
Announcements in our meetings	30	32
Announcements in distributed community bulletins or schedules	37	39
Announcement in our written newsletter	56	59
Announcement in our electronic newsletter	36	38
Promotion on our website	49	52
Promotion on social media	53	56
Other platforms	14	15
We would not promote this program	5	5

[a]The percentages do not sum to 100%, as community organization representatives were able to select more than 1 response.

DISCUSSION

In this survey of 101 representatives from community agencies serving older adults in Wisconsin, most participants perceived continence promotion as valuable and relevant to their organization and members. Participants were interested in an online program, and most were willing to advertise it to their members. Few were interested in providing an in-person program through their organization, and many who valued it preferred that it be sponsored and organized by a partner organization.

Our results suggest that community agencies serving older adults would be willing to balance the benefits and drawbacks of online continence promotion programs. Participants perceived that technology may present a challenging learning curve for their organizations' members; however, they were still willing to offer the program as it could improve reach and access. More recently, due to COVID-19, several studies found that older adults have increased their use of technology to meet their health needs.[6-8] Sixsmith et al administered the same technology use questionnaire in 2019 and 2020. They found older adults were signifi-

Table 3. Community Agency Representatives' Perceptions of Community-based Continence Promotion

Domain	Theme	Description	Exemplars
Need for education about bladder and bowel health	Information equals power	Education is a way to empower older adults to take active roles in improving their health.	"Any way we can help older women help themselves to have a better quality of life is of interest to our senior center."
	Prevalence	Representatives recognized incontinence as a common health issue among aging populations.	"I think this is an issue that affects many women, and it is beneficial for them to know that others are going through the same thing."
	Fills unmet needs	Despite its prevalence, incontinence is an under-addressed issue that many women have no venue to discuss.	"Many women suffer silently with this and isolate themselves. If they can start to learn how to prevent and live with this issue it will only improve their lives moving forward."
Stigma	Initiating the discussion (stigma)	Many women feel embarrassed, do not seek care, and do not discuss their incontinence with clinicians.	"Some women may be uncomfortable speaking with their health care professional but might access a website for information."
Organizational fit	Scope of services	Representatives noted health promotion was (or was not) within their organization's scope of services.	"Our organization is not directly responsible for health promotion."
	Alignment with mission	Representatives commented on program alignment (or lack thereof) with their organization's mission.	"That is what we are here for – to provide information and resources to enhance the lives of older adults."
	Lack of resources	Many representatives reported that resource or staffing limitations would make it difficult for their organization to offer a program independently.	"I am a single employee and cannot do it all and do it all well."

Table 4. Community Agency Representatives' Preferences for Delivery Format

Domain	Theme	Description	Exemplars
Stigma	Privacy	The online platform would allow people to engage confidentially and keep health information private.	"For a potentially embarrassing issue such as incontience, one may not want to meet in a group. Many seniors are tech-savvy now and could learn from the online version."
Technology	Technological literacy	Some older adults have limited technological literacy, while a younger group of older adults is more interested in and connected to the Internet.	"Lots of incontinence out there but not as much computer literacy as one might like." "The younger generation of seniors (Baby Boomers) would definitely benefit from the online program."
	Access to electronic resources	Many older adults lack access to Internet services and Internet-connected devices. At the same time, the online platform has the potential to reach a broader audience compared to in-person activities.	"It's great information but many older women do not use the Internet or web-based products. So, many women who may find this useful will be missed." "Some of the women in our community are unable to take the Mind Over Matter seminar but will be able to do the online program. For those who work, do caregiving, do not have transportation, and cannot attend a workshop or are just simply uncomfortable in a group setting."
Member preferences	In-person preference	Many older adults prefer in-person activities and benefit from social contact.	"[Older adults] also prefer to have a face-to-face presentation so they are able to ask questions."

cantly more likely to use computers and smartphones to communicate online. Furthermore, most older adults stated they would continue to utilize technology after COVID-19 social distancing restrictions were lifted.[6]

Using a convenience sample limits this study as it may not represent all community organizations or their employees, and those most likely to support an online continence promotion program are more likely to have responded to this survey. Those who did participate offered their perceptions of what would be valuable and relevant to their members. The global pandemic beginning in 2020 has almost certainly changed the landscape for older adults and the organizations serving them; however, these results provide a roadmap for future health promotion programming delivery.

CONCLUSIONS

Most community agency representatives perceived that a continence promotion program would be valuable to their members and reported that they would be willing to promote such a program. Although most representatives preferred to implement an online program that did not require maintenance from their organization, many identified both advantages and disadvantages of an online program for their members. The advantages of an online program included the unmet need for bladder and bowel health education, accessibility, and privacy. Representatives noted several disadvantages to an online program for their members, including a lack of access to electronic resources, reduced social interaction, and challenges with technological literacy. Although the continence promotion program initially was developed as an in-person

program, community organizations would prefer an online delivery, aligning with the preferences of women with incontinence. Future research should focus on developing an online continence promotion program and exploring other in-person health promotion programs to determine if an online format would be more optimal.

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REFERENCES

1. Brown HW, Wexner SD, Lukacz ES. Factors associated with care seeking among women with accidental bowel leakage. *Female Pelvic Med Reconstr Surg.* 2013;19(2):66-71. doi:10.1097/SPV.0b013e31828016d3

2. Patel UJ, Godecker AL, Giles DL, Brown HW. Updated prevalence of urinary incontinence in women: 2015-2018 national population-based survey data. *Female Pelvic Med Reconstr Surg.* 2022;28(4):181-187. doi:10.1097/SPV.0000000000001127

3. Brown HW, Braun EJ, Wise ME, et al. Small-group, community-member intervention for urinary and bowel incontinence: a randomized controlled trial. Obstet Gynecol. 2019;134(3):600-610. doi:10.1097/AOG.0000000000003422

4. Schmuhl NB, Brow KA, Wise ME, Myers S, Mahoney JE, Brown HW. After the randomized trial: implementation of community-based continence promotion in the real world. *J Am Geriatr Soc*. 2020;68(11):2668-2674. doi:10.1111/jgs.16771

5. Brown HW, Wise ME, LeCaire TJ, et al. Reasons behind preferences for community-based continence promotion. *Female Pelvic Med Reconstr Surg*. 2020. doi:10.1097/SPV.0000000000000806

6. Sixsmith A, Horst BR, Simeonov D, Mihailidis A. Older people's use of digital technology during the COVID-19 pandemic. *Bull Sci Technol Soc.* 2022;42(1-2):19-24. doi:10.1177/02704676221094731

7. McIlduff CD, Acharibasam J, Starr V, Chapados M. Engaging Indigenous older adults with technology use to respond to health and well-being concerns and needs. *Healthc Manage Forum.* 2022;35(5):257-264. doi:10.1177/08404704221103521

8. Qin W. Technology learning and the adoption of telehealth among community-dwelling older adults during the COVID-19 outbreak. *J Appl Gerontol.* 2022;41(7):1651-1656. doi:10.1177/07334648221085473

Transition Practices in Wisconsin Health Care Systems: What Do We Know?

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ABSTRACT

Background: The transition from youth to adult health care is a complex process, and only 25% of all youth and less than 35% of youth with special health care needs in Wisconsin receive support.

Objectives: This article describes the process and results from the Wisconsin Youth Health Transition Initiative's assessment of transition support provided in health care.

Methods: Key informant interviews were undertaken with clinicians from several Wisconsin health care systems.

Results: Fifty percent of health care systems interviewed had a formal policy or guideline supporting health care transition. Additionally, several barriers consistent with national trends were confirmed.

Conclusions: Health care transition for Wisconsin youth remains suboptimally supported in practice. Continued funding and work towards this important maternal and child health objective are needed.

BACKGROUND

Transitioning from pediatric to adult health care can be complex for youth and their families, along with their clinicians. Health care transition (HCT) is defined as the process of an individual moving from a pediatric to an adult model of health care with or without a transfer to a new clinician.[1]

According to the 2020-2021 National Survey of Children's Health, only 34.6% of Wisconsin youth with special health care needs and 25% of youth without special health care needs receive adequate HCT assistance from their health care providers.[2] In this survey, parents of youth ages 12 to 17 responded to questions related to whether the health care professional (1) spent time alone with the youth, (2) discussed the HCT process (skills and changes at age 18), and (3) discussed the need to transfer to clinicians for adults.

To address the problem that less than half of all youth are getting the help needed for successful transitions to adult care, best practices have been defined and endorsed by White and coauthors, including the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Physicians.[1] These best practices include structured implementation processes for HCT called the Six Core Elements. The Six Core Elements are intended to be customized depending on patient population and practice type and include: (1) transition and/or care policy, (2) tracking and monitoring, (3) transition readiness and/or orientation to adult practice, (4) transition planning and/or integration into adult approach to care, (5) transfer of care and/or initial visit, and (6) transition completion/ongoing care. Policy development is the first step, with consideration for starting HCT planning as early as age 12 when changes in confidentiality occur.

Clinician barriers to HCT most often reported in the literature include not being given enough time for transition,[1] lack of available clinicians,[1] lack of current knowledge/awareness of available resources,[3] having transition resources but not using them,[4] and hesitancy to transfer patients with active care or disease.[5] Although current literature promotes best HCT practices (eg, the Six Core Elements), there is little evidence for improved

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out comes using a common set of strategies for all clinics/systems.

Families and youth may experience HCT barriers with respect to accessing HCT support, including feeling alone in the process;[3] lack of anticipation/awareness of HCT;[6] difficulty trusting new clinicians;[4] and reluctance to transition.[7] Those achieving HCT frequently reported increasing awareness as being helpful for transition.[7] Two models of HCT described that the use of a care navigator facilitated successful transitions.[8] In a 2023 scoping review, Markoulakis et al[9] described 5 themes that support HCT, including holistic supports, proactive preparation, empowering youth and families, collaborative relationships, and systemic considerations.

In 2021-2022, the Wisconsin Youth Health Transition Initiative (YHTI), funded by the Wisconsin Department of Health Services Maternal and Child Health Block grant on a contract with the Waisman Center University Center for Excellence in Developmental Disabilities at the University of Wisconsin-Madison, was asked to report on HCT practices, which included identifying those Wisconsin health care systems with HCT policies or practice guidelines, the extent of HCT implementation, and the facilitators and barriers of that implementation. This report reflects "what we know" about HCT in Wisconsin during the COVID-19 pandemic.

METHODS

Using a systematic approach, the YHTI chose to conduct interviews with informants from selected Wisconsin health care systems. The YHTI identified the number of hospital beds as the most readily available measure to capture those systems serving the largest population and utilized a state-based database cross-referenced with a national hospital directory for this measure. While the focus of the YHTI is youth with special health care needs, the team sought key informants in the 10 largest systems providing primary and specialty care to pediatric and adult patients. This project met the criteria for "quality improvement" utilizing the University of Wisconsin-Madison Quality Improvement/Program Evaluation Self-Certification Tool and did not require institutional review board approval.

Conducting Interviews

Interview questions were generated to identify the extent of HCT implementation utilizing the Six Core Elements, with a focus on whether the interviewee knew if there was an existing system-wide HCT policy or practice guideline. All interviews (20-60 minutes each, 2 of which included more than 1 respondent in the interview) were conducted over a 15-month period via Zoom by an adult nurse practitioner with lived experience as a parent of a child with a disability. Three pilot interviews, conducted with 3 clinicians known to the YHTI, finalized 19 questions. Seven subsequent interviews involving 10 clinicians were conducted (Table 1).

Table 1. Description of Interview Sample

	No.	(%)
System size (n = 8)		
Top 10 largest	5	(62.5)
Other	3	(37.5)
Interviewee system size (n = 13)		
Top 10 largest	8	(61.5)
Other	5	(38.5)
Interviewee credential (n = 13)		
Physician	5	(38.5)
Advanced practice provider[a]	4	(30.8)[a]
Registered nurse	1	(7.7)
Social worker	2	(15.4)
Bachelor of Science	1	(7.7)
Interviewee primary role (n = 13)		
Administrative/non-direct patient care	4	(30.8)
Direct patient care	9	(69.2)
Interviewee primary population served (n = 13)		
Adult	1	(7.7)
Medicine pediatrics	3	(23.1)
Adolescent	1	(7.7)
Pediatrics	8	(61.5)

[a]Due to rounding, percentages may add up to more than 100%.

The YHTI encountered significant challenges in identifying, contacting, and interviewing key informants in 5 of the 10 largest Wisconsin health care systems. Therefore, additional interviews with smaller health care systems with known contacts, as well as the 3 pilot interviews, were included in the analysis.

Performing Data Analysis

Interview recordings were transcribed verbatim by one of the authors. A qualitative codebook was developed based on literature review and a seminal HCT article.[1] A single experienced coder performed a thematic analysis of the interview transcripts in QSR NVivo 12 Software (Lumivero). Themes were reviewed by all authors and confirmed that saturation was achieved.

RESULTS

Analysis began with the first of the Six Core Elements (ie, having a HCT policy or guidelines in place) and then focused on facilitators or barriers of additional elements. Four out of the 8 (50%) systems interviewed met the criteria of having a policy or guideline in place. The Six Core Elements further recommends the policy or guideline be consistently communicated and supported by administration, with funded time for implementation, and shared in an accessible format. All 4 systems with a HCT policy or guideline in place indicated limited policy or guideline communication, administrative support, or additional time for HCT. Table 2 includes quotes from interviewed clinicians.

The Six Core Elements includes the availability of electronic medical record (EMR)-embedded tools as a facilitator of HCT implementation. Examples of these tools include the ability to identify, track, and monitor patients during transition; transi-

tion readiness assessments; HCT report queries; clinician registries; shared plans of care or summary statements, and transfer of care materials. Interviews identified that few systems had any of these tools embedded into their EMR. Those that did have access to some EMR-embedded tools indicated their usefulness in HCT implementation and quality improvement initiatives (Table 2).

HCT practice leaders are included as important factors in HCT implementation.[1] Those interviewed indicated both the importance of having system or clinical leadership to keep focus and momentum on HCT, as well as being able to identify clinicians willing to see adults with different conditions. Staff indicated challenges when HCT leaders retired and in identifying enough adult clinicians to transition patients.

Table 2. Quotes Illustrating Reported Facilitators and Barriers of Health Care Transition Implementation

THEME/Representative Quotes
ADMINISTRATIVE SUPPORT OF HCT POLICY/GUIDE
"I think there's the intention, so the theoretical support [for HCT], but not the time and dollars support."
"We did write a transition policy, which I don't know that anyone is really necessarily supporting that or making it something that teams need or have to follow. From my perspective, we really don't have a whole lot of support just from a system-wide standpoint."
"We do have a policy in place that states that we will be doing this. However, that's as far as we've gotten…I think there's a lack of awareness beyond a few people in the organization, especially in the management and higher level… I think there's a lack of resource allocation to even move forward with the project."
"I think that grant opportunities and the connections that I've had with the [CYSHCN] regional center for many years have both really helped with this whole process…to serve as a catalyst for some of the work that we've done in our health systems."
COVID
"I know with COVID too, you know, that that's kind of putting a lot of regular work that we're doing to the side while we're just trying to manage that weekly changes as you know."
"…So, we work those lists. It's supposed to be every 3 months unless you're in a pandemic or unless you're in a surge of pediatric respiratory cases like right now."
"COVID has changed a lot of our protocols."
HCT LEADER
"We had a couple departments that were doing it … very well. Now those providers, the two that were kind of our headstrong for leading the transition project have now retired…and I really feel like the transition work has kind of just fizzled out."
"[Many adult] medical providers have no education on this [YSHCN] population. And that's [why there is] really no formal system like a welcome center that has 'okay, these are providers who are interested and willing'."
"I feel like you always need a clinician, a chair cheerleader…but I think it's taking on a lot for someone who is already busy."
"We latch onto somebody that's taking a few [transition patients] and keep adding to their pile."
EMR-EMBEDDED TOOLS
"There is no way to identify them as they're making the appointments as someone who has special needs or complex care. They get slotted into the same 30-minute appointment that all of my new patients would get slotted into. If I happen to preview them enough in advance then I may be able to move them around in my schedule, find them a little more time, some of those sorts of things."
"But I think that we do in this day and age have many opportunities with our EMR's and our systems that we have in place that we could do that. We just don't have the resources to make it happen right now."
"I think the only thing that we really have at a system level right now as we have a process that we send out a letter to all patients 17 years, 9 months. And then we have like a brochure turning 18."
"Yes [we have tools in EMR]. That [HCT readiness] checklist. And then ultimately the shared plan of care will reflect that transition."
"I can do manual audits to see like how often the transition checklists are being used and the questionnaires are being used because those get scanned into the medical record under a specific content type."

Abbreviations: HCT, health care transition; EMR, electronic medical record; YSHCN, youth with special health care needs; CYSHCN, children and youth with special health care needs.

DISCUSSION

The YHTI identified that systems were more likely to have met the primary measure of having an HCT policy or guideline if there was previous HCT support, including grant funding, access to targeted training or technical assistance, financial support for professional continuing education opportunities, or the presence of HCT practice leaders within the health care system.

The interview results indicate that HCT continues to occur within practice silos, primarily by clinicians (physician/nurse practitioner/physician assistant) with intermittent evidence of nursing, social work, or other professional support and, typically, without identified system-wide supports. HCT supports were more prevalent in specialty care than primary care settings. There was evidence that HCT work often was initiated and carried out by individual leaders with a passion for the work, which subsequently floundered when the clinician left or retired.

The timing of the COVID-19 pandemic had an impact on both the interview process and HCT practices within health care systems. While the use of virtual platforms facilitated the interview process, the pandemic disrupted the project timeline. With time and efforts saturated by the day-to-day care of patients, it was difficult for clinicians to have time for interviews. Additionally, many of those interviewed reported the pandemic severely affected HCT work and progress in their system. These impacts on HCT implementation are likely to persist for many years beyond the pandemic.

The interviews were limited to 1 or 2 clinicians within a health care system, and it was difficult to find an individual within an organization that could speak to HCT implementation on a systems level. Nonetheless, interviewees were able to identify HCT facilitators in their organization. Two contacts reported that the recent systemic focus on diversity, equity, and inclusion offered a renewed avenue of conversation regarding equitable care of indi-

viduals with disabilities within their organizations. This has the potential to elicit change in the delivery of health care to youth with special health care needs and to be a potential source of quality improvement for systems to implement HCT practices for all patients. Another positive outcome of these interviews was the identification of leaders with potential to expand HCT implementation. These interviews confirmed Wisconsin has similar barriers to those reported nationally, and this knowledge provides a focus for future work in the state.

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REFERENCES

1. American Academy of Pediatrics; American Academy of Family Physicians; American College of Physicians; Transitions Clinical Report Authoring Group, Cooley WC, Sagerman PJ. Supporting the health care transition from adolescence to adulthood in the medical home. *Pediatrics*. 2011;128(1):182-200. doi:10.1542/peds.2011-0969

2. 2020-2021 National Survey of Children's Health. Data Resource Center for Child and Adolescent Health. Accessed May 9, 2023. https://www.childhealthdata.org/

3. Cady RG, Erickson C, Harris DS, Nickelsen T. Successful healthcare transition for youth with special healthcare needs is a team effort. *Nurse Pract*. 2021;46(11):38-43. doi:10.1097/01.NPR.0000794524.42202.4c

4. Momplaisir F, McGlonn K, Grabill M, et al. Strategies to improve outcomes of youth experiencing healthcare transition from pediatric to adult HIV care in a large U.S. city. *Arch Public Health*. 2023;81(1):49. Published 2023 Mar 31. doi:10.1186/s13690-023-01057-8

5. Johnson KR, Edens C, Sadun RE, et al. Differences in healthcare transition views, practices, and barriers among North American pediatric rheumatology clinicians from 2010 to 2018. *J Rheumatol*. 2021;48(9):1442-1449. doi:10.3899/jrheum.200196

6. Christian BJ. Translational research - Healthcare transition readiness, stress, and resilience among youth with chronic conditions and disabilities. *J Pediatr Nurs*. 2022;67:172-175. doi:10.1016/j.pedn.2022.11.005

7. Halyard AS, Doraivelu K, Camacho-González AF, Del Río C, Hussen SA. Examining healthcare transition experiences among youth living with HIV in Atlanta, Georgia, USA: a longitudinal qualitative study. *J Int AIDS Soc*. 2021;24(2):e25676. doi:10.1002/jia2.25676

8. Garland BH, Caldwell KL, Acosta AB, Wiemann CM, Gonzales SA, Wolfe RS. Clinical considerations for emerging adults with eating disorders and transfer to adult-based care. *Evid Based Pract Child Adolesc Ment Health*. 2018;4(2):187-201. doi:10.1080/23794925.2018.1504637

9. Markoulakis R, Cader H, Chan S, et al. Transitions in mental health and addiction care for youth and their families: a scoping review of needs, barriers, and facilitators. *BMC Health Serv Res*. 2023;23(1):470. doi:10.1186/s12913-023-09430-7

Delta-8 Tetrahydrocannabinol in the Emergency Department: A Case Series

Kyle Gibbons, PharmD; Jacob Morris, MD

ABSTRACT

Introduction: "Delta-8," or delta-8 tetrahydrocannabinol (delta-8 THC), is a cannabinoid product that is growing in popularity for recreational use across the nation. This report aims to characterize the clinical presentation of acute delta-8 ingestions presenting to the emergency department.

Case Series: This is a case series of 6 patients who presented to a regional network of small- and medium-volume emergency departments in northwest Wisconsin. Patient histories confirmed that all patients had delta-8 exposure. Patient ages ranged from 5 to 57 years old. Amounts ingested and routes of ingestions varied from patient to patient. The most common symptoms reported were respiratory depression, unresponsiveness, altered mental status, tachycardia, and chest pressure.

Conclusions: This case series is a snapshot of the burden experienced by emergency departments because of delta-8 availability. Clinicians should maintain a high index of suspicion for delta-8 use, especially in patients with altered mental status, anxiety, or cardiac.

INTRODUCTION

"Delta-8," or delta-8 tetrahydrocannabinol (delta-8 THC), is a cannabinoid product that is growing in popularity for recreational use across the nation. It is widely advertised on billboards, television, and social media and is even available for purchase at gas stations. But what is delta-8 and what side effects should emergency departments (ED) be prepared to treat? This report is a case series of 6 patients who presented to a regional network of small- and medium-volume EDs in northwest Wisconsin during June 2021 to October 2022. The patients' history confirmed delta-8 exposure, and their ED presentation was attributed primarily to this exposure. To our knowledge, this is the largest case series involving delta-8-related ED presentations in a non-urban ED system. It provides insight into several phenotypes of delta-8-related symptoms, including altered mental status, anxiety, and cardiac symptoms and also demonstrates the burden placed on EDs secondary to widespread legal access of delta-8. The paper concludes with education on the regulatory status of delta-8 and on the presentation, testing, and management of delta-8 intoxication.

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CASE PRESENTATIONS

Case 1

A 36-year-old female presented to the ED via emergency medical services (EMS). According to EMS and the patient's son, she was using a vape pen with delta-8 THC prior to arrival. Her son stated that she became less responsive while sitting on the couch. He propped her head up with a few pillows. After an hour of her becoming increasingly unresponsive he called EMS.

When EMS arrived, she was minimally responsive. Naloxone was administered without improvement. Upon arrival to the ED, she remained unresponsive to any stimuli and was given a Glasgow Coma Scale (GCS) score of 4. Her oxygen saturation was in the mid to high 90s on nasal cannula with respirations between 12 and 16. Blood gas showed pH 7.38, carbon dioxide (CO_2) 34, and bicarbonate 20. Initial vital signs were heart rate (HR) 77 and blood pressure (BP) 127/86 mmHg. Given her continued altered mental status, she was intubated for airway protection. Her urine drug screen came back positive for amphetamines (not methamphetamines) and THC. The positive screen for amphetamines was likely a false positive due to her home medication of trazodone. The other toxicology labs (ethyl alcohol, acetaminophen level,

salicylate level) were negative. Computed tomography (CT) of the head was unremarkable.

The patient was admitted to the intensive care unit and was extubated later that evening. She had 1 seizure-like episode that evening and was treated with lorazepam. Neurology was consulted and no other cause for her altered mental status or seizure were identified—both were attributed to the ingestion of delta-8. She spent a total of 7 days in the hospital and was discharged home in her baseline neurologic state.

Case 2

A 45-year-old female presented to the ED by ambulance for a syncopal episode at work. According to EMS, the patient had normal vital signs and blood sugar upon their arrival, but she remained "unconscious" with occasional nonpurposeful movements. Upon arrival to the ED, the clinician performed a sternal rub, at which point the patient's eyes opened, she localized to push hands away, and said "stop that." Her GCS was 12. She did not respond to naloxone. Vital signs on arrival were HR 87 and BP 140/83 mmHg. Urine drug screen was positive for THC. Head CT was negative.

An hour after arrival, the patient's behavior was still altered. She occasionally would follow commands and state, "I am tired," but then would not answer any more questions and would blink her eyes and smack her lips. At this point, her mental status level was only A and O (alert and oriented) x 1.

Two hours after arrival, she became increasingly lucid and began to answer questions appropriately. She stated that the evening of her presentation, just before going to work, she consumed 2 delta-8 gummies, which she had never tried before. She denied any other substance use. She eventually was discharged in a normal mental state 6 hours after her initial arrival. Her transient severe altered mental status was attributed to delta-8.

Case 3

A 5-year-old female presented to the ED with her mother with concerns of dizziness, abdominal pain, pallor, and lethargy. When her mother picked her up from her father's house, he noted that she was complaining of dizziness and stomach pain. Her mother noted that she seemed unsteady with ambulation and was lethargic. When the clinician entered the room, the patient was staring at the ceiling and unable to answer questions. She was looking around the room, opening and closing her eyes, but she was not responsive to commands from her mother or the clinician.

She continued to be somnolent with a GCS of 10 and her oxygen level briefly desaturated to 80%. She was started on 0.5 L nasal cannula oxygen, was placed on end-tidal CO_2 monitoring, and remained responsive to physical stimuli. Her urine drug screen was positive for THC. At that time, it was revealed that on the day of presentation while in her father's care, she had consumed 12 delta-8 THC gummies, total of approximately 324 mg. Poison Control recommended 4-hour observation and supportive care, after which the patient was transferred to Minnesota Children's Hospital for further monitoring. She improved in the ED and was discharged home.

Case 4

A 21-year-old female presented to the ED via EMS with altered mental status, agitation, and concern for overdose. On the way to the ED, EMS reported she was agitated, screaming, and hallucinating. She became aggressive and was given 5 mg of midazolam en route.

Upon arrival to the ED, the patient was somnolent but still intermittently thrashing on the cot. She followed 1-step commands and spoke nonsensical words. Her GCS score was 12, HR 121, BP 116/81, respiratory rate 18, oxygen saturation (SPO_2)96%, and temperature 36.8 °C. She eventually became violent with staff due to hallucinations and received another 5 mg of midazolam. Over the next hour, her SPO_2 desaturated to the upper 90% with some sonorous respirations. She responded to jaw thrusts and eventually received a nasal trumpet for airway support overnight. Throughout the night, she was intermittently agitated attending to auditory and visual hallucinations. After these episodes, she would fall back to sleep, again requiring the nasal trumpet. Labs were significant for ethyl alcohol 249 and a urine drug screen positive for THC. Head CT was negative. Her significant other reported that she ingested delta-8 with alcohol that evening.

Nine hours after she presented to the ED, she was able to be assessed. She reported that she was smoking delta-8 and drinking the previous night. After a total of 14 hours in the ED, she was discharged home at her baseline mental status. The altered mental status, hallucinations, and erratic behavior all attributed to the ingestion of delta-8 with alcohol.

Case 5

A 25-year-old male presented to the ED for what he described as a sensation of chest tightness associated with "anxiety and a racing heart." He stated that prior to the onset of his symptoms, he ingested a delta-8 THC oil that he had purchased that day from a dispensary. Prior to arrival, he took approximately 13 mL of a 30 mL bottle; the recommended dose was 0.5 mL.

Vital signs at presentation included HR 146, BP 172/98, respiratory rate 25. Labs were unremarkable. No urine drug screen was performed. Poison Control was contacted and recommended a 4-hour observation. He received lorazepam 1mg intravenously, as well as 1L of normal saline. At time of discharge, his heart rate was 90 beats per minute. His tachycardia and anxiety were attributed to delta-8 intoxication.

Case 6

A 57-year-old male presented to the ED for dizziness, diaphoresis and "an odd feeling in his chest." He stated that he took his normal regimen of morphine and methocarbamol with dinner. Approximately 30 minutes later, he took 3 delta-8 gummies,

which he had not tried previously. An hour after ingestion, he started to feel sweaty, weak, dizzy, and had chest pressure leading to the ED visit.

Vital signs at presentation were HR 87-97, BP 152/92. Electrocardiogram and cardiac markers were negative for acute coronary syndrome. Urine drug screen was positive for opioids (prescribed home medication) and THC. He was given intravenous (IV) fluids and monitored. Five hours after presentation, his chest pressure resolved and he was discharged home in stable condition. His diaphoresis, dizziness, and chest discomfort were attributed to delta-8 ingestion.

DISCUSSION

What is Delta-8?

Delta-8 tetrahydrocannabinol (delta-8 THC) is a cannabinoid that is a double-bond isomer of the better-known delta-9 THC. Delta-8 THC was first derived from the cyclization of cannabidiol (CBD) in the 1940s and was found to be highly psychoactive in humans. By the 1960s, it was discovered that delta-8 THC was naturally present in small amounts of cannabis and cannabis-derived products.[1]

Delta-8 THC occurs naturally in hemp and marijuana in very low quantities. In order to get larger quantities of delta-8 THC, additional chemicals are needed to convert other cannabinoids in hemp into delta-8 THC, hence the term "synthetic THC." This synthesizing process is not regulated by the US Food and Drug Administration (FDA). Therefore, the manufacturing of delta-8 THC products may occur in uncontrolled or unsanitary settings, which may lead to the presence of unsafe contaminants or other potentially harmful substances.[2]

Regulatory Status

There is much debate around the legality of delta-8 THC. Its regulatory status changes almost monthly and varies from state to state. The Agriculture Improvement Act of 2018[3] (ie, the "Farm Bill") legalized hemp, its derivatives, and extracts. Hemp is defined as a cannabis plant containing no more than 0.3% of delta-9 THC. As previously discussed, very small quantities of delta-8 are found in synthesized hemp.[4] With this definition, delta-8 THC is a "legal" hemp derivative.

At authorship of this case series, delta-8 THC is legal in 29 states, including Wisconsin, and 1 district. Nine other states have rules and regulations surrounding the use of delta-8 THC.[5] In the states like Wisconsin where delta-8 THC is legal, it is readily accessible to patients over the counter in many vape or smoke shops, gas stations, other convenience stores, and in online retailers.

Healthcare Burden

According to the FDA, national poison control centers received 2362 exposure cases of delta-8THC products between January 1, 2021 through February 28, 2022.[2] Of the reported cases, 58% involved adults, and 41% involved pediatric patients. Forty percent of ingestions were unintentional exposures to delta-8 THC, and 82% of these unintentional exposures affected pediatric patients.[2] Seventy percent required evaluation at a health care facility, and 8% of these resulted in admission to a critical care unit. Most patients requiring evaluation at a health care facility were pediatric patients, and there was 1 report of a pediatric fatality during this time frame.[2]

Delivery Mechanism

Delta-8's 2 most common forms of ingestion are oral consumption and smoking/inhalation. Delta-8 THC is available in the form of edibles, such as gummies or candy, with colorful packaging that makes them more attractive to children and in vape cartridges to be inhaled by the user. Other available products include pure delta-8 THC oil, "flower," "crumble," prerolled blunts, cigarettes, soft gels, capsules, drink flavorings, and sodas. As with the synthesis of delta-8 THC, there is no regulation of the products containing the chemical.

Symptoms

Delta-8 THC has psychoactive and intoxicating effects, similar to that of delta-9 THC.[1] THC is known to act at a number of receptor sites. Dopaminergic, cholinergic, noradrenergic, serotonergic, and γ-aminobutyric acid are all receptors affected, as well as a number of neuropeptides that all play a role in the symptoms seen in patients presenting to the ED.[6]

In mild to moderate cases of delta-8 THC intoxication, symptoms are what one would expect to see with marijuana intoxication, including somnolence, euphoria, alterations of senses and time perception, depersonalization, loss of social inhibition, giddiness, and mood alterations.[6] Severe symptoms of toxicity include lethargy, uncoordinated movements and decreased psychomotor activity, slurred speech, increased heart rate progressing to slowed heart rate, hypotension, difficulty breathing, seizures, sedation, and, eventually, coma. These effects occur regardless of ingestion route.[6]

Testing for Delta-8

Currently, there is not a widely available test specifically for delta-8 THC. As with the cases presented here, a urine drug screen will likely be positive for THC. A study published in 2022 determined that if someone is using delta-8-THC, the method initially developed to detect THC is able to detect it in the urine sample.[7] Once an immunoassay positive sample has been identified, a chromatographic method would be necessary to differentiate between delta-8 and delta-9 because they are so structurally similar.[7]

In the current ED practice setting, determining what strain of THC the patient ingested comes down to a good patient history and report from EMS or family. It is often helpful to ask specifically about delta-8 use versus a general question about rec-

reational drug use, as some patients may not consider delta-8 a recreational drug.

Treatment Options

There is no antidote or reversal for delta-8 THC like that available for acetaminophen and opioid intoxications. Management for delta-8 ingestion consists primarily of supportive care and includes benzodiazepines for agitation, tachycardia, and seizures. Fluids can be given for hypotension followed by vasopressors if necessary.[6]

In severe toxicity, altered mental status and obtundation may require airway support. There have also been reports of atrial fibrillation and other cardiac dysrhythmias in patients after ingesting that should receive supportive care the appropriate corresponding care. Poison control centers also have reported patients presenting with hypomagnesemia. These patients should be treated with the appropriate corresponding IV magnesium replacement for their age and current magnesium level.[6]

CONCLUSIONS

With widespread access to delta-8 THC in Wisconsin and across the rest of the United States, EDs will see an increase in delta-8 THC intoxications. This case series is a snapshot of the burden experienced by EDs due to the availability of delta-8 THC. Though there is no antidote, good supportive care is effective in caring for these patients. Since delta-8 and delta-9 THC are structurally similar, a patient who has ingested delta-8 THC will test positive for THC on a urine drug screen. Clinicians should maintain a high index of suspicion for delta-8 use, especially in patients with altered mental status, anxiety, or cardiac symptoms

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REFERENCES

1. Tagen M, Klumpers LE. Review of delta-8-tetrahydrocannabinol (delta-8-THC): comparative pharmacology with delta-9-THC. *Br J Pharmacol.* 2022;179(15):3915-3933. doi:10.1111/bph.15865

2. 5 things to know about delta-8 tetrahydrocannabinol – delta-8 THC | FDA. US Food and Drug Administration. Reviewed May 4, 2022. Accessed February 3, 2023. https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc

3. An act to provide for the reform and continuation of agricultural and other programs of the Department of Agriculture through fiscal year 2023, and for other purposes, HR 2, 115th Congress (2017-2018). Accessed September 3, 2023. https://www.congress.gov/bill/115th-congress/house-bill/2

4. Gussow L. Toxicology rounds: your ED Patients are likely using delta-8. *Emer Med News.* 2021;43(8):18. Accessed February 3, 2023. https://journals.lww.com/em-news/fulltext/2021/08000/toxicology_rounds__your_ed_patients_are_likely.17.aspx

5. Is delta-8 THC legal? A state-by-state analysis. Updated October 31, 2023. Accessed February 3, 2023. https://cbdoracle.com/news/policy/delta-8-thc-legal/

6. Marijuana. Micromedex (electronic version). Merative; 2023. Accessed April 2, 2023. https://www.micromedexsolutions.com

7. Garg U, Baird S, Frazee C. Can current immunoassay and gas-chromatography mass spectrometry (GC-MS) methods for delta-9-tetrahydrocannabinol carboxylic acid (delta-9-THC-COOH) detect delta-8-THC-COOH? Poster presented at: AACC Annual Scientific Meeting and Clinical Lab Expo; July 24-28, 2022; Chicago, IL. Accessed February 3, 2023. https://www.abstractsonline.com/pp8/#!/10594/presentation/293

Prolonged COVID-19 Pneumonitis and Severe Lung Injury in a Patient with a History of Diffuse Large B-cell Lymphoma after CAR-T Therapy: Highlighting the Role of Corticosteroids

Mark Ehioghae, MSc; Harini Shah, BS; Anu Taylor, MD; Brian Buggy, MD; Gabriel Mikhael, MD

ABSTRACT

Introduction: COVID-19 can have severe consequences for immunocompromised individuals, including those with hematological malignancies. Prolonged infections causing pneumonia and lung injury are rare in patients with diffuse large B-cell lymphoma (DLBCL) treated with chimeric antigen receptor T-cell (CAR-T).

Case Presentation: A 43-year-old male with a history of DLBCL, in remission for 2 years after CAR-T therapy, developed a persistent COVID infection, as confirmed via positive polymerase chain reaction. This slowly progressed to symptomatic hypoxemic pneumonitis and biopsy-proven diffuse alveolar damage, which responded to corticosteroid treatment.

Discussion: COVID-19 poses increased risks to patients with a history of hematologic malignancies and can lead to severe respiratory distress and mortality. Studies have shown prolonged pneumonitis may require corticosteroids for improvement. However, data on appropriate regimen for managing prolonged COVID-19 pneumonitis are lacking.

Conclusions: This case highlights challenges of the treatment of COVID-19 infections in immunocompromised individuals with hematological malignancies. Corticosteroid treatment shows benefits, but dosing and duration should be based on individual patient response. Extended monitoring, individualized treatment plans, and research are crucial for optimizing outcomes in this vulnerable population.

INTRODUCTION

As of May 2023, the United States has witnessed the significant impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in terms of 98 million COVID-19 cases and 1 128 903 deaths.[1] While most COVID-19 infections have been mild, immunocompromised individuals with hematological malignancies are at a higher risk of developing severe disease and experiencing increased mortality, even following a mild infection.[2] Immunocompromised patients have been observed to have persistent and prolonged COVID-19 infections, leading to secondary organizing pneumonia or severe lung injury, including the presence of hyaline membranes consistent with diffuse alveolar damage.[3,4] However, such manifestations are seen rarely in patients who are 2 years removed from treatment of diffuse large B-cell lymphoma (DLBCL) with chimeric antigen receptor T-cell (CAR-T) therapy.

In this report, we present a case of a patient who exhibited persistent COVID-19 positivity for 2.5 months, presenting as organizing pneumonia, despite being 2 years post-CAR-T treatment for DLBCL. Notably, clinical improvement was achieved only after the initiation of high-dose systemic corticosteroids.

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CASE PRESENTATION

A 43-year-old male with a history of mediastinal DLBCL in remission for 2 years after CAR-T therapy presented with cough, myalgia, and headache on day 1. Chest x-ray and computed tomography (CT) of the chest were normal (Figure 1). A qualitative antigen test for the presence of SARS- CoV-2 (Abbott BinaxNOW) was positive. He was given symptomatic treatment. Prior COVID vaccinations were with Moderna mRNA-1273 vaccine 13, 12, 11, and 6 months prior to presentation.

The patient had persistent cough, malaise, and mild exertional dyspnea. He then developed a severe diffuse headache and presented to hospital again on day 21 of his illness. CT of the head suggested mild cerebral edema, which was confirmed on magnetic resonance imaging, with the addition of diffuse dural thickening. Cerebrospinal fluid analysis was completely normal with a nega-

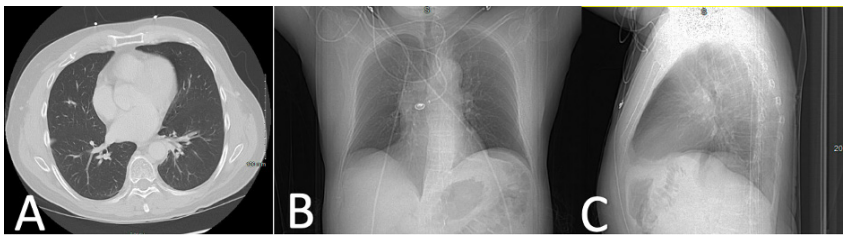
tive viral encephalitis panel and negative cytology. Peripheral blood analysis showed total white blood cell count was 2.4 K/mcl with an absolute neutrophil count of 2.2 K/mcl and a total lymphocyte count of 0.5 K/mcl. COVID-19 polymerase chain reaction (PCR) (Cepheid Xpert N-2 platform) was positive with a cycle threshold of 36.3. He was treated symptomatically without remdesivir or steroids, but symptoms persisted with continued fever, chills, nonproductive cough, and increasing dyspnea. However, his headache resolved by day 35.

Respiratory symptoms worsened, and on day 51, chest x-ray revealed bilateral ground glass opacities. Pulse oximetry on room air at rest was 93%. He was treated with empiric azithromycin and ceftriaxone. Blood cultures, urinary antigens for *Legionella pneumophila* and *Streptococcus pneumoniae*, and a multiplex viral respiratory panel were negative. COVID PCR remained positive at a cycle threshold of 34.5. Total lymphocyte count remained at 0.6 K/mcl. IgG was 406 mg/dl (reference range 700-1600), IgA was 38 (reference range 70-400), and IgM was 37 (reference range 40-250). He refused treatment with remdesivir and was given prednisone 40 mg daily (approximately ½ mg/kg/day) with a 3-week taper with no clinical improvement.

Two weeks later on day 65, he presented to the hospital again with worsening infiltrates on both chest x-ray and chest CT (Figure 2), now with resting hypoxemia of 83%. This improved to 96% on 4 liters/minute of supplemental oxygen. COVID cycle threshold was unchanged at 34.6. Bronchoscopy was performed, and all infectious diagnostic studies on lavage fluid (bacterial, fungal, mycobacterial, viral) were negative except for a barely detectable *Aspergillus galactomannan* antigen on 1 of 2 bronchoalveolar lavage specimens (index value of 0.60 with threshold of <0.50, ARUP Labs). He was given posaconazole while awaiting 16s ribosomal DNA analysis for bacteria and mycobacteria with 28s ribosomal DNA for fungi (University of Washington), all of which were ultimately negative. Transbronchial biopsy revealed diffuse alveolar damage with hyaline membrane formation (Figure 3).

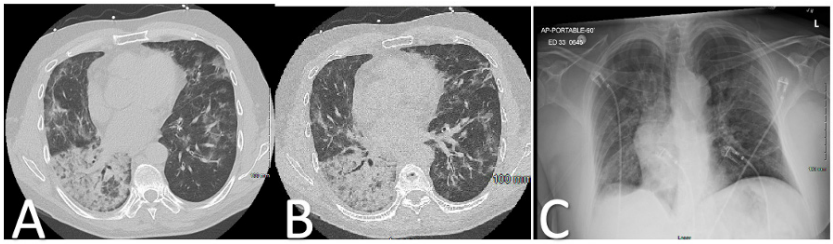
Intravenous methylprednisolone at 1 mg/lg/day for 5 days was administered with rapid clinical improvement. He was placed on a prolonged (2 month) prednisone taper starting at 0.75 mg/kg/day with sustained clinical resolution of his symptoms and clearance of the infiltrates on chest x-ray.

Figure 1. Computed Tomography (CT) and Chest X-ray of the Patient on Day 1



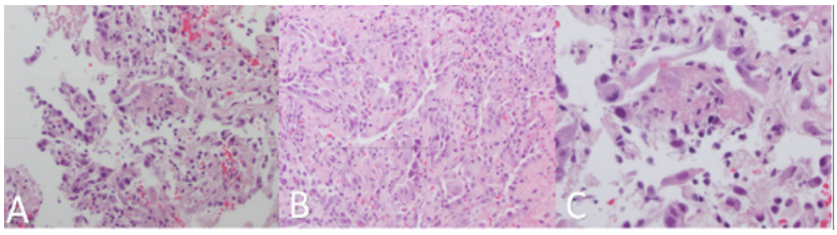
A: Axial chest CT.
B and C: Anterior/posterior and lateral chest x-ray.

Figure 2. Computed Tomography (CT) and Chest X-ray of Patient on Day 65



A and B: Axial chest CT of bilateral ground glass opacities.
C: Anterior/posterior chest x-ray of interstitial infiltrates

Figure 3. Biopsy Images



A and B: Biopsy of intact alveolar membranes within alveolar spaces.
C: Biopsy of organizing phase of hyaline membranization.

DISCUSSION

In immunocompetent individuals, a mild COVID-19 infection typically resolves within 4 weeks.[3] However, patients with malignancies who contract COVID-19 often experience severe respiratory distress and higher mortality rates.[2,3]

Similar cases have been described by Golbets et al,[5] where a patient with a history of DLBCL and receiving maintenance rituximab showed improvement after introducing corticosteroids to treat secondary organizing pneumonitis associated with COVID-19. Siafarikas et al[6] presented 2 cases of patients who deteriorated rapidly with organizing pneumonia after acute COVID-19 infec-

tion, with clinical improvement seen after corticosteroid (methylprednisolone at 1 mg/kg/day) intervention. Dayco et al[7] described a patient in remission from DLBCL after chemotherapy who contracted COVID-19, developed pulmonary fibrosis, and showed improvement following high-dose corticosteroid treatment starting with prednisone 40 mg for 1 week, subsequently decreasing by 5 mg every 7 days.

In contrast, Hensley et al[8] presented a patient with prolonged COVID-19 positivity who did not receive early high-dose corticosteroid treatment. The patient, an immunocompromised individual on CAR-T therapy, received standard COVID-19 interventions but ultimately died from respiratory failure. The timing, dosage, and severity of COVID-19 are crucial factors influencing the outcomes of corticosteroid treatment, which has been associated with decreased all-cause mortality in hospitalized COVID-19 patients.[9,10] However, no standardized protocol currently exists for managing patients with prolonged COVID-19 pneumonitis and pulmonary manifestations. We believe that our patient's initial lack of response to prednisone was based on insufficient dosing of steroids, and his prompt response to higher dosing supports this conclusion.

It is important to note that in our case, the patient had not undergone CAR-T therapy for nearly 2 years. Studies have shown that patients who have undergone CAR-T therapy may experience neutropenia beyond 3 months[11] and cytopenia lasting 15 to 21 months post-therapy.[12] Despite our patient's total leukocyte count being within normal limits, lymphocyte counts remained consistently below the reference range, potentially impairing effective clearance of the COVID-19 virus and resulting in persistent positivity.[13,14] Hill et al[15] reported that viral infections are the most common pathogens within 28 days after CAR-T infusion, with fungal infections such as aspergillus increasing after 90 days. However, as demonstrated in our patient's case, these infection risks may extend far beyond the expected timeframe—as seen in our case for up to 2 years—which emphasizes the importance of extended monitoring.

CONCLUSIONS

This case report underscores the enduring challenges posed by severe COVID-19 in individuals, persisting up to 2 years following CAR-T therapy for hematological malignancies. The occurrence of prolonged viral activity in these patients accentuates the potential role of sustained lymphopenia, indicating the need for prolonged vigilance and monitoring. Notably, the positive response to high-dose steroids demonstrated in this case suggests a viable therapeutic avenue for managing severe COVID-19 complications in immunocompromised individuals with a CAR-T therapy history. However, the absence of a standardized protocol highlights the complexity of prolonged COVID-19 pneumonitis in this unique population, emphasizing the urgent necessity for further research. The imperative for ongoing investigation is clear, as elucidating the timing, dosage, and overall efficacy of interventions is paramount to refining treatment strategies and ultimately improving outcomes in this specific and vulnerable patient cohort.

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REFERENCES

1. COVID data tracker. Centers for Disease Control and Prevention. Accessed September 20, 2023. https://covid.cdc.gov/covid-data-tracker

2. Acar IH, Guner SI, Ak MA, et al. Impact of COVID-19 on outcomes of patients with hematologic malignancies: a multicenter, retrospective study. *Mediterr J Hematol Infect Dis*. 2022;14(1):e2022074. doi:10.4084/MJHID.2022.074

3. Fung M, Babik JM. COVID-19 in immunocompromised hosts: what we know so far. *Clin Infect Dis*. 2021;72(2):340-350. doi:10.1093/cid/ciaa863

4. Cappell KM, Kochenderfer JN. Long-term outcomes following CAR T cell therapy: what we know so far. *Nat Rev Clin Oncol*. 2023;20(6):359-371. doi:10.1038/s41571-023-00754-1

5. Golbets E, Kaplan A, Shafat T, et al. Secondary organizing pneumonia after recovery of mild COVID-19 infection. *J Med Virol*. 2022;94(1):417-423. doi:10.1002/jmv.27360

6. Siafarikas C, Stafylidis C, Tentolouris A, et al. Radiologically suspected COVID-19-associated organizing pneumonia responding well to corticosteroids: a report of two cases and a review of the literature. *Exp Ther Med*. 2022;24(1):453. doi:10.3892/etm.2022.11379

7. Dayco JS, El-Reda Z, Sumbal N, Alhusain R, Raheem S. Perpetually positive: post-COVID interstitial lung disease in an immunocompromised patient with diffuse large B-cell lymphoma. *J Investig Med High Impact Case Rep.* 2021;9:23247096211041207. doi:10.1177/23247096211041207

8. Hensley MK, Bain WG, Jacobs J, et al. Intractable coronavirus disease 2019 (COVID-19) and prolonged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication in a chimeric antigen receptor-modified T-cell therapy recipient: a case study. *Clin Infect Dis.* 2021;73(3):e815-e821. doi:10.1093/cid/ciab072

9. Amponsah SK, Tagoe B, Adams I, Bugyei KA. Efficacy and safety profile of corticosteroids and non-steroidal anti-inflammatory drugs in COVID-19 management: a narrative review. *Front Pharmacol*. 2022;13:1063246. doi:10.3389/fphar.2022.1063246

10. Matthay MA, Wick KD. Corticosteroids, COVID-19 pneumonia, and acute respiratory distress syndrome. *J Clin Invest*. 2020;130(12):6218-6221. doi:10.1172/JCI143331

11. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1-2 trial. *Lancet Oncol*. 2019;20(1):31-42. doi:10.1016/S1470-2045(18)30864-7

12. Cordeiro A, Bezerra ED, Hirayama AV, et al. Late events after treatment with CD19-targeted chimeric antigen receptor modified T cells. *Biol Blood Marrow Transplant.* 2020;26(1):26-33. doi:10.1016/j.bbmt.2019.08.003

13. Dao TL, Hoang VT, Gautret P. Recurrence of SARS-CoV-2 viral RNA in recovered COVID-19 patients: a narrative review. *Eur J Clin Microbiol Infect Dis*. 2021;40(1):13-25. doi:10.1007/s10096-020-04088-z

14. Devonshire AL, Makhija M. Approach to primary immunodeficiency. *Allergy Asthma Proc.* 2019;40(6):465-469. doi:10.2500/aap.2019.40.4273

15. Hill JA, Li D, Hay KA, et al. Infectious complications of CD19-targeted chimeric antigen receptor-modified T-cell immunotherapy. *Blood*. 2018;131(1):121-130. doi:10.1182/blood-2017-07-793760

Nonsurgical Management of a Traumatic, Full-Thickness Corneal Laceration: A Case Report

Leslie Huang, MS; Jennifer Larson, MD

ABSTRACT

Introduction: In this report, we describe a case of a large, full-thickness traumatic cornea laceration that was managed nonsurgically.

Case Presentation: A 22-year-old male presented with a red, painful right eye 4 days after a work-related injury. He was found to have a 6.5 mm full-thickness corneal laceration. The wound was Seidel negative, so the decision was made to manage the laceration nonsurgically. The patient did not develop endophthalmitis or wound complications, and his corrected visual acuity recovered to 20/25.

Discussion: Full-thickness cornea lacerations and lacerations larger than 3 mm routinely necessitate surgical intervention in a sterile environment, while medical management is typically reserved for partial-thickness or small, self-sealing lacerations. Surgical repair of lacerations can lead to resultant astigmatic problems, even when performed in ideal conditions and, therefore, should be avoided when possible. Through careful examination and close follow-up, our patient with a large full-thickness laceration was successfully treated nonsurgically and able to avoid associated complications.

Conclusions: This report expands the literature of the appropriate management of cornea lacerations.

INTRODUCTION

Corneal lacerations represent an important sequela of ocular trauma that can cause significant ocular morbidity. Eliciting a detailed history regarding the nature of the injury and performing a thorough examination are crucial in determining the best course of management. All lacerations require prompt treatment to minimize risk of infection and permanent visual disability, with the ultimate goal of restoring meaningful vision.[1]

Specific management of a corneal laceration is dependent on many different factors, notably the extent of the injury and the risk of complications. For example, larger lacerations are more likely to require surgical repair, whereas smaller or partial-thickness lacerations may be treated with conservative medical management.[2] Additionally, the mechanism of injury may prompt further evaluation; traumas that involve possible fragments necessitate radiologic imaging to rule out the presence of intraocular foreign bodies.[3] Developing a cohesive treatment plan for corneal lacerations is complex and requires careful evaluation of the injury to determine the risks and benefits of medical versus surgical management.

Here, we present a case of nonsurgical management of a large, traumatic, full-thickness corneal laceration in a young male patient.

CASE PRESENTATION

A 22-year-old male patient was referred for ophthalmological evaluation after sustaining a traumatic corneal laceration. He presented with right eye pain, redness, and tearing 4 days after a work-related injury. He reported possible metal hitting his right eye underneath protective safety glasses, with no noticeable bloody drainage or loss of fluid. Despite prompt irrigation and use of artificial tears, his symptoms continued without improvement, so he sought ophthalmological care.

At initial presentation, a full ocular examination was per

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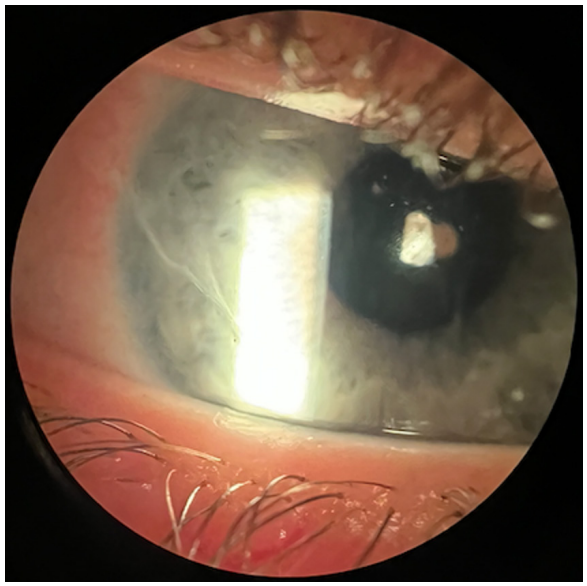
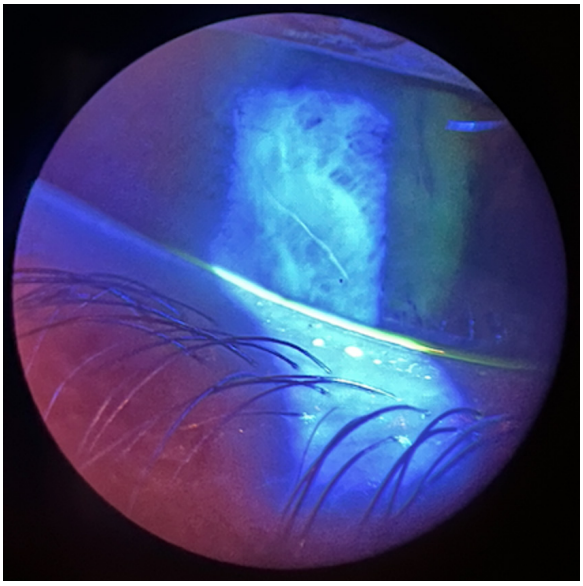
Figure 1. Slit Lamp Photograph of the Right Eye Taken During Initial Ophthalmic Evaluation Four Days After Eye Injury



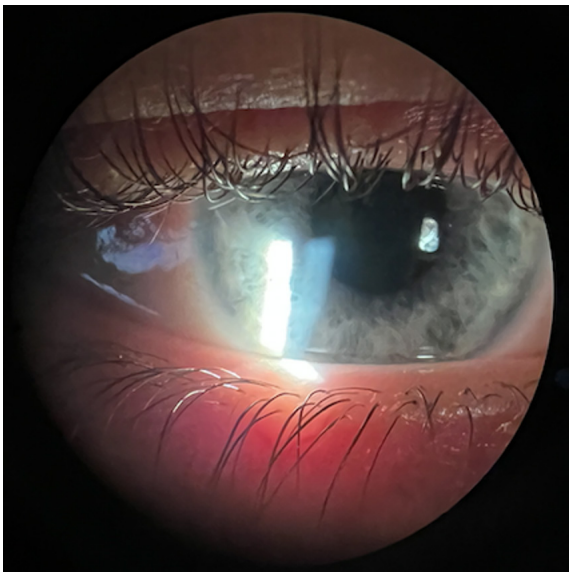
A 6.5 mm diagonal corneal, full-thickness laceration is noted (black arrow). Subtle corresponding Descemet's fold are also seen.

Figure 2. Fluorescein Staining of the Right Eye



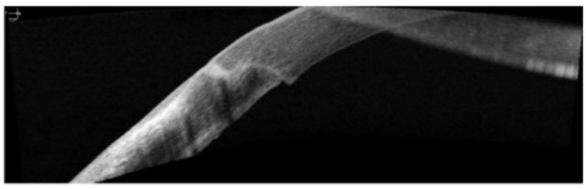
The cornea laceration was Seidel negative and remained so even when pressure was applied to the globe.

Figure 3. Slit Lamp Photograph of the Right Eye



The anterior chamber is deep and well formed. No hyphema or hypopyon is seen.

Figure 4. Anterior Segment and Cornea Optical Coherence Tomography of the Right Eye



A full-thickness laceration is demonstrated.

formed. Best corrected visual acuity was 20/30 in the right eye and 20/40 in the left eye. The right pupil was noted to be smaller than the left but reacted appropriately without an afferent pupillary defect. Anterior segment examination revealed a 6.5 mm diagonal, well-approximated corneal-limbal laceration with corresponding Descemet's fold (Figure 1). The wound was Seidel negative (Figure 2), even with pressure applied to the globe. The anterior chamber was formed with trace anterior chamber cells (Figure 3). The remainder of the anterior and posterior segment examination was unremarkable. Anterior segment and cornea optical coherence tomography confirmed the laceration was full thickness (Figure 4). Intraocular pressure was not measured to avoid unnecessary manipulation of the globe. A maxillofacial computed tomography scan revealed no intraocular or intraorbital foreign body. The patient received tetanus prophylaxis and prophylactic intravenous antibiotics (moxifloxacin).

After the initial evaluation, the patient's eye was covered with a rigid Fox eye shield, and he was given strict orders of bed rest and prescribed topical steroid (prednisolone) and topical antibiotic (moxifloxacin) eye drops. Prophylactic oral antibiotics were not prescribed as they are not used routinely for open globe injuries.

The patient returned for follow-up 1 day and 1 week after the initial ophthalmologic exam, and he reported adhering to the

medication regimen and activity restrictions with improving photophobia and eye discomfort. At the 6-week follow-up appointment, best corrected visual acuity improved to 20/25-2 in the right eye, and he recovered without further ocular co morbidity, endophthalmitis, or wound complications.

DISCUSSION

Corneal lacerations are most commonly managed with surgical repair, however there are some limited circumstances where these injuries may be managed medically. Many patients with eye trauma present to primary care, urgent care, or the emergency department and not the eye clinic, so it is imperative for these clinicians to be comfortable with the initial workup and management of ocular trauma—including corneal lacerations—and to initiate emergent consultation with an ophthalmologist when an open globe injury is suspected.

Further, the majority of ocular traumas presenting to the emergency department involve corneal injury, including full-thickness corneal lacerations due to traumatic foreign bodies.[4] Clinical course and visual outcomes vary widely depending on the mechanism of injury, the extent of the injury, and the time to treatment. A rapid and thorough evaluation of the injury is needed to determine whether the best course of action is medical or surgical intervention.

A patient presenting with ocular trauma should first be evaluated for other traumatic injuries. Clinicians must complete a primary and secondary trauma survey unless the injury is limited to the eye. When the patient is deemed medically stable, it is then important to evaluate the extent of the ocular injury. Broadly, ocular trauma can be characterized as open globe or closed globe. Open globe injuries (OGI) are full-thickness lacerations and penetrating or perforating injuries to the eye.[5] History should focus on the mechanism and timing of injury, as these circumstances can raise suspicion for an open globe and risk for endophthalmitis. If possible, visual acuity assessment, pupillary responses, and external examination should be completed prior to ophthalmologic consultation. Clinicians should avoid placing direct pressure on the eye due to the concern for extrusion of ocular contents and worsening the extent of the injury; therefore, intraocular pressure should not be measured.[6] Any leakage or extrusion of intraocular contents is diagnostic of OGI. To aid in the visualization of aqueous humor loss, a Seidel test may be performed by placing fluorescein on the ocular surface and looking for a stream of leaking fluid under cobalt blue lighting.[5] Other suggestive signs of OGI include a shallow anterior chamber, peaked pupil (as a result of iris tissue being pulled toward the wound by a strand of vitreous tissue), 8-ball hyphema (complete filling of the anterior chamber with blood), 360-degree subconjunctival hemorrhage, and irregular scleral or corneal contour. Finally, it is important to perform a complete examination of the uninjured eye as well. If an OGI is suspected or detected, the eye should be covered with a rigid Fox shield, and ophthalmologic consultation should be requested immediately.

The goals of traumatic corneal injury repair are to maintain a watertight globe, prevent hypotony, restore anatomy, and prevent infection.[7] For partial-thickness or small corneal lacerations, the options for medical management are well-established. Patching and therapeutic soft contact lenses can provide structural support by acting as mechanical splints and preventing leakage in pinpoint lacerations or very small perforations.[8] Tissue adhesives, such as cyanoacrylate, also may be used to approximate irregular wound edges and additionally provide the advantage of allowing immediate closure of a wound that can be done in the outpatient setting.[2]

In our case, the size of the laceration was larger than those typically managed conservatively; full-thickness cornea lacerations and lacerations larger than 3 mm routinely necessitate surgical intervention and are most often managed through surgical repair in a sterile environment.[8] The conventional method of repair is utilizing 10-0 nylon interrupted sutures to restore the original anatomy and create watertight wound closure.[9] However, there are advantages to nonsurgical management of corneal lacerations, such as avoiding the risks associated with general anesthesia and avoiding surgically induced irregular astigmatism from the corneal sutures. A significant cause of visual disability in patients with corneal lacerations is the development of high astigmatism due to irregularity in the corneal surface.[1] Even with careful surgical techniques and perfect approximation of wound edges, there is still a risk of visually significant surgically induced irregular astigmatism postoperatively.[10] Furthermore, self-sealing lacerations have been found to confer higher risks of intraocular foreign bodies, endophthalmitis, and other complications that should lead to prompt evaluation for surgical management. Watanachai et al reported a study with 591 OGI patients in which a higher distribution of endophthalmitis and delayed presentation to the hospital were observed in patients with self-sealing wounds compared to patients requiring primary wound repair (P values < 0.001).[11] The self-sealing nature of our patient's laceration, combined with the delayed presentation and size of the wound, made this an unusual case of medical management of a traumatic corneal laceration.

We reported here a case of a large traumatic, full-thickness corneal laceration that was managed nonsurgically. The patient presented 4 days following the initial injury. Full ophthalmological examination revealed a self-sealing, full-thickness, peripheral laceration with no iris or vitreous prolapse and no evidence of infection, despite the passage of 4 days since the initial injury. We speculate that healing may have occurred in the time between injury and initial presentation—especially given the peripheral location of the laceration. The increased thickness of the peripheral cornea, as well as the involvement of the limbus—a critical reservoir for corneal epithelial stem cells, likely accelerated wound healing and helped prevent OGI complications.[12]

This case was reported to show that with careful evaluation and

conservative management, we were able to avoid surgery and associated complications and, importantly, achieve good visual acuity. Surgical care remains the standard of care for open globe injuries, however, conservative management was appropriate here because of the lack of intraocular foreign body and self-sealing nature of the wound. Reviewing return precautions (asking the patient to return immediately for worsening eye pain, redness, or decrease in vision) was also important for safely managing this wound conservatively.

CONCLUSIONS

Developing an optimal treatment plan for corneal lacerations is dependent on a thorough and rapid examination to evaluate the extent of the injury. Although the standard of care is to surgically repair full-thickness corneal lacerations, there are advantages to avoiding surgery, and select lacerations may be appropriate for nonsurgical management as this case demonstrates.

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REFERENCES

1. Hamill MB, Thompson WS. The evaluation and management of corneal lacerations. *Retina*. 1990;10 Suppl 1:S1-S7. doi:10.1097/00006982-199010001-00003

2. Vote BJ, Elder MJ. Cyanoacrylate glue for corneal perforations: a description of a surgical technique and a review of the literature. *Clin Exp Ophthalmol.* 2000;28(6):437-442. doi:10.1046/j.1442-9071.2000.00351.x

3. Beatty RF, Beatty RL. The repair of corneal and scleral lacerations. *Semin Ophthalmol.* 1994;9(3):165-176. doi:10.3109/08820539409060012

4. Channa R, Zafar SN, Canner JK, Haring RS, Schneider EB, Friedman DS. Epidemiology of eye-related emergency department visits. *JAMA Ophthalmol.* 2016;134(3):312-319. doi:10.1001/jamaophthalmol.2015.5778

5. Zhou Y, DiSclafani M, Jeang L, Shah AA. Open globe injuries: review of evaluation, management, and surgical pearls. *Clin Ophthalmol*. 2022;16:2545-2559. doi:10.2147/OPTH.S372011

6. Colby K. Management of open globe injuries. *Int Ophthalmol Clin*. 1999;39(1):59-69. doi:10.1097/00004397-199903910-00008

7. Hamill MB. Corneal and scleral trauma. *Ophthalmol Clin North Am*. 2002;15(2):185-194. doi:10.1016/s0896-1549(02)00018-4

8. Lin DT, Webster RG Jr, Abbott RL. Repair of corneal lacerations and perforations. *Int Ophthalmol Clin*. 1988;28(1):69-75. doi:10.1097/00004397-198802810-00010

9. Vora GK, Haddadin R, Chodosh J. Management of corneal lacerations and perforations. *Int Ophthalmol Clin*. 2013;53(4):1-10. doi:10.1097/IIO.0b013e3182a12c08

10. Swinger CA. Postoperative astigmatism. *Surv Ophthalmol*. 1987;31(4):219-248. doi:10.1016/0039-6257(87)90023-3

11. Watanachai N, Choovuthayakorn J, Chokesuwattanaskul S, et al. Risk factors and outcomes of post-traumatic endophthalmitis: a retrospective single-center study. *J Ophthalmic Inflamm Infect.* 2021;11(1):22. doi:10.1186/s12348-021-00254-2

12. Yoon JJ, Ismail S, Sherwin T. Limbal stem cells: central concepts of corneal epithelial homeostasis. *World J Stem Cells*. 2014;6(4):391-403. doi:10.4252/wjsc.v6.i4.391

Orofacial Actinomycosis Eroding Through Hard Palate: A Case Report

Stephanie Liu, MD; Charissa M. Etrheim, MD; Kevin M. McDonald, MD

ABSTRACT

Introduction: Actinomycosis is a rare, chronic, progressive bacterial infection caused by *Actinomyces* species with a reported incidence of 1 in 300 000. Actinomycosis has variable presentations and is commonly mistaken for malignancy and other infections, leading to delays in diagnosis and appropriate treatment. *Actinomyces* is a commensal bacteria found in the mouth, gut, and genitourinary tract. Actinomycosis tends to take advantage of anatomical defects for contiguous spread and can cause fistulas, sinus tracts, abscesses, and intrauterine device-associated infections.

Case Presentation: A 78-year-old White male with known dental caries came to a primary care clinic 2 days after noticing a painless, nonbleeding mass eroding from his hard palate. After a tissue biopsy of the mass showed a diagnosis of actinomycosis and advanced imaging showed no intracranial involvement, he was treated with a 6-month course of antibiotics, including oral amoxicillin, oral amoxicillin-clavulanate, and intravenous ertapenem.

Discussion: There are several case reports of actinomycosis with variable presentations, such as cutaneous nodules and sinus tracts. These cases frequently are associated with dental infections and procedures, trauma, oral surgery, or prior head and neck radiation. The condition is often mistaken for other infections or malignancy, which can delay appropriate treatment and increase the risk of complications.

Conclusions: Actinomycosis is a rare bacterial infection with variable presentations occurring throughout the body. This patient responded well to a prolonged course of intravenous and oral antibiotics and had complete healing of his hard palate defect. Actinomycosis is frequently misdiagnosed, leading to delays in appropriate treatment.

INTRODUCTION

Actinomycosis is a rare, chronic, progressive bacterial infection with a reported incidence of 1 in 300 000.[1] It is caused by *Actinomyces*, a commensal bacteria found in the mouth, gut, and genitourinary tract. Actinomycosis has variable presentations and is commonly mistaken for malignancy and other infections, leading to delays in diagnosis and appropriate treatment. It tends to take advantage of anatomical defects for contiguous spread and can cause fistulas, sinus tracts, abscesses, and IUD-associated infections.

In this report, we present the case of patient who presented with orofacial actinomycosis eroding through his hard palate.

CASE PRESENTATION

A 78-year-old White male with a history of hypertension presented to the primary care clinic with concerns of a painless mass eroding from his hard palate. He had no known allergies and was not taking any medications on a regular basis. He first noticed a dangling piece of tissue emerging from a hole in his right hard palate about 2 days earlier. He had no recent dental procedures and denied any significant trauma or injuries to the oral cavity. He reported otherwise feeling well, except for mild decreased energy and appetite over the previous month. He was not experiencing any associated bleeding, drainage, pain, fevers, or difficulty swallowing. Of note, his dentist recently had recommended extraction of tooth no. 1, where he had been experiencing mild pain.

Additionally, the patient had been seen 1 week prior in the primary care clinic for dizziness, intermittent right-sided head

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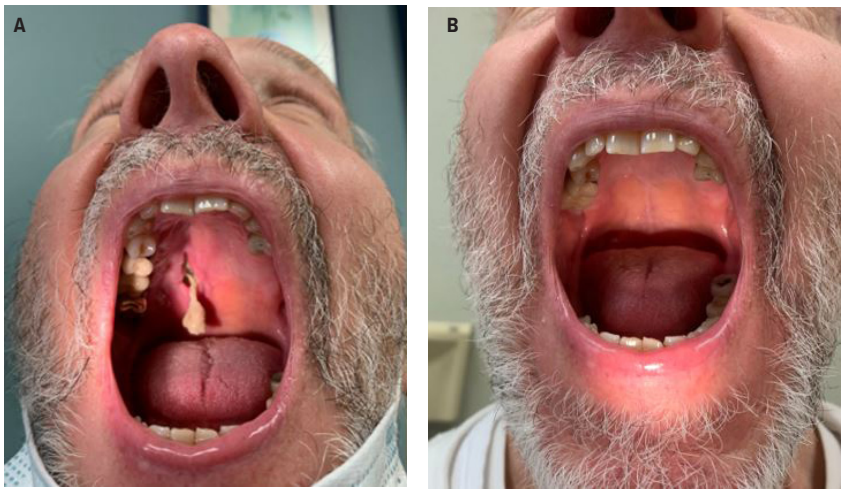
aches, and subtle static facial asymmetry. At the time of the previous clinic visit for dizziness, his hard palate was not examined, and he was sent to the emergency department for a stroke workup that was negative, including fast brain magnetic resonance imaging (MRI) that did not show any acute abnormalities.

On examination, the patient appeared well overall. His vital signs were normal, including his temperature. His speech sounded normal, and his previous dizziness and facial drooping had improved. In his mouth, he had multiple cavities and a visible hole in the right side of the hard palate with a white, soft lesion emerging into the oral cavity (Figure 1A). The lesion and hard palate were not tender to touch. For diagnostic purposes, the lesion was truncated by excising the accessible portion with scissors. The hard palate defect was not probed to its depth. The eroding mass was sent for surgical pathology evaluation. The patient had no bleeding or discomfort when the lesion was cut, and he did not require local anesthesia. There was some initial concern for cancer given the cavitary nature of the lesion. The subsequent histopathology report returned with clumped colonies of *actinomyces* sulfur granules.

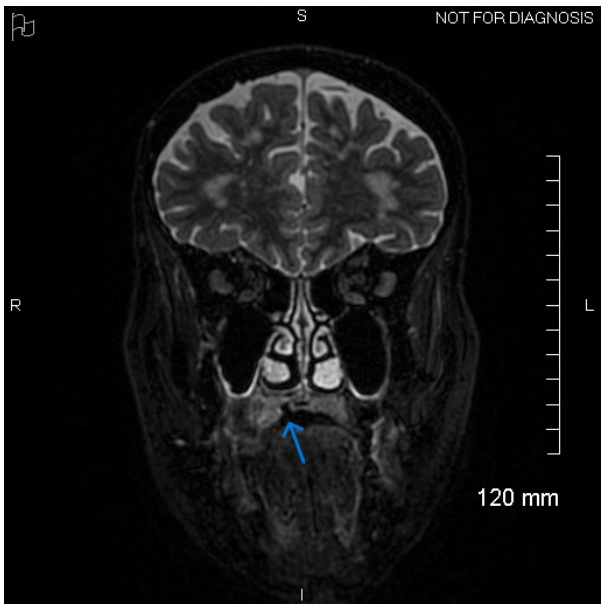
Figure 1. Photos of Patient's Oral Cavity



1A. Photo demonstrating mass eroding through the right hard palate, taken prior to biopsy.
1B. Photo demonstrating resolution of hard palate defect at 6-month follow-up.

The patient was referred to the Infectious Disease clinic for further evaluation and management of his orofacial *actinomyces* infection. Computed tomographic (CT) maxillofacial imaging with contrast demonstrated asymmetric enlargement of the right greater palatine foramen with a defect in the right palatine and with abnormal soft tissue attenuation in the right pterygopalatine fossa. An MRI brain with and without contrast was then performed to rule out intracranial involvement. This demonstrated an ulcerative lesion of the right hard palate and contiguous inflammatory changes in the right maxillary alveolus, right greater palatine canal, and right pterygopalatine fossa without extension into the orbit, central skull base, or brain parenchyma (Figure 2). He also was evaluated by an ear, nose, and throat (ENT) specialist for possible surgical intervention. The ENT specialist performed a punch biopsy at the base of the cavitary lesion to rule out malignancy. This biopsy was benign and showed squamous mucosa with evidence of inflammation. After reviewing the images, the ENT specialist indicated that surgical intervention was not needed.

Figure 2. Coronal Magnetic Resonance Imaging.



Arrow pointing to hard palate defect.

Per Infectious Disease recommendations, the patient was initiated on amoxicillin 500 mg and amoxicillin-clavulanate 875/125 mg every 8 hours, which served as a bridging therapy for 3 days until treatment with intravenous (IV) ertapenem was able to be coordinated in the outpatient setting. He completed 3 weeks of IV ertapenem, 1 gram every 24 hours, and was then transitioned to a regimen of amoxicillin-clavulanate acid and amoxicillin for an additional 4 weeks. On repeat evaluation after 7 weeks of antimicrobial therapy, the defect in the hard palate had healed, and he was transitioned to single agent amoxicillin 1 g every 8 hours to complete a total of 6 months of treatment. During his treatment course, he had dental extraction of tooth no. 1, which had been causing pain and was thought to be the inciting factor for the *actinomyces* infection.

At his 6-month follow-up visit, the patient had complete healing of the defect in the right hard palate (Figure 1B). Infectious

Table. Characteristics of Seven Case Reports Describing Actinomycosis

Author/Date	Age	Symptoms	Location	Treatment
Mehta et al[8] (2007)	11 y	Otorrhea, otalgia, facial weakness	Temporal bone involving facial nerve	Debridement, 9 weeks of ampicillin/sulbactam
Bose et al[10] (2014)	32 y	Painless nodules, draining sinuses	Back and axilla	Penicillin and TMP-SMX followed by amoxicillin and TMP-SMX (unspecified duration)
Almarzouq et al[11] (2019)	35 y	Painless mass	Great toe	Local excision, 6 weeks of clindamycin
Han et al[12] (2020)	54 y	Lower abdominal pain, anorexia, vomiting	Pelvic cavity	2 weeks of penicillin
Sah et al[13] (2020)	35 y	Headache, weakness, vomiting	Brain	Excision, ampicillin-sulbactam followed by oral antibiotics (unspecified duration)
Mou et al[7] (2021)	5 y	Fevers, pain, erythema, sores	Popliteal fossa	Debridement, 7 weeks of ampicillin-sulbactam followed by 6 weeks of oral amoxicillin-clavulanate
Yuan et al[14] (2022)	47 y	Productive cough, dyspnea, fever	Lung	10 days of piperacillin-sulbactam and 7 months of amoxicillin-clavulanate

Abbreviations: y, years; TMP-SMX, trimethoprim-sulfamethoxazole.

Disease recommended that he have a follow-up MRI to confirm eradication of the deep infection; however, he said he was feeling well and declined the MRI. Since he had demonstrated an initial rapid response to antibiotic therapy with complete healing of the hard palate, he was discharged from Infectious Disease care with guidance on monitoring for relapse of symptoms.

DISCUSSION

Actinomyces are nonmotile, filamentous, gram-positive, non-acid fast, and obligate anaerobic bacteria found as a commensal organism of the oropharynx, gastrointestinal tract, genitourinary tract, and skin.[2] Actinomycosis is a rare, progressive, chronic granulomatous disease that can occur in cervicofacial, thoracic, abdominopelvic, cerebral, and other forms.[2-4] *Actinomyces israelii* is the most encountered species, but many different species have been described to cause infections in various anatomical sites.[5] Peak incidence occurs in the fourth to fifth decade of life, with males more commonly affected than females in a 3:1 ratio.[6] Risk factors for actinomycosis include dental caries, infections of erupting teeth, gingivitis, dental extractions, the presence of intrauterine and intravaginal devices, diabetes, alcohol use disorder, malnutrition, and malignancy.[7]

Actinomycosis can spread directly into adjacent tissue by taking advantage of defects in anatomic barriers to form abscesses, sinus tracts, necrosis, fibrosis, and fistulae. Actinomycosis lesions are often painless, as in this patient's case, but they have been described to cause pain.[8] This patient had been seen a week prior to evaluation of the mass for complaints of dizziness and headache. Actinomycosis was thought to be a possible explanation for these symptoms. There has been at least 1 other case report describing facial nerve palsy from actinomycosis.[9] Actinomycosis presents in a variety of forms and can easily mimic other infections and neoplasms, leading to misdiagnosis or delay in diagnosis. Cervicofacial actinomycosis is the most common clinical presentation and is often described as "lumpy jaw syndrome," with a tendency to affect the upper and lower mandibles.[7,10] The literature on actinomycosis is limited, but there are several case reports describing variable presentations (Table)[8-9,11-15] This patient had a history of known dental caries that had been recommended for extraction, which was performed during his antibiotic regimen.

The most accurate method of diagnosis is made via isolation of *Actinomyces* species on cultures of clinical specimens. *Actinomyces* species are slow growing in nature, so cultures should be observed for up to 21 days to allow time for adequate detection. The presence of characteristic yellow "sulfur" granules on histopathology sections is strongly suggestive of *Actinomyces*, although granules are not seen consistently on all clinical specimens. Species-specific monoclonal antibody staining has been shown to improve identification of various *Actinomyces* species,[4] which could be useful when this diagnosis is suspected. Recently, molecular techniques using 16s rRNA gene probes also have assisted greatly in the diagnosis of actinomycosis.[16] In this patient's case, a diagnosis was able to be made with histopathology.

Actinomycosis is typically treated with high-dose penicillin G, with amoxicillin, amoxicillin-clavulanate, ampicillin-sulbactam, and doxycycline used as alternatives. Actinomycosis historically has been treated with prolonged antibiotic courses up to 1 year in duration, with shorter treatment courses of 1 to 4 weeks described in more recent reports.[17,18] Of note, actinomycosis infections can respond temporarily to shorter courses of broad-spectrum antibiotics prescribed for presumed odontogenic bacterial infections. This can lead to repeated short courses of antibiotics, promoting chronicity and formation of woody induration and fibrosis that can mimic malignancy. Increased clinician awareness of this condition can help prevent misdiagnosis and treatment delays.

This patient was treated with oral amoxicillin, amoxicillin-clavulanate, and IV ertapenem per Infectious Disease recommendations. While IV penicillin is typically the agent of choice

for actinomycosis, ertapenem was chosen over penicillin due to the invasive and erosive nature of this patient's actinomycosis infection.

CONCLUSIONS

This case report discusses a patient with a white mass eroding from his hard palate that was found to be a rare infection. The case adds to the limited literature describing various clinical presentations of actinomycosis affecting different organ systems and highlights how actinomycosis can invade through structures and mimic malignancy and other disease processes. Actinomycosis often is associated with dental infections and can take advantage of defects in anatomical barriers to spread and form abscesses, sinus tracts, and fistulas. Increased clinician awareness of the condition and appropriate methods of diagnosis can help prevent delays in treatment and complications from spreading infection.

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REFERENCES

1. Boyanova L, Kolarov R, Mateva L, Markovska R, Mitov I. Actinomycosis: a frequently forgotten disease. *Future Microbiol.* 2015;10(4):613-628. doi:10.2217/fmb.14.130

2. Li J, Li Y, Zhou Y, Wang C, Wu B, Wan J. Actinomyces and alimentary tract diseases: a review of its biological functions and pathology. *Biomed Res Int.* 2018;2018:3820215. doi:10.1155/2018/3820215

3. Gajdács M, Urbán E, Terhes G. Microbiological and clinical aspects of cervicofacial actinomyces infections: an overview. *Dent J (Basel).* 2019;7(3):85. doi:10.3390/dj7030085

4. Smego RA Jr, Foglia G. Actinomycosis. *Clin Infect Dis*. 1998;26(6):1255-1263. doi:10.1086/516337

5. Bonnefond S, Catroux M, Melenotte C, et al. Clinical features of actinomycosis: a retrospective, multicenter study of 28 cases of miscellaneous presentations. *Medicine (Baltimore).* 2016;95(24):e3923. doi:10.1097/MD.0000000000003923

6. Bennhoff DF. Actinomycosis: diagnostic and therapeutic considerations and a review of 32 cases. *Laryngoscope*. 1984;94(9):1198-1217. doi:10.1288/00005537-198409000-00013

7. Sharma S, Hashmi MF, Valentino DJ III. Actinomycosis. In: *StatPearls.* StatPearls Publishing; 2023. Accessed November 20, 2023. https://www.ncbi.nlm.nih.gov/books/NBK482151/

8. Mou Y, Jiao Q, Wang Y, et al. Musculoskeletal actinomycosis in children: a case report. *BMC Infect Dis*. 2021;21(1):1220. doi:10.1186/s12879-021-06890-2

9. Mehta D, Statham M, Choo D. Actinomycosis of the temporal bone with labyrinthine and facial nerve involvement. *Laryngoscope*. 2007;117(11):1999-2001. doi:10.1097/MLG.0b013e318133a127

10. Valour F, Sénéchal A, Dupieux C, et al. Actinomycosis: etiology, clinical features, diagnosis, treatment, and management. *Infect Drug Resist.* 2014;7:183-197. doi:10.2147/IDR.S39601

11. Bose M, Ghosh R, Mukherjee K, Ghoshal L. Primary cutaneous actinomycosis: a case report. *J Clin Diagn Res.* 2014;8(7):YD03-YD5. doi:10.7860/JCDR/2014/8286.4591

12. Almarzouq SF, Almarghoub MA, Almeshal O. Primary actinomycosis of the big toe: a case report and literature review. *J Surg Case Rep*. 2019;2019(11):rjz292. doi:10.1093/jscr/rjz292

13. Han Y, Cao Y, Zhang Y, Niu L, Wang S, Sang C. A case report of pelvic actinomycosis and a literature review. *Am J Case Rep*. 2020;21:e922601. doi:10.12659/AJCR.922601

14. Sah R, Nepal G, Sah S, et al. A rare case of brain abscess caused by *Actinomyces meyeri. BMC Infect Dis.* 2020;20(1):378. doi:10.1186/s12879-020-05100-9

15. Yuan Y, Hou Z, Peng D, Xing Z, Wang J, Zhang S. Pulmonary Actinomyces graevenitzii infection: case report and review of the literature. *Front Med (Lausanne).* 2022;9:916817. doi:10.3389/fmed.2022.916817

16. Kuyama K, Fukui K, Ochiai E, et al. Identification of the actinomycete 16S ribosomal RNA gene by polymerase chain reaction in oral inflammatory lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2013;116(4):485-491. doi:10.1016/j.oooo.2013.06.027

17. Moghimi M, Salentijn E, Debets-Ossenkop Y, Karagozoglu KH, Forouzanfar T. Treatment of cervicofacial actinomycosis: a report of 19 cases and review of literature. *Med Oral Patol Oral Cir Bucal*. 2013;18(4):e627-e632. doi:10.4317/medoral.19124

18. Könönen E, Wade WG. Actinomyces and related organisms in human infections. *Clin Microbiol Rev.* 2015;28(2):419-442. doi:10.1128/CMR.00100-14

STRN-ALK Fusion in Advanced Salivary Gland Carcinoma With Response to Anaplastic Lymphoma Kinase Inhibition: Case Report and Literature Review

Varinder Kaur, MD; Sara Zadeh, MD

ABSTRACT

Salivary gland carcinomas are a heterogeneous group of rare tumors. There is no established standard of care therapy for metastatic disease. We describe the case of a patient with metastatic salivary gland adenocarcinoma harboring *STRN-ALK* translocation, with tumor response and clinical benefit from anaplastic lymphoma kinase (*ALK*) inhibition. Our patient experienced clinical benefit from first and second generation *ALK* inhibition in a chemotherapy refractory tumor. Tumor mutation profiling can identify mutations that may render tumors sensitive to targeted therapy with tyrosine kinase inhibitors.

INTRODUCTION

Salivary gland carcinomas are heterogeneous tumors that affect less than 2500 adults in United States annually.[1] While the era of precision oncology has transformed the treatment paradigms for solid tumors like non-small cell lung cancer (NSCLC) and melanoma, the development of biomarker-driven therapy for advanced salivary gland tumors remains challenging due to rarity of the disease and limited actionable targets.[2,3] Treatment of metastatic disease is still mostly based on chemotherapy, despite the low response rates. Recent availability of targeted therapies, such as *NTRK* inhibitors, has been a welcome addition to treatment options, but they represent less than 5% patients with salivary gland adenocarcinomas, not otherwise specified (NOS).[4] We present a challenging case of aggressive salivary gland adenocarcinoma with dramatic, clinically meaningful response to *ALK* inhibition.

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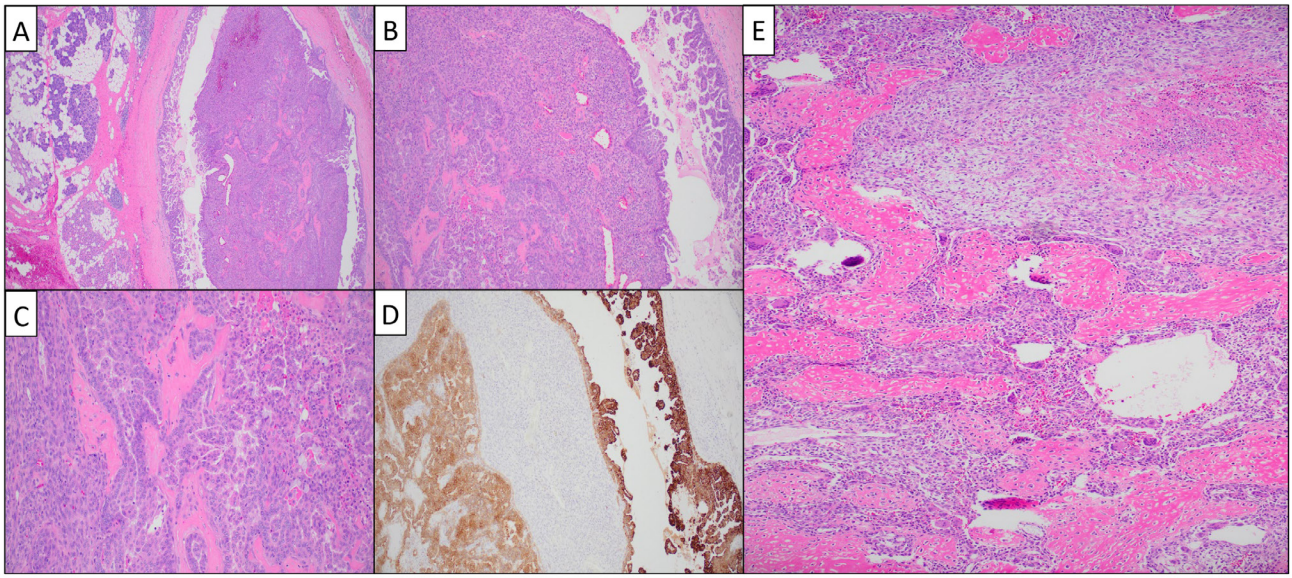
CASE PRESENTATION

A 50-year-old White male was diagnosed initially with AJCC (American Joint Committee on Cancer) 7th edition stage IVA (pT1pN2bcM0) adenocarcinoma NOS of the right parotid gland, for which he underwent right parotidectomy and right neck dissection. Pathology review showed a 1.5 cm unifocal adenocarcinoma with papillary and micropapillary architecture and focal spindle features (Figure 1). Sixteen of the 64 lymph nodes examined were positive, with largest nodal diameter of 3.5 cm with extracapsular extension. Other notable features included presence of perineural invasion and lymphovascular invasion (LVI). Immunohistochemical (IHC) stains showed tumor expression of pankeratin, mammaglobin, and S100 with focal p16 immunoreativity. Fluorescence in situ hybridization (FISH) showed intact *ETV6*, *RET*, and *MAML2* genes. He received adjuvant chemoradiotherapy (66Gy in 33 fractions together with weekly carboplatin and paclitaxel) and subsequently pursued close surveillance with clinical examination every 3 months and scans every 6 months.

Three years after his initial surgery, the patient developed right cervical and axillary nodal recurrence, for which he underwent right radical and central neck dissection and right axillary dissection. Pathology showed metastatic adenocarcinoma, morphologically similar to the prior parotid tumor. Similarly, LVI and extracapsular extension were identified again. Additional workup showed no immunoreactivity for the androgen receptor by IHC, an intact *NTRK1* gene by FISH, and no amplification of HER2 by chromogenic in situ hybridization. PD-L1 IHC was negative. He received additional hyperfractionated radiotherapy regimen (45Gy in 30 fractions) to the right neck and axilla.

Seven months later, the patient again presented with new

Figure 1. Microscopic Images



A) Low-power hematoxylin and eosin (H and E) image demonstrating the tumor interface to the background parotid parenchyma; B) Medium-power H and E image highlighting the epithelioid component and adjacent spindle cell component of the tumor; prominent papillary architecture is accentuated at the periphery of the tumor; C) High-power H and E image showing tumor cells with abundant eosinophilic cytoplasm and occasional mucinous differentiation; D) Mixed cytokeratin immunohistochemical stain is diffusely and strongly expressed in the epithelial component and is absent in the sarcomatoid component; E) H and E section of the recurrent tumor demonstrates sheets of epithelioid to spindled tumor cells. Islands of malignant osteoid admixed with osteoclast-like giant cells are prominent. Necrosis and lymphovascular space invasion are frequent. An epithelial component is notably absent in the recurrent tumor.

right cervical adenopathy, right lower neck subcutaneous mass, and left supraclavicular adenopathy. Fine needle aspiration cytology from the left supraclavicular lymph node showed metastatic adenocarcinoma, consistent with his prior parotid tumor. Computed tomography of the lung showed up to 0.2 cm bilateral lung micronodules that were indeterminate but new compared to his scans 7 months prior. Due to lack of clinical trial availability, his tumor was sent for FoundationOne testing. This revealed a microsatellite stable tumor and the presence of a *STRN* (NM_003162)-*ALK* (NM_004304) fusion (S2; A20). He was started on crizotinib therapy and tolerated it with minimal side effects, most notably mild nausea and diarrhea. His follow-up scans 2 months after crizotinib initiation showed interval tumor response (Figure 2).

Subsequent 2-month follow-up scans showed interval progression in the right neck mass, despite continuation of crizotinib. A core needle biopsy of the right neck lesion showed metastatic carcinoma. He underwent wide excision of the right neck mass and right neck dissection. Pathology review of the surgical excision specimen showed sarcomatoid carcinoma, with osteosarcomatous differentiation characterized by islands of malignant osteoid admixed with multinucleated osteoclast-like giant cells in a background of high-grade epithelioid to spindled cells (Figure 1E). The tumor sample was again sent for FoundationOne testing and showed a *STRN* (NM_003162)-*ALK* (NM_004304) fusion (S2; A20) but no additional mutations. He started cytotoxic chemotherapy with cyclophosphamide, Adriamycin, and cisplatin and experienced marked progression following cycle 2 (Figure 3A1 and A2). He was subsequently started on alectinib and experienced marked improvement in his disease burden (Figure 3B and 3C). Clinically, he noted significant improvement in his pain, bleeding, and tenderness of skin/subcutaneous nodules and improved energy. He also was able to stop his opioid pain medications, which enabled him to continue his employment. He remained in remission for 12 months, after which he had rapid disease progression and subsequently elected to pursue hospice care.

DISCUSSION

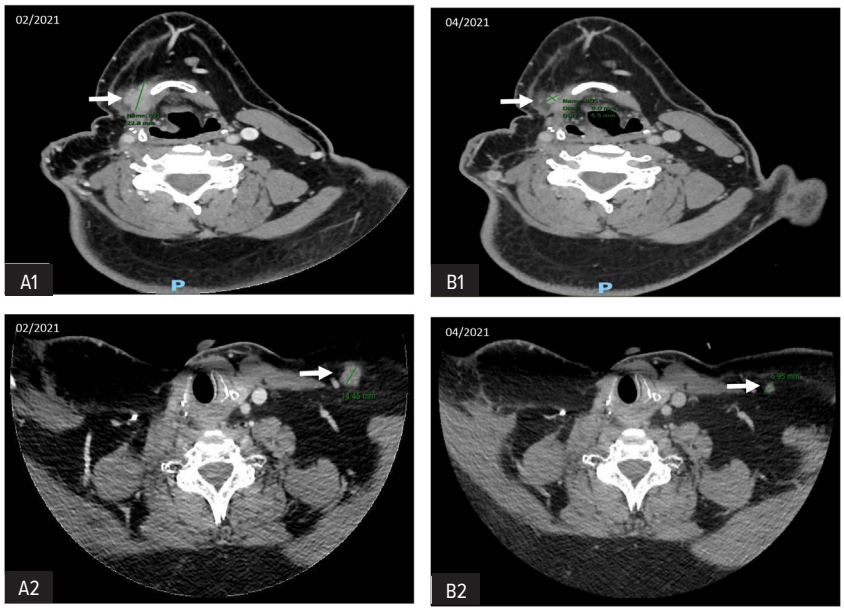
Chromosomal rearrangements in *ALK* are well-described targets for specific tyrosine kinase inhibitors (TKI) in lung cancer. *ALK* encodes a receptor tyrosine kinase whose activation induces downstream pathways associated with cell proliferation, cell survival, and angiogenesis. Oncogenic *ALK* fusions involve an N-terminal partner gene that promotes activation of *ALK* domain by dimerization.[5] More than 90 fusion partners for ALK have been identified in NSCLC.[6] The striatin (*STRN*) gene is an uncommon fusion partner of *ALK* rarely reported in solid tumors.[7,8] STRN is located on the short arm of chromosome 2—the same location as the more common fusion partner echinoderm microtubule-associated protein-like 4 gene (*EML4*). The *STRN-ALK* fusion involves chromosomal translocation of exons 1 to 3 of *STRN* to exons 20 to 29 of fusion partner ALK

within the short arm of chromosome 2.[1] *STRN-ALK* fusion has been associated with an aggressive tumor behavior in solid tumors.[8] Only 9 cases of ALK –fusion-positive salivary gland carcinomas have been reported previously (Table).[5-9] To our knowledge, this is the first reported case of *STRN-ALK* fusion in metastatic salivary gland cancer with response to *ALK* inhibition therapy.

Although genetic alterations are frequent in advanced salivary gland carcinomas, *ALK* rearrangements are rare.[9-13] Salivary gland carcinoma with *STRN-ALK* alteration has been described to have a cribriform histology and mucinous differentiation.[7] Our patient harbored a parotid gland tumor with unique morphologic features, including prominent papillary and micropapillary architecture with oncocytic and focal mucinous differentiation.

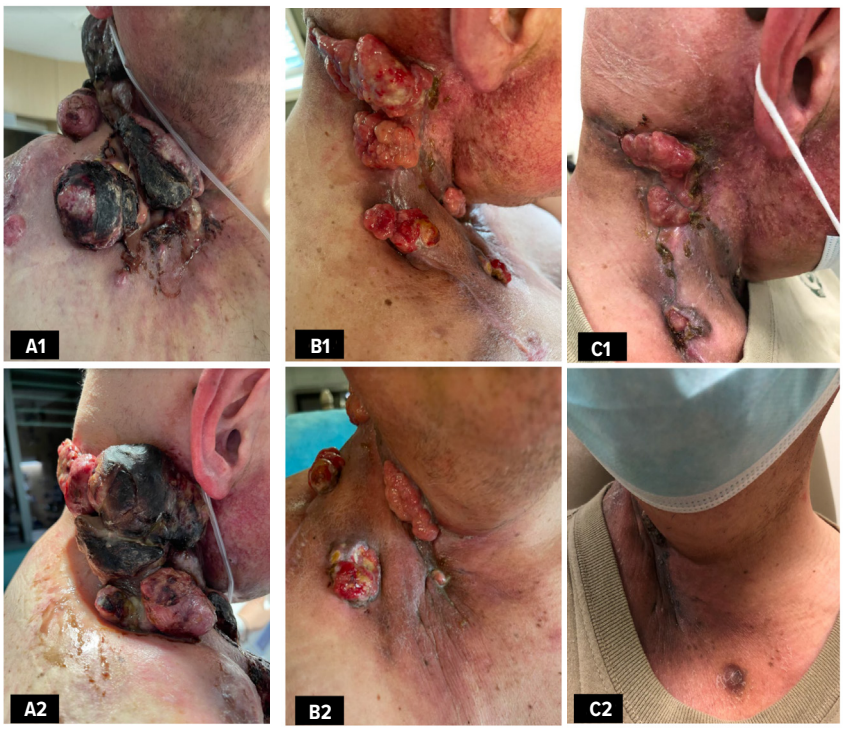
ALK fusions are effective therapeutic targets in lung cancer. Whether they represent a therapeutic target in salivary gland carcinomas has not been well established. Multiple *ALK* fusion types respond variably to *ALK*-TKIs. Crizotinib is a potent ATP-competitive inhibitor of the *ALK* and *MET* kinases and is approved by the US Food and Drug Administration (FDA) as therapy for *ALK-EML4* fusion NSCLC. It shows a therapeutic response in approximately 57% of patients with *ALK* rearrangement positive NSCLC.[14] Rare case reports in NSCLC patients also have shown sensitivity of this fusion peptide to crizotinib.[15] Both a clinical response[16] and lack of a response have been described with alectinib in *STRN-ALK* fusion-positive non-small cell lung cancer.[17] Our patient experienced a measurable, albeit short-lived, response with crizotinib and subsequently attained marked decline in clinical tumor burden with alectinib.

Figure 2. Computed Tomography Soft Tissue Neck With Contrast Images



A1 and A2: Prior to crizotinib initiation; B1 and 1B2: 2 months after crizotinib initiation.

Figure 3. Clinical Images



A1 and A2: Prior to alectinib initiation; B1 and B2: 2 weeks after alectinib initiation; C1 and C2: 4 weeks after alectinib initiation.

The standard of care management of metastatic salivary gland tumors is not well established. Chemotherapy has been utilized in patients with symptomatic or progressive disease affecting quality of life performance status with a goal to achieve cytoreduction. But whether chemotherapy alters the natural history of most salivary gland cancers subtypes remains unclear as trials employing chemotherapy have not shown improvement in overall survival. More recently,

Table. *ALK* Fusion-Positive Salivary Gland Carcinoma Cases Described in Literature

Case	Age/Sex	Subsite	*ALK* Fusion Partner	Salivary Gland Carcinoma Subtype	Treatment	Clinical Course
1[7]	NA	Parotid	*EML4-ALK*	Salivary ductal carcinoma de novo	NA	NA
2[7]	NA	Parotid	*HNRNPH3-ALK*	Salivary ductal carcinoma de novo	NA	NA
3[8]	82/M	Parotid	*CTNNA1-ALK*	Secretory carcinoma of salivary gland dissection	Surgical resection and selective neck	Indolent
4[9]	84/F	Intra-parotid lymph node	*STRN-ALK*	Salivary intra-ductal carcinoma	Surgical resection	Indolent
5[5]	73/F	Minor salivary gland of lip	*MYO18A-ALK*	Salivary intraductal carcinoma/low grade cribriform cystadenocarcinoma	Surgical resection`	Indolent
6[6]	67/M	Parotid	*STRN-ALK*	Salivary ductal carcinoma	Surgical resection, then palliative therapy following recurrence	NA
7[6]	79/M	Parotid	*EML4-ALK*	Salivary ductal carcinoma	Surgical resection	NA
8[6]	72/M	Parotid	*EML4-ALK*	Salivary ductal carcinoma	Surgical resection, then palliative chemotherapy	NA
9[6]	69/F	Parotid	*EML4-ALK*	Intercalated-type intraductal carcinoma	NA	NA
10[a]	46/M	Parotid	*STRN-ALK*	Adenocarcinoma NOS	Surgical resection, chemo-radiotherapy, Crizotinib, Alectinib	Aggressive

Abbreviations: NA, not available; NOS, not otherwise specified
[a]Index case described in this report.

RET fusion TKI and NTRK fusion TKI larotrectinib have received site agnostic FDA approvals.

In the absence of a standard of care therapy for metastatic salivary gland cancer without *NTRK* or *RET* fusion mutations, we obtained FoundationOne medicine genetic analysis for our patient and identified a rare *STRN-ALK* fusion in his tumor. Since the tumor sent for analysis was a surgical specimen from his initial surgery, this rare fusion was likely an early event in tumorigenesis. Given his noticeable clinical and radiographic response, *STRN-ALK* fusion in this patients' tumor was likely the oncogenic driver as well. There were other important considerations for our patient before crizotinib could be initiated. Due to QTc prolongation and CYP3A inhibition with critozinib, his antidepressant was switched from escitalopram to paroxetine, and statin therapy had to be switched from simvastatin to rosuvastatin. He tolerated both of these medication changes well. Thus, clinicians should keep these important drug interactions in mind while using critozinib. The patient's subsequent clinical benefit to second like *ALK* inhibition with alectinib also demonstrates the utility of considering additional *ALK* inhibition following progression on first generation *ALK* inhibitors, such as crizotinib. Our patient experienced prolonged response to alectinib; thus, considering second generation *ALK* inhibitors in the front line may be a reasonable approach.

CONCLUSIONS

Tumor mutation profiling can yield potentially targetable mutations and should be considered in rare tumors with limited standard of care options. This is particularly important given the expanding repertoire of targeted therapeutic agents.

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REFERENCES

1. Tagen M, Klumpers LE. Review of delta-8-tetrahydrocannabinol (delta-8-THC): com1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin*. 2015;65(1):5-29. doi:10.3322/caac.21254

2. Schwartzberg L, Kim ES, Liu D, Schrag D. Precision oncology: who, how, what, when, and when not? *Am Soc Clin Oncol Educ Book*. 2017;37:160-169. doi:10.1200/EDBK_1741

3. Ferrell JK, Mace JC, Clayburgh D. Contemporary treatment patterns and outcomes of salivary gland carcinoma: a National Cancer Database review. *Eur Arch Otorhinolaryngol*. 2019;276(4):1135-1146. doi:10.1007/s00405-019-05282-2

4. Wang K, Russell JS, McDermott JD, et al. Profiling of 149 salivary duct carcinomas, carcinoma ex pleomorphic adenomas, and adenocarcinomas, not otherwise specified reveals actionable genomic alterations. *Clin Cancer Res*. 2016;22(24):6061-6068. doi:10.1158/1078-0432.CCR-15-2568

5. Grande E, Bolós MV, Arriola E. Targeting oncogenic ALK: a promising strategy for cancer treatment. *Mol Cancer Ther*. 2011;10(4):569-579. doi:10.1158/1535-7163.MCT-10-0615

6. Ou SI, Zhu VW, Nagasaka M. Catalog of 5' fusion partners in ALK-positive NSCLC circa 2020. *JTO Clin Res Rep*. 2020;1(1):100015. doi:10.1016/j.jtocrr.2020.100015

7. Majewska H, Gorczyński A, Czapiewski P, et al. ALK alterations in salivary gland carcinomas. *Virchows Arch*. 2021;478(5):933-941. doi:10.1007/s00428-020-02971-w

8. Pérot G, Soubeyran I, Ribeiro A, et al. Identification of a recurrent STRN/ALK fusion in thyroid carcinomas. *PLoS ONE*. 2014;9(1):e87170. doi:10.1371/journal.pone.0087170

9. Agaimy A, Baněčková M, Ihrler S, et al. ALK rearrangements characterize 2 distinct types of salivary gland carcinomas: clinicopathologic and molecular analysis of 4 cases and literature review. *Am J Surg Pathol*. 2021;45(9):1166-1178. doi:10.1097/PAS.0000000000001698

10. Dogan S, Ng CKY, Xu B, et al. The repertoire of genetic alterations in salivary duct carcinoma including a novel HNRNPH3-ALK rearrangement. *Hum Pathol*. 2019;88:66-77. doi:10.1016/j.humpath.2019.03.004

11. Sasaki E, Masago K, Fujita S, Suzuki H, Hanai N, Hosoda W. Salivary secretory carcinoma harboring a novel ALK fusion: expanding the molecular characterization of

carcinomas beyond the etV6 Gene. *Am J Surg Pathol.* 2020;44(7):962-969. doi:10.1097/PAS.0000000000001471

12. Rooper LM, Thompson LDR, Gagan J, Oliai BR, Weinreb I, Bishop JA. Salivary intraductal carcinoma arising within intraparotid lymph node: a report of 4 cases with identification of a novel STRN-ALK fusion. *Head Neck Pathol*. 2021;15(1):179-185. doi:10.1007/s12105-020-01198-0

13. Kato S, Elkin SK, Schwaederle M, et al. Genomic landscape of salivary gland tumors. *Oncotarget*. 2015;6(28):25631-25645. doi:10.18632/oncotarget.4554

14. Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. *N Engl J Med.* 2010;363(18):1693-1703. doi:10.1056/NEJMoa1006448

15. Yang Y, Qin SK, Zhu J, et al. A rare STRN-ALK Fusion in lung adenocarcinoma identified using next-generation sequencing-based circulating tumor DNA profiling exhibits excellent response to crizotinib. *Mayo Clin Proc Innov Qual Outcomes.* 2017;1(1):111-116. doi:10.1016/j.mayocpiqo.2017.04.003

16. Su C, Jiang Y, Jiang W, et al. STRN-ALK fusion in lung adenocarcinoma with excellent response upon alectinib treatment: a case report and literature review. *Onco Targets Ther.* 2020;13:12515-12519. doi:10.2147/OTT.S282933

17. Nakanishi Y, Masuda S, Iida Y, Takahashi N, Hashimoto S. Case report of non-small cell lung cancer with STRN-ALK translocation: a nonresponder to alectinib. *J Thorac Oncol.* 2017;12(12):e202-e204. doi:10.1016/j.jtho.2017.08.009

Tropical Myositis: A Not-So-Tropical Diagnosis in a Febrile Type 1 Diabetic Patient

Jack Bullis, MD; Kenneth Fiala, MD; Nicole Werner, MD

ABSTRACT

Introduction: Tropical myositis – also known as pyomyositis – is a subacute, primary infection of skeletal muscle. Long considered a diagnosis exclusive to tropical climates, recently it has been reported increasingly in historically nontropical climates. We present a case of tropical myositis in Madison, Wisconsin, occurring in a febrile type 1 diabetic patient without travel or known exposure.

Case Presentation: A 35-year-old male with a history of von Willebrand disease, type 1 diabetes, and financial insecurity resulting in insulin rationing presented with 2 weeks of generalized weakness. On exam, he had a multitude of large, erythematous "bumps" across his body, which had been increasing in size for more than 2 weeks. His blood glucose was 518, with leukocytosis and labs supportive of diabetic ketoacidosis. Computed tomography revealed extensive intramuscular and subcutaneous abscesses of the left chest, bilateral erector spinae, right gluteal muscles, bilateral thighs, left leg, and left upper and lower arm. Broad-spectrum antibiotics were initiated, as was treatment for diabetic ketoacidosis. Blood and urine cultures revealed oxacillin-susceptible *Staphylococcus aureus*. After clinical stabilization, he underwent initial incision and drainage of the abscesses. His condition would require 14 more operative incision and drainage procedures and wound closure attempts before he was discharged to a rehab facility after more than a month-long hospitalization.

Discussion: Severe tropical myositis is associated with high morbidity and high use of health care resources. The exponential rise in cases in the United States in recent years risks further stressing an already-burdened health care system. We explore potential causes of the increase in cases of tropical myositis in nontropical regions, including increasing rates of diabetes and poverty and climate change. Recent data suggest that the large majority of tropical myositis cases are caused by Panton-Valentine leukocidin toxin-producing *Staphylococcus aureus* strains. There is a theoretical mitigation of disease severity when patients receive early protein synthesis inhibitor antibiotic treatment, though these findings are limited to case reports and observational studies and lack controlled clinical trials. This case highlights the need for early identification, antibiotic administration, and surgical source control in suspected cases of tropical myositis.

INTRODUCTION

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Tropical myositis – or pyomyositis – is a subacute deep primary infection of skeletal muscle long considered to be a diagnosis exclusive to tropical climates. However, in the last 2 decades, tropical myositis increasingly has been reported worldwide.[1]

Tropical myositis was first described in detail in 1885 and first characterized within the United States in 1971.[2] Although more common in immunocompromised individuals, tropical myositis can be found in the immunocompetent – especially in tropical climates.[1] Tropical myositis has been reported to account for as much as 4% of all hospital admissions in tropical regions.[3] The rates of infection have been climbing in temperate climates, where tropical myositis was once extremely rare. In the United States, there was a three-fold increase in tropical myositis admissions from 2002 to 2014.[4] Australia saw an almost four-fold increase in pediatric tropical myositis cases during the same time period.[5]

Tropical myositis is associated with immunodeficient states, including HIV infection, diabetes, organ transplantation, chemotherapy, rheumatologic diseases, and malignancy, and it occurs more commonly in males, with a 6:1 male-to-female ratio.[3]

Tropical myositis commonly manifests with fevers, myalgias, and cramping in a specific muscle or multiple muscles.[3] The lower extremities and pelvic girdle muscles are the most common site of infection, but it can affect other muscles, including the pectoralis

major, serratus anterior, iliopsoas, biceps, and spinal muscles.[3,6] Multiple muscle groups are involved in 12% to 40% of cases.[7] The most common causative organism is *Staphylococcus aureus* (*S aureus*).[6] The etiology is likely related to transient bacteremia with or without muscular trauma inducing seeding of the muscle leading to subsequent infection.[8]

Clinically, tropical myositis presents in 1 of 3 stages.[7] In the first stage of disease, patients present with generalized complaints – usually muscle aches or mild fever without clear formation of abscesses. Instead, affected muscles may feel "wooden" on palpation.[7] If untreated, it will progress to the second stage of disease, which is characterized by abscess formation.[7] Around 90% of diagnoses are made at this stage.[7] Patients present with worsened muscle pain, fever, and irregular muscle swelling, or fluctuance on exam. If missed in the second stage, patients may then progress to the third stage, which is characterized by severe systemic infection.[3]

It is imperative that tropical myositis be considered as part of the differential diagnosis for a patient presenting with generalized muscle complaints, fevers, and risk factors for tropical myositis (diabetes, muscular trauma, or immunocompromise). Our case describes a patient with tropical myositis who evaded early detection of disease and presented in the third stage of disease, resulting in a protracted hospital course. Our discussion focuses on the intersection of specific risk factors and their potential role in increasing rates of tropical myositis in nontropical areas. We discuss a theoretical framework by which a rise in temperate climate tropical myositis could be explained, highlighting the necessity of managing tropical myositis not only from a medical and surgical standpoint but also the social and environmental factors that put populations at risk for development of this debilitating disease process.

CASE PRESENTATION

A 35-year-old male who lost his balance in a public setting and was subsequently transported to the emergency department for severe weakness presented in the summer months with a past medical history of poorly controlled type 1 diabetes, von Willebrand disease, and financial insecurity resulting in insulin rationing. On arrival, he complained of excessive weakness lasting for 2 weeks. He endorsed dizziness, frequent urination, and severe thirst. Secondarily, he noted large "red bumps" on his left chest, left forearm, left thigh, and right calf. He described muscle aches for multiple weeks prior, though he was unsure of the exact time period. Aside from diabetes, he had no other history of immunocompromise or prior severe infections, nor did he have a history of illicit drug use.

On physical examination, the patient was alert and oriented, albeit in moderate distress with notable malaise. He had dry mucous membranes and was appreciably tachycardic. Muscle strength and sensation were grossly intact. Multiple large, erythematous masses were present on his left forearm, right hip, left chest wall, left thigh, and bilateral calves (the right draining purulent fluid). He had full passive range of motion in his extremities without pain out of proportion on exam. He was febrile, tachycardic, and normotensive. Initial laboratory analysis revealed significant leukocytosis, blood glucose of 518, metabolic acidosis, and elevated beta-hydroxybutyrate – concerning for diabetic ketoacidosis. Diabetic ketoacidosis protocol was begun in the emergency department.

Empiric antibiotic therapy of vancomycin, cefepime, and metronidazole also was initiated, with additional concern for severe infection given the patient's purulent abscesses on exam. Blood, body fluid, and urine cultures were drawn prior to initiation of antibiotics. Computed tomography of the chest, abdomen, pelvis, left forearm, and left knee was obtained, revealing diffuse intramuscular abscesses (Figures 1-3). Given the imaging findings, he was admitted to the general surgery inpatient floor for stabilization and plans for surgical management of his disease.

All cultures were gram-stained and revealed gram-positive cocci. Due to concern for bacteremia, the patient underwent transthoracic and transesophageal echocardiography on hospital days 1 and 2, respectively – both of which showed an absence of cardiac vegetations. Cultures speciated to oxacillin-susceptible *S aureus*, and antibiotics were narrowed to intravenous oxacillin. Additional infectious disease workup revealed normal oxidative burst via dihydrorhodamine test and negative HIV antibody/antigen testing.

On day 3 of hospitalization, the patient underwent extensive incision and drainage of the previously identified abscesses – producing copious amounts of purulent fluid from each. Achieving adequate source control of the infection proved difficult. He underwent extensive procedures, having 14 total operative debridements, fasciotomies, and attempted wound closures throughout his more than 30-day hospital stay. Given his diffuse muscular abscesses without clear nidus for infection, a diagnosis of primary pyomyositis – or tropical myositis – was made. By the end of his hospital stay, all wounds had been closed aside from the left forearm and left calf incisions, which were covered with wound vacuum with plans for surgical closure in the outpatient setting. Once medically stable and with confidence that source control had been achieved, the patient was discharged to a skilled nursing facility.

DISCUSSION

From 1971 to 1992, there were only 98 reported cases of tropical myositis within North America.[9] Since then, rates have increased significantly. From 2002 to 2014, there were more than 13 000 cases of tropical myositis in the United States.[4] During the same time period, rates of tropical myositis more than tripled, with an

incidence of 0.0054% per hospital discharge in 2002 to 0.0209% in 2014.[4] A diagnosis of tropical myositis during that time period was significantly associated with a history of diabetes (type 1 and type 2),[4] of which our patient also had a history. He also faced financial insecurity, which resulted in insulin rationing that likely contributed in large part to his diabetic ketoacidosis. We believe this led to the immune compromise that produced the initial infection, as no obvious site of inoculation could be determined. Poverty and financial insecurity are well-known contributors to uncontrolled diabetes and increasing rates of diabetic ketoacidosis.[10] Incidence of both type 1 and type 2 diabetes increased each year during 2002-2012.[11] It is possible that the increased incidence of diabetes may have contributed to a rise in tropical myositis cases, though it may not explain the whole picture.

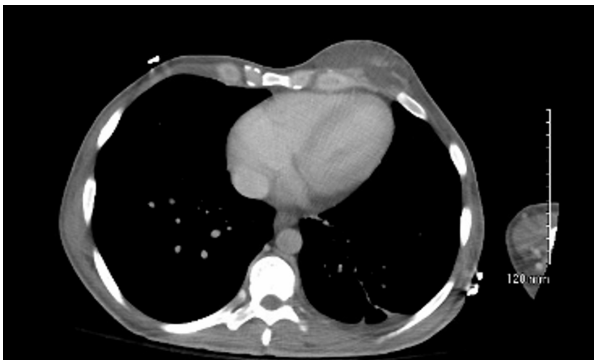
In temperate climates, the causal agent of tropical myositis is *S aureus* in more than 75% of all cases,[1] including our patient. *S aureus* strains containing the Panton-Valentine leucocidin (PVL) locus are associated with the development of soft tissue infections.[12] This locus codes for a specific pore-forming protein toxin secreted by the staphylococcal species. A recent genome-wide association study determined that *S aureus* containing the PVL locus alone increased odds of tropical myositis by more than 130-fold in Cambodian children, suggesting that *S aureus*-associated tropical myositis is critically dependent on the PVL locus.[13] For example, in sub-Saharan Africa – an area with high rates of tropical myositis – almost half of *S aureus* isolates contain PVL toxin.[14] Meanwhile, in Germany, where rates of tropical myositis are low, almost no *S aureus* isolates contain the PVL toxin.[14] This data may suggest a link between climate and the development of PVL-containing *S aureus* species.

We were unable to find any studies detailing the overall incidence of the PVL locus in *S aureus* species within the United States. However, new variations of *S aureus* species among cases of tropical myositis have been appreciated. Rates of oxacillin-resistant *S aureus* in cases of tropical myositis increased substantially from 1994 to 2006.[15] It is possible that variations in antibiotic usage over time have led to increased rates of PVL-containing *S aureus* species.

Recent evidence also suggests that climate change could offer a means by which once tropics-specific bacteria could colonize the skin microbiome of those living in historically temperate climates. Changes in average temperature and humidity associated with climate change could offer a potential mechanism for significant alterations in skin microbiome,[16] potentially favoring tropical myositis-associated pathogens like PVL-containing *S aureus* species. This warrants further investigation, though it may offer an explanation for the increasing incidence of tropical myositis in nontropical climates.

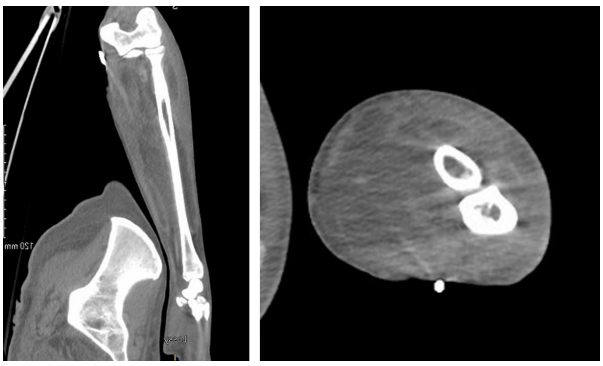
The suggestion that tropical myositis is critically dependent on toxin-secreting PVL-positive *S aureus* may offer insight into effec-

Figure 1. Computed Tomography of Patient's Chest



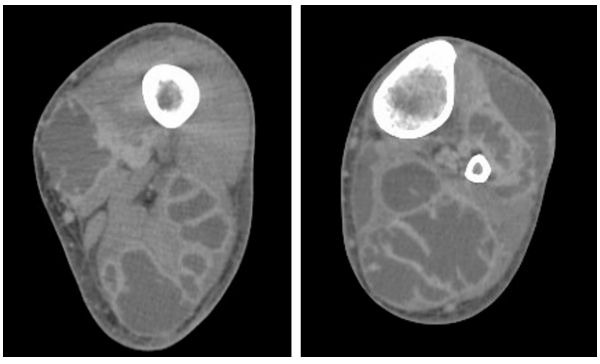
Left anterior lower chest wall abscess measuring 2.5 x 4.5 x 7.4 cm with surrounding soft tissue thickening and overlying phlegmonous soft tissue. Simple, small left pleural effusion.

Figure 2. Computed Tomography of Left Upper Extremity, Forearm, Coronal and Axial Views



Large complex, multiloculated, peripherally enhancing fluid collection within the brachioradialis and flexor musculature (7.7 x 5.7 x 18 cm). Intramuscular fluid collection with subcutaneous involvement along the posterior forearm (6.4 x 2.2 x 14.5 cm).

Figure 3. Computed Tomography of Left Lower Extremity, Thigh (Left) and Leg (Right)



Large multiloculated fluid collections within the distal hamstring musculature (7.6 x 4.5 x 11.5 cm); fluid and gas-filled collection within the medial thigh, predominantly within vastus medialis (4.3 x 6.4 x 17.7 cm). Loculated fluid collection within the medial head of the gastrocnemius (6.4 x 6.2 x 13.1 cm).

tive antibiotic management of tropical myositis. Empiric therapy with broad-spectrum antibiotics is the most beneficial initial management of presumed tropical myositis,[17] which fortunately was initiated promptly in our case. Because *S aureus*-associated tropical myositis may be critically dependent on toxin production,[13] early inhibition of bacterial toxin production with protein-synthesis inhibitors could theoretically prevent advancement of disease or lead to earlier resolution.[17] This also could prove helpful in preventing morbidity or mortality associated with severe disease. Multiple antibiotic classes have been shown to reduce production of PVL in vivo: macrolides, lincosamides (like clindamycin), rifampicin, and oxazolidinone.[18] To date, there is no current data on the favoring of one protein-synthesis inhibitor over another in the treatment of PVL-associated tropical myositis or their effects on limiting hospital course.

CONCLUSIONS

Tropical myositis, formally known as pyomyositis, is no longer a disease exclusive to the tropics. As such, it remains an important consideration as part of the differential diagnosis for immune-compromised patients presenting with diffuse myalgias and fever. There is a theoretical role for early adjunct initiation of protein-synthesis inhibitors given its association with PVL-containing *S aureus* species, though this remains an important area of investigation. The high systems cost associated with treatment of late-stage tropical myositis coupled with increasing rates of tropical myositis in temperate regions could further burden already highly stressed health care systems. Because of its association with diabetes, increasing rates of poverty, and possibly even climate change, the development of tropical myositis in historically temperate regions highlights the importance of appreciating and advocating for management of social determinants of health, such as poverty and climate change. Early recognition of tropical myositis and its risk factors is critical in preventing morbidity and mortality, as well as the high costs of treatment for patients and health care systems alike.

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REFERENCES

1. Agarwal V, Chauhan S, Gupta RK. Pyomyositis. *Neuroimaging Clin N Am.* 2011;21(4):975-x. doi:10.1016/j.nic.2011.07.011

2. Levin MJ, Gardner P, Waldvogel FA. "Tropical" pyomyositis. An unusual infection due to Staphylococcus aureus. *N Engl J Med*. 1971;284(4):196-198. doi:10.1056/NEJM197101282840407

3. Sharma A, Kumar S, Wanchu A, et al. Clinical characteristics and predictors of mortality in 67 patients with primary pyomyositis: a study from North India. *Clin Rheumatol.* 2010;29(1):45-51. doi:10.1007/s10067-009-1277-x

4. Maravelas R, Melgar TA, Vos D, Lima N, Sadarangani S. Pyomyositis in the United States 2002-2014. *J Infect*. 2020;80(5):497-503. doi:10.1016/j.jinf.2020.02.005

5. Moriarty P, Leung C, Walsh M, Nourse C. Increasing pyomyositis presentations among children in Queensland, Australia. *Pediatr Infect Dis J.* 2015;34(1):1-4. doi:10.1097/INF.0000000000000470

6. Crum NF. Bacterial pyomyositis in the United States. *Am J Med.* 2004;117(6):420-428. doi:10.1016/j.amjmed.2004.03.031

7. Chiedozi LC. Pyomyositis. Review of 205 cases in 112 patients. *Am J Surg.* 1979;137(2):255-259. doi:10.1016/0002-9610(79)90158-2

8. Bickels J, Ben-Sira L, Kessler A, Wientroub S. Primary pyomyositis. *J Bone Joint Surg Am*. 2002;84(12):2277-2286. doi:10.2106/00004623-200212000-00024

9. Christin L, Sarosi GA. Pyomyositis in North America: case reports and review. *Clin Infect Dis.* 1992;15(4):668-677. doi:10.1093/clind/15.4.668

10. Kurani SS, Heien HC, Sangaralingham LR, et al. Association of area-level socioeconomic deprivation with hypoglycemic and hyperglycemic crises in US adults with diabetes. *JAMA Netw Open.* 2022;5(1):e2143597. doi:10.1001/jamanetworkopen.2021.43597

11. Ingelfinger JR, Jarcho JA. Increase in the incidence of diabetes and its implications. *N Engl J Med.* 2017;376(15):1473-1474. doi:10.1056/NEJMe1616575

12. Shallcross LJ, Fragaszy E, Johnson AM, Hayward AC. The role of the Panton-Valentine leucocidin toxin in staphylococcal disease: a systematic review and meta-analysis. *Lancet Infect Dis*. 2013;13(1):43-54. doi:10.1016/S1473-3099(12)70238-4

13. Young BC, Earle SG, Soeng S, et al. Panton-Valentine leucocidin is the key determinant of *Staphylococcus aureus* pyomyositis in a bacterial GWAS. *eLife.* 2019;8:e42486. doi:10.7554/eLife.42486

14. Ruffing U, Alabi A, Kazimoto T, et al. Community-associated *Staphylococcus aureus* from sub-Saharan Africa and Germany: a cross-sectional geographic correlation study. *Sci Rep*. 2017;7(1):154. doi:10.1038/s41598-017-00214-8

15. Zalavras CG, Rigopoulos N, Poultsides L, Patzakis MJ. Increased oxacillin resistance in thigh pyomyositis in diabetic patients. *Clin Orthop Relat Res.* 2008;466(6):1405-1409. doi:10.1007/s11999-008-0198-3

16. Isler MF, Coates SJ, Boos MD. Climate change, the cutaneous microbiome and skin disease: implications for a warming world. *Int J Dermatol.* 2023;62(3):337-345. doi:10.1111/ijd.16297

17. Shittu A, Deinhardt-Emmer S, Vas Nunes J, Niemann S, Grobusch MP, Schaumburg F. Tropical pyomyositis: an update. *Trop Med Int Health*. 2020;25(6):660-665. doi:10.1111/tmi.13395

18. Hodille E, Rose W, Diep BA, Goutelle S, Lina G, Dumitrescu O. The role of antibiotics in modulating virulence in *Staphylococcus aureus*. *Clin Microbiol Rev.* 2017;30(4):887-917. doi:10.1128/CMR.00120-16

Statistical Thinking Part 2: Relative Risk, Absolute Risk, and Number Needed to Treat

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Clearly communicating the risks and benefits of (and alternatives to) a treatment to patients is one of the most important tasks of clinicians. The data informing the task of communication can take many forms. For example, small differences in risks can appear very impressive and provide a false perception of benefit. Therefore, clinicians should have the skills to critically evaluate the data presented within research articles.

When reading studies, clinicians will invariably come across terms that describe effect size, such as relative risk, relative risk reduction, absolute risk difference, odds ratio, and hazard ratio (Table). Both patients and clinicians may be confused by the differences between percentage decreases in these terms. In part 2 of this limited series on statistical thinking, we present a story of risk that sets the stage for defining statistical terms that describe effect size and the number needed to treat, an intuitive term that helps clinicians and patients better express absolute effect size.

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A Story About Risk

Suppose one of your favorite patients, Mrs Smith, a 70-year-old retired algebra teacher, asks you to prescribe a new medicine she just read about in an online newspaper. The article reported a 50% reduction in heart attacks with this medicine. Mrs Smith noted that this result came from a large study of over 15 000 patients, and she astutely noted that she had many of the personal characteristics of the people in this 2-year study and, therefore, the results should apply to her. Furthermore, the authors described the results as "highly statistically significant," and the study was published in a prestigious medical journal. Based on this information alone, would you prescribe the new medicine for Mrs Smith?

Having read the article, suppose you respond to Mrs Smith by stating that "there is a 99% chance that you will not benefit from this new treatment in the next 2 years" (reflecting the length of the study). Stated differently, Mrs Smith has a 1% chance of benefiting from this new treatment in the next 2 years. How could a "highly statistically significant" 50% relative risk reduction (RRR) benefit only 1 person in 100 (1%) over 2 years?

When Mrs Smith requested this new treatment, she thought her risk of a heart attack was going to be reduced in half, eg, from a 100% chance to a 50% chance. Indeed, that is a 50% RRR. However, let's assume she was more optimistic and gauged her risk of heart attack to be reduced from 40% to 20%, which would also represent a 50% RRR. In reality, suppose that in the study she referenced the absolute risk of heart attack was reduced from 2% (in the placebo group) to 1% (in the treatment group). That also represents a 50% RRR. However, the absolute risk difference (ARD) was only 1% in this 2-year study. Given a 1% decrease in absolute risk, 100 people like Mrs Smith would have to be treated over a 2-year period to prevent, on average, 1 heart attack. Her next question is likely to be, "what will this new medicine cost?" "I may not be the one who benefits!" Indeed, chances are she will not benefit, and we haven't even considered the possible side-effects of or alternatives to this new treatment.

Stories such as the one presented here are not uncommon.[1] Studies presented in the lay media report treatment "x" reduces the risk of outcome "y" without reporting the probability of the outcome or precise statistics that describe the effect size, which creates a perception of benefit for lay individuals and confusion for clinicians. A fundamental understanding of statistical terms to describe effect size (relative risk, RRR, ARD, and number needed to treat) is paramount for understanding the results of a study and communicating with patients. In the "Critical Thinking in Medicine" thread within the Fusion Curriculum at the Medical College of Wisconsin, we teach medical students how to have a conversation with their patients by first explaining these terms using practical, story-like formats and analogies.

Relative Risk and Relative Risk Reduction

Relative risk (RR) is the ratio of 2 probabilities. For example, suppose 1 group of people has a 10% risk of a heart attack in the next 5 years and another group has a 5% risk. The RR of a heart attack for the second group, compared to the first, is 5% divided by 10% or 0.5. RRR is the proportional amount that a risk is decreased in 1 group versus another. Numerically, it is the control group event rate (CER) minus the experimental group event rate (EER) divided by the CER. In the example above, the RRR is calculated (10% – 5%)/10% or 50%. RR is a very useful concept, especially for identifying risk factors for disease. A problem occurs, however, if RR and RRR are presented without their corresponding absolute risks. Another problem arises when the benefits of some treatment are presented in terms of RRRs and the risks of the treatment are presented as absolute risks.[1] In this way, the same thing can be stated in very different ways. For example, in the study that Mrs Smith read, the authors stated that the treatment caused a 50% reduction in heart attacks (which is actually the RRR), but suppose they stated that only 1% of the subjects in the study experienced an adverse event. In that case, the same proportion of people avoided a heart attack as experienced an adverse event (1% in each case).

To summarize, the RR is a ratio of the probability of an event occurring in a treatment versus a control population, and the RRR is the proportional amount that a risk is decreased in 1 group compared to another.

Table. Definitions and Calculations of Common Statistical Terms Describing Effect Size

Statistical Term	Definition	Calculation
Absolute Risk (AR)	The probability of an event occurring in a population	Number of events in a population divided by the total number of individuals at risk for the event in a population
Relative Risk (RR)	The ratio of the risk of an event between 2 groups	The ratio of 2 probabilities, for example, experimental group event rate (EER) divided by control group event rate (CER)
Relative Risk Reduction (RRR)	The proportional amount that a risk is decreased in 1 group compared to another	Control group event rate (CER) minus experimental group event rate (EER) divided by CER
Absolute Risk Difference (ARD)	The measure of the absolute effect size of an intervention	Control group event rate (CER) minus experi mental group event rate (EER)
Number Needed to Treat/Harm (NNT/NNH)	Measures the effectiveness of an intervention by identifying the number of, patients, on average, that would need to be treated with an intervention for patient to benefit (NNT) or be harmed (NNH)	The NNT is the reciprocal of the ARR (1/ARR) and the NNH is the reciprocal of the ARI (1/ARI)
Odds	The probability of an event compared to the probability of it not occurring	Probability of an event (P) divided by the probability of it not occurring (1-P)
Odds Ratio (OR)	The odds (likelihood) of an event occurring in 1 group (eg, exposed) compared to another group (eg, nonexposed)	Odds of an event occurring in an exposed group ($P_{exposed}/1-P_{exposed}$) divided by the odds of it occurring in the nonexposed group ($P_{nonexposed}/1-P_{nonexposed}$)
Hazard Ratio (HR)	A measure of effect in a time-to-event survival analysis	The hazard rate in the treatment group divided by the hazard rate in the control group

Abbreviations: ARR, absolute risk reduction; ARI, absolute risk increase.

Absolute Risk

Absolute risk is a probability—and a very complex topic that is the subject of a future article. Probability is generally interpreted in 2 ways: as a long-run frequency (the "frequentist" view) or as a degree of belief that can be modified with additional data (the "Bayesian view").

When viewed as a long-run frequency, probability is the proportion of times that some event occurs over many repetitions of some process, carried out under similar conditions. For example, if a coin lands on heads 50 times out of 100 flips, we would say that there is a 50% probability of the coin landing on heads. There are a few problems here, however. What number (of flips) constitutes "many repetitions?" Is 100 enough? How about 500? Another problem with this definition is "similar conditions." What does that mean exactly? If all conditions, such as which side of the coin is facing up when flipped, exactly how vigorously the coin was flipped, the precise wind conditions, etc, were exactly the same, we could predict with certainty whether it would land heads or tails. Therefore, a coin flip appears to be random because we cannot measure or control the many variables that determine whether it lands heads or tails.

Another problem with the frequentist view is that many important processes do not occur "many times under similar conditions." Your favorite football team is only going to play this year's season once, not 100 times under similar conditions. Accordingly, what does it mean to state that there is a 10% chance of your team playing in the championship game?

To address some of these concerns with the frequentist view, another conception of probability has been advanced, referred to as the "Bayesian view," and named after the English clergyman, Thomas Bayes, who studied probability in the late 18th century.[2] In the Bayesian view, probability is a degree of belief that is modifiable with additional data. For example, before the start of the football season, we may feel that our team has a 10% chance of getting to the championship game, based on factors such as the results of the previous year and the current team makeup. As the year progresses and the team wins and loses games, we will probably revise our estimation of how likely the team will be in the championship game based on the new data. The revision of probability based on new data is the heart of the Bayesian view, which is especially useful when determining whether a patient has some disease. After taking a careful history, you develop some idea of the likelihood of a particular disease and then, after doing a physical exam and perhaps getting various lab tests, you revise your estimate of the likelihood of disease based on this additional data. In fact, our brain operates under a Bayesian framework on a day-to-day basis. For example, before the school

year begins, you have some idea of how well you will do in a particular course. As the year progresses and you see the results of various exams and quizzes, you then revise your impression (and perhaps your study habits) of how well you'll do.

Most statistical tests in the medical literature today are based on the frequentist view of probability. In part, this is because our first conception of probability was based on predicting games of chance. When outcomes are equally likely, the frequentist view works well. Also, the frequentist view is generally computationally much easier to understand and use. However, in time, with improvements in computer technology and artificial intelligence, the Bayesian approach is becoming more prevalent. We will rely heavily on the Bayesian approach in the next article in this series regarding interpreting laboratory tests.

Absolute risk, or probability, is a proportion, and a proportion is different than a rate. A rate has time in the denominator. For example, miles per hour or heart attacks per 100 patient-years are rates. Unfortunately in medicine, many terms that are really proportions are called "rates." For example, the "attack rate" is the number of patients who contract a given disease out of the total population at risk. Obviously, this is a proportion and not a rate, since it is a number between 0 and 1 and time is not in the denominator. It is important to keep the distinction between rates and proportions in mind because a ratio of rates is different from a ratio of proportions (probabilities). A proportion ranges from 0 to 1, whereas a rate ranges from 0 to infinity. So, a ratio of 2 proportions is different from a ratio of 2 rates, unless the rates and proportions are very small (as discussed below).

To summarize, the absolute risk is a probability—or the number times that some event occurs over many repetitions of some process—carried out under similar conditions and is measured as a proportion and, therefore, ranges between 0 and 1 (or 0% and 100%).

Number Needed to Treat and Absolute Risk Difference

In addition to RR and RRR, the effect of a therapy also can be expressed by the number of patients needed to treat (NNT) to prevent some event (or "cause" some good event). Conversely, the number needed to harm (NNH) is the number of people who would have to be treated over some time period to cause 1 "bad" event. This intuitive concept first appeared in medical literature in 1988,[3] which is very surprising given the simplicity of this measure.

The ARD is the difference in risk of some specific outcome between control and experimental groups. When the experimental group experiences greater harm compared to the control, the ARD is also known as the absolute risk increase (ARI). When the experimental group receives more benefit compared to the control group, the ARD is also known as the absolute risk reduction (ARR).

The NNT and NNH (NNT/NNH) is calculated as the reciprocal of the ARD (1/ARD) in the treatment groups, and the calculation always implies a certain follow-up time. In the example above with absolute risks of 10% and 5% heart attacks, the ARD is 5%. (This is also referred to as the "attributable risk," but we see no need to introduce extra terminology when teaching this concept for the first time.) The reciprocal of 5% or 0.05 is 1/0.05 (or 100%/5%), which equals 20. When calculating the NNT/NNH, it is crucial to state the time interval involved; after all, in the long run we all experience the same fate so we must state a time interval reflecting the study involved.

To make this concept clearer, suppose we have a treatment that cures everyone who receives it, and those who don't receive it all die. In that case, the risk difference is 100%, and 100%/100% equals 1. We would only have to treat 1 person to cure the disease. Moreover, if we have a treatment that cures 50% (and everyone not receiving the treatment dies), we would have to treat 2 people, on average, to cure 1 (100%/50% = 2). Similarly, if we have a treatment that cures 25%, we would need to treat 4, on average, to cure 1 person (100%/25% = 4).

Another way to remember how to calculate NNT/NNH is with a basketball analogy. If my free throw percentage is 50%, on average, I am going to have to go the free throw line twice to make 1 free throw. If my percentage is 25%, I am going to have to go the line 4 times, on average, to make 1 free throw.

To summarize, the ARD is the difference in risk of some specific outcome between control and experimental groups, and the NNT/NNH is calculated as the reciprocal of the ARD (1/ARD) and is a practical way to communicate the risks and benefits of an intervention.

Number Needed to Treat and Baseline Risk

Assuming a constant RRR, the NNT is inversely proportional to the baseline risk (the number of adverse events in the control group). As the baseline risk increases, the NNT is reduced (implying fewer patients would need to be treated with the therapy for 1 patient to benefit). Consider an example of patients with coronary heart disease (CHD). Suppose we have a group of CHD patients who have a 10-year risk of another heart attack of 20% (the absolute risk). If we provide a lipid lowering treatment to this group that decreases their risk by 30% at 10 years (the RRR), we will have decreased their absolute risk of a heart attack from 20% to 14% (20% x 0.3 = 6%; where 20% is the absolute risk and 0.3 is the RRR), and the absolute risk decreases from 20% to 14% (20% – 6%, or an ARR of 6%). The reciprocal of this 6% ARR is about 17 (100/6 = 16.67). In this high-risk population, 17 patients would need to be treated for 10 years (the risk period in this example) to prevent, on average, 1 heart attack.

Now suppose we have another group of people who have a 10-year risk of a heart attack of 1% (the absolute risk). If we provide them the same treatment that decreases their risk by 30% (the RRR), we would reduce their absolute risk to 0.7% (1% x 0.3 = 0.3%; where 1% is the absolute risk and 0.3 is the RRR of the treatment; 1% – 0.3% = 0.7%) and an ARR of 0.3% (1% – 0.7%). Therefore, the reciprocal of 0.3% ARR is 333 (100/0.3 = 333). In this low-risk population, we would have to treat 333 people for 10 years to prevent, on average, 1 heart attack.

To summarize, when the baseline risk is high, the NNT is low. When the baseline risk is low, the NNT is high because we are taking the reciprocals of absolute risk differences.

Additional Risk Ratios

Odds Ratio

Odds is less intuitive than probability. Recall that the probability measures how likely an event will occur divided by the total number of possible outcomes. Consider the following example: if some event occurs in 50% of a population, then the probability of it occurring is 50%/100% = 50%. The odds FOR an event occurring is the ratio of the probability of the event occurring divided by the probability of it not occurring. For example, if the probability of some event is 50%, the probability that it will occur is 50% and the probability that it will not occur is also 50%. The ratio of these is 50%/50%, which reduces to 1:1 or even odds. If some event has a 75% chance of occurring, there is a 25% chance that it will not occur, and this ratio – 75%/25%, which reduces to 3:1 – is the equivalent odds to a 75% probability. When the probability of some event is 5%, the probability that it will not occur is 95%, giving odds of 5:95 or 1:19. Notice when the event is relatively rare – in this case 5%, the probability and the odds are quite similar.

The odds ratio (OR) is a ratio of 2 odds, just as the RR is the ratio of 2 probabilities. When odds and probability are fairly similar—as they are when the risks are low, such as above—the OR and the RR are very similar. However, when the probability of an event is much higher, the OR and the RR can be quite different. For example, if the probability of an event is 75%, as noted above, the odds are 3:1. If the probability of this event in another group is 50%, then the RR for the event in 1 group versus the other is 75%/50% or 1.5. For this same comparison, the OR would be 3:1/1:1 or 3. Thus, in this example, the OR is twice the RR. Only when the risks are low (under about 10%) are the odds and probability reasonably comparable and, therefore, the OR and the RR are nearly equal.

Hazard Ratio

The hazard ratio (HR) is a measure of effect in a time-to-event survival analysis (to be covered in a subsequent article). In brief, a survival analysis is used when the outcome of interest is the time between the start of a study to when the event of interest (eg, heart attack) occurs. The hazard rate is the instantaneous rate of failure at some given time, given that the person has "survived" up to that time.

Mathematically, the HR is the ratio of hazard rates and is calculated by the hazard rate in the treatment group divided by the hazard rate in the control group. It is frequently more informative to compare the rates of the occurrence of 2 events rather than the cumulative number of events in each group at the end of the study (which the RR does). For example, if all subjects in the treatment group of a 4-year study experience the event of interest in the last year of the study (with no events in the first 3 years), their survival experience would be very different from a control group that experienced the event at a constant rate throughout the study. If, at the end of the study, the same number of events occurred in each equal-sized group, we would much rather be in the group that experienced events only in the last year of the study. Those 3 years of event-free survival would be very important! Survival analysis allows this kind comparison using HRs. In this example, the RR of the event would be 1.0 because the same proportion of patients experienced the event over the course of the study. However, the HR would be very different and would reflect the different hazard rates in each group.

When risks are below approximately 10%, the RR, OR, and HR are all comparable. For example, the event rates in cardiovascular studies are often less than 10%, and the RR, OR, and HR are similar. On the contrary, the event rates can be much higher in oncology studies, causing the RRs to be much different than the HRs and the ORs.

To summarize, the OR is the odds of an event occurring in an exposed group compared to the odds of it occurring in a nonexposed group (a ratio of 2 odds). The HR is measure of effect in a time-to-event survival analysis and informative to compare the rates of the occurrence of 2 events during a study.

Conclusion

Statistics of effect are measures used to describe, for example, the strength of a therapy in a study. Common measures include RR, RRR, ARD, and NNT. Reporting RRR without absolute risk may be misleading (eg, large RRR may have little clinical meaning if the absolute risks are small [and the NNT is large]). The NNT/NNH incorporate baseline risk and are practical ways to express the effectiveness of a treatment to facilitate clinical decision-making. Probabilities in the frequentist approach are proportions (and not rates) and range from 0 to 1 (0% to 100%). As the baseline risk increases, the NNT decreases. The RR is a ratio of probabilities, the OR is a ratio of odds, and the HR is a ratio of hazard rates. Each of these measures have different uses, meanings, and limitations; and in future articles, we will expound on the appropriate uses of these measures of effect. In part 3 of this series, we will utilize the Bayesian approach and demonstrate how to interpret diagnostic tests with probabilistic thinking.

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REFERENCES

1. Gigerenzer G, Wegwarth O, Feufel M. Misleading communication of risk. *BMJ*. 2010;341:c4830. doi:10.1136/bmj.c4830

2. Stigler SM. *The History of Statistics*. Belknap Press; 1986:88,97-98.

3. Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med*. 1988;318(26):1728-1733. doi:10.1056/NEJM198806303182605

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