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WMJ

2023 • volume 122 • issue 3

Q fever, West Nile virus, leprosy & more:

Infectious Disease

in the Midwest

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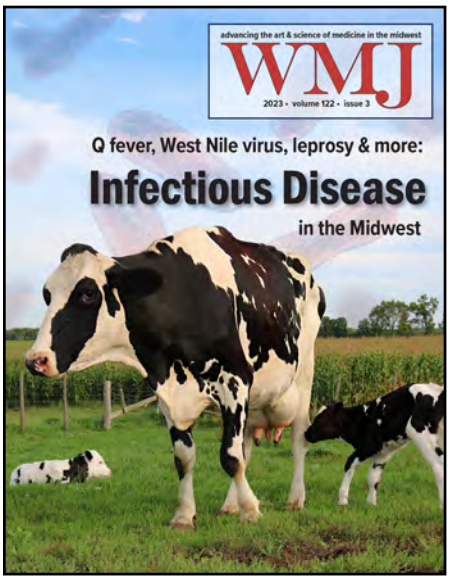

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WMJ

advancing the art & science of medicine in the midwest

COVER THEME

Infectious Disease

From a pediatric case of Q fever to cases of West Nile virus presenting with ocular symptoms and leprosy with no known exposure or travel to endemic areas, a series of reports in this issue of WMJ *explores some of the myriad infectious diseases that affect patients in the Midwest.*

Cover design by Kendi Neff-Parvin

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EDITORIAL

ORIGINAL RESEARCH

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BRIEF REPORTS

CASE REPORTS

REVIEW

Do Internal Medicine Advanced Practice Providers Perceive a Benefit in Mentorship?

Dear Editor:

Mentorship programs across medicine have shown multiple benefits, including increased professional satisfaction and retention, participation in academic scholarship, and development of leadership skills.[1] Historically, opportunities for advancement to faculty positions within academic institutions have not existed for advanced practice providers (APPs); however, the Medical College of Wisconsin (MCW) is changing that. Faculty promotion typically requires involvement in scholarly work, research, and education. APP education models focus on clinical knowledge and work, offering limited exposure to research and publication, with the goal of filling clinical shortages. Therefore, APPs rarely participate in academic scholarship early in their careers.[2] Recent studies show the first 3 to 5 years of an academic provider's career are the most important in developing research and publishing skills, because after that time, they are often recruited by other nonacademic organizations.[3]

In January 2023, an anonymous Qualtrics survey was sent to all 61 APPs in the Division of General Internal Medicine at MCW to assess their perception of mentorship among general internal medicine APPs. A total of 50 APPs completed the survey, with a response rate of 81% (64% hospitalists, 14% primary care, 14% perioperative medicine, and 8% observation unit). Ninety percent of respondents were female, and 62% had less than 5 years of experience as an APP. About 90% of APPs said mentorship was important, and of those who have had a mentor, 74% reported finding it beneficial. Perceived benefits of mentorship included advancing clinical knowledge, gaining skills for precepting students, and building your CV for career advancement and leadership opportunities. Perceived barriers to mentorship included time constraints, mentor availability, and lack of structured mentorship program. Regarding structure preference in a mentorship program, 74% of APPs prefer a mentor from the same section; and 26% prefer APP to APP, 20% prefer MD to APP, and 26% prefer mixed APP and MD to APP, depending on career interests.

Based on the interest and perceived benefits, our division is developing a mentor program for APPs. Participation will be optional, and pairing mentors and mentees will be aligned with career interests. Our future work will be focused on evaluating the effectiveness of this formal program. This mentorship model might encourage other institutions to implement similar programs to support APP career development and advancement.

—Andrea Bequest, PA-C; Paige Gioia, PA-C; Sanjay Bhandari, MD; Pinky Jha, MD, MPH

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Fahad Aziz, MD, FASN

Compassionate Care Essential for Better Clinical Outcomes, Burnout Prevention

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

On February 27, 2007, a crash occurred before 9 AM between two buses on a snowy road in central Sweden. In this terrible accident, at least six people died, nine were seriously injured, and 42 suffered minor injuries. Most of the wounded were taken to Uppsala University Hospital. Two of the most seriously injured were airlifted to a Stockholm hospital.[1]

In 2014, Doohan et al conducted telephone interviews with the survivors. The sample consisted of 54 of 56 survivors: 21 women and 33 men. The questions asked were about prehospital discomfort, lack of compassionate care, and dissatisfaction with crisis support. Even after so many years, the survivors remembered not only the physical pain but also the lack of compassion they received in the emergency department. The authors concluded that a lack of compassion among health care professionals affected the patients' well-being to the degree that it remains one of the worst memories of the crash seven years later.[2] While patients and families may not remember the name or face of a doctor or nurse who cared for them on one of the worst days of their life, the slightest compassion they receive from health care professionals may stick with them long after.

Derived from a Latin word that means "together suffering" or "fellow in feelings," compassion arises in response to someone's suffering and includes a motivation to relieve their suffering. And while similar to pity, sympathy, and empathy, there are clear differences. Pity is a simple expression of sorrow; sympathy goes a step further; it is composed of a range of feelings and means understanding what the other person is feeling. Finally, empathy is feeling what the other person is feeling but does not require action or sustain itself over time.[3] (See Figure.)

> "The most exciting breakthroughs of the 21st century will not occur because of technology, but because of an expanding concept of what it means to be human."
>
> —James Nasibitt

Physician/scientists Stephen Trzeciak and Anthony Mazzarelli wrote in their book *Compassionomics, The Revolutionary Scientific Evidence That Caring Makes a Difference,* "Empathy is like a one-way street running toward the health care provider: detecting, processing, understanding, and even feeling the incoming emotional cues from the patient. Compassion, on the other hand, is a street that runs in the other direction, a responsive action toward the one who is suffering. Empathy can happen through a one-way mirror. Compassion cannot."[4] In other words, compassion has two components: (1) feeling someone's suffering, and (2) the ability to take action to relieve them from that suffering.[5,6]

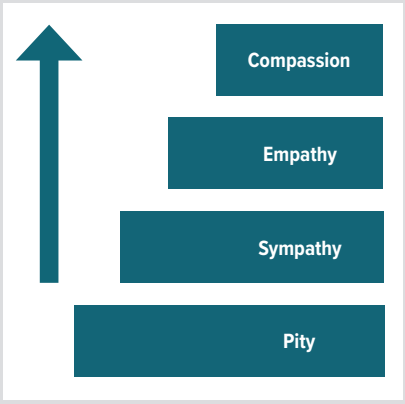
WHY DOES COMPASSION MATTER?

Patient Outcomes

The release of *Compassionomics* ignited a conversation about the relationship between physician compassion and patient outcomes, and several studies have demonstrated that health care providers' compassion significantly improved patients' clinical outcomes – especially those with chronic medical conditions.

Watts et al aimed to elucidate the role of compassionate care in various aspects of medicine and health care delivery. They conducted a literature review of four databases and included 22 articles in the study. Their analysis showed that along with enhanced patient outcomes, compassionate care was associated with reduced care costs, lower rates of compassion fatigue and burnout, and fewer malpractice claims.[7]

Figure. Staircase to Compassion



In another study, Hojat et al tested the hypothesis that health care compassion is associated with favorable clinical outcomes in diabetic patients. The study included 891 diabetic patients and showed that patients of physicians with high empathy scores were significantly more likely to have reasonable control of their hemoglobin A1c (56%) than were patients of physicians with low empathy scores (40%, $P<.001$). The study concluded that health care providers' compassion is an essential factor associated with better clinical outcomes in patients with diabetes.[8] Several other studies showed that compassionate care by physicians, physician assistants, and nurses predicts faster recovery, significant autonomy, lower intensive care utilization, and more responsible healthcare management.[9-12]

The above data showed that the healthcare provider's compassion significantly improved patients' clinical outcomes, especially those with chronic medical conditions.

Clinician Burnout

In their 2022 book *Wonder Drug: 7 Scientifically Proven Ways That Serving Others Is the Best Medicine for Yourself,* Trzeciak and Mazzarelli demonstrate that providing compassionate care to patients is extremely important for health care providers. It prevents burnout and compassion fatigue and is also a source of happiness and accomplishment.[13] "You don't lose anything by serving others, you only gain. Giving is a powerful therapy for the giver, any giver," said Trzeciak.

COMPONENTS TO COMPASSIONATE CARE

There are three essential components of companionate care:

1. **Serve by intention:** In the words of leadership expert and author John C. Maxwell, "Good intentions turn into good actions." A genuine intention to help people in their suffering is the most essential and crucial step to compassionate care.
2. **Be humble:** Humility and gratitude are also crucial to compassionate care. In his interview with Oprah Winfrey in 2001, Nelson Mandela said, "Humility is the most important thing you should have to succeed. If you make people realize you are no threat to them, they will take no time to embrace you." Being a humble and grateful health care professional does not equal weakness or being soft; rather, it reduces arrogance and strengthens the clinician.
3. **Spread hope:** Believing is a significant factor in a patient's recovery.[13] Spreading hope does not mean giving false information but rather showing "silver linings" in difficult medical conditions. When a patient has hope, it can have a positive impact on their quality of life, leading to better adaptation and lower stress levels, anxiety, and depression.

American author John Nasibitt once said, "The most exciting breakthroughs of the 21st century will not occur because of technology, but because of an expanding concept of what it means to be human."

With the pressures we face as clinicians every day, providing compassionate care is essential. Not only does it produce better clinical outcomes for patients, but it is a defense against burnout. Unfortunately, in conventional medical education, the importance of compassionate care is rarely taught. It is crucial that we put extra effort into incorporating "compassionate care" teaching into the curriculum of our future medical providers.

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Improving Health Equity Through the Integration of Mental Health Services Within Primary Care

Jeffrey D. Shahidullah, PhD; Rachel A. Petts, PhD

This commentary demonstrates how the integration of mental health services within primary care aligns with calls for improving health equity and access within the health care system.[1] By recognizing the advantages of a range of integrated care models within primary care, clinicians, health care administrators, and policymakers can advocate for the model within their systems not just to improve health and wellness outcomes, but also to improve opportunities for all individuals – particularly those from minoritized groups – to access quality, whole-person health care.

Disparities in accessing quality mental health care among minoritized groups and individuals living in poverty is a widespread problem. For instance, data from the National Health Interview Survey in 2021 found that around 30.4% of White adults received mental health treatment within the past year, compared to 14.8% of Black, 12.8% of Hispanic, and 10.8% of Asian adults.[2] Further, geographic data across the United States demonstrate that communities within the lowest income quartile are less likely than those within the highest income quartile to have access to a physician mental health specialist (8% vs 25.3%), a nonphysician mental health professional (12.9% vs 35.1%), and any community-based mental health treatment resource (23.1% vs 42.5%).[3] A variety of structural and perceptual barriers may affect access to quality mental health care. Structural barriers include lack of insurance status or limited financial resources, while perceptual barriers could include stigma or lack of trust with the health care system.[4] Relatedly, experiences of discrimination or racism also affect willingness to continue with care in communities of color.[5]

Delaying or failing to access timely, quality mental health care can lead to chronic mental health problems and impaired functioning. Lack of access to mental health treatment in minoritized communities also is associated with lack of access to health care in general and poorer health outcomes.[6] For instance, Black and Brown communities have higher rates of chronic illnesses, such as obesity, diabetes, and hypertension, and are less likely to receive needed care for these conditions.[6,7] Psychosocial factors, such as untreated depression, can affect health, including attendance at appointments and follow-through with a medical regimen, while impaired health status can further exacerbate one's health problems. In other words, mental health disparities are associated – and often exacerbate – other health disparities and vice versa.

> Integrated care increases access to services and improves patient outcomes, improves primary care clinicians' efficiency and self-reported competency and satisfaction with care delivery, and increases follow-up with mental health referrals.

Primary care may be the ideal setting to address these mental health and health disparities. Mental health care is considered specialty (secondary) care and is, by definition, less accessible. Workforce shortages of psychiatrists and psychologists – particularly in rural medically underserved areas – create long waitlists for specialty mental health care in the community.[8] As a result, primary care physicians are often the first professionals that individuals go to in order to discuss mental health problems and provide most mental health care.[9,10] For the patient, there may be comfort in discussing concerns with a provider they have seen previously.

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It is also convenient and does not require a referral or transfer of care to an unfamiliar clinic or provider. As the first point of care for most in the health system, primary care clinics may be well-positioned to improve access to mental health care for underserved communities.

Despite its promise, there are many barriers to primary care clinicians addressing mental health problems in primary care.[9,10] These barriers include a lack of collaborative infrastructure (eg, shared electronic medical record, shared space, curbside consults, warm hand-offs) to address mental health needs in a way that is effective and coordinated with mental health clinicians. They also include a lack of time in addressing mental health concerns, as typical reimbursement systems do not incentivize assessment or treatment. Further, if needs do arise that necessitate further treatment or consultation, some practices may not have systems in place to facilitate referrals to specialized care and, thus, many individuals do not receive the level of care that is necessary.

Fortunately, there are a range of models that integrate mental health clinician services in primary care, spanning from offsite coordinated care to onsite collaborative care and integrated care. Coordinated care models use offsite psychiatrists to provide training and case-based consultation to increase the knowledge, skills, and confidence of primary care clinicians around mental health (eg, Massachusetts Child Psychiatry Access Project [MCPAP]).[11] Collaborative care models collaborate in patient care onsite by screening for a specific, high-frequency condition (eg, depression, attention deficit hyperactivity disorder) and engaging in a protocol-driven decision process that may include onsite or coordinated mental health services using care managers and offsite psychiatric consultation (eg, Reaching Out to Adolescents in Distress [ROAD], Improving Mood-Promoting Access to Collaborative Treatment [IMPACT]).[12,13] Integrated care models embed mental health clinicians onsite for shared patient care that may include same-day access, joint treatment plans, and shared real-time collaboration with primary care clinicians.[14]

Integrated care increases access to services and improves patient outcomes, improves primary care clinicians' efficiency and self-reported competency and satisfaction with care delivery, and increases follow-up with mental health referrals.[15,16] These models also improve equity in access and outcomes since receiving mental health care where patients receive their physical health care is less stigmatizing and more comfortable, particularly for Black and Brown patients who face the greatest disparities in mental health access.[1,17-18] Mental health in primary care also improves overall health and health disparities.[19,20] Addressing mental health and psychosocial factors that affect chronic health conditions, such as asthma, diabetes, and obesity, has enormous potential to improve physical health and wellness and reduce unnecessary medical procedures, hospitalizations, and emergency department visits.[1,19]

The sustained and widespread implementation of models that integrate mental health in primary care to improve health equity will require transformations in practice, policy, and payment. Health insurer reimbursement must account for the downstream cost savings that results from reduction of unnecessary medical procedures, hospitalizations, and emergency department visits when patients receive high-quality and whole-person primary care that addresses mental health and physical health needs proactively in primary care.[21,22] This cost savings can be reinvested in paying for upfront costs of hiring and training mental health clinicians and other primary care team members (eg, care managers, social workers, system navigators, health educators) and covering annual physical health and mental health wellness check-ups, including mental health screening in primary care.

Moving forward it will be important to increase the accessibility of the integrated primary care model. Evaluations show that the model can yield improved care outcomes and cost savings, while reducing ethnic/racial disparities in care.[9] The integration of mental health services within primary care faces a number of implementation challenges, such as reimbursement, confidentiality rules for mental health, limited capacity, and resistance to change.[23] We must have a call to action to continue to advance this model given its potential to improve not only health and wellness outcomes, but also health equity.

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Inpatient Pediatric Care and Clinician Workforce in Wisconsin: The State of the State

Samantha Busch, BS; Ann Allen, MD; Jen Birstler, MS; Andrea Ildiko Martonffy, MD

ABSTRACT

Introduction: Availability of inpatient pediatric services declined across the United States from 2008 through 2018, with rural areas experiencing steepest declines. Despite the movement of pediatric care to children's centers, most children are still cared for in community hospitals nationally. Assessing the availability and providers of inpatient pediatric care in Wisconsin is an important step in ensuring the health care needs of children in the state continue to be met.

Methods: A cross-sectional survey was distributed to Wisconsin hospitals to determine pediatric services and physician workforce. The response rate was 130/138 (94%), including 56/58 (97%) critical access hospitals. Results of specific inpatient pediatric subdivisions were analyzed by descriptive statistics.

Results: Hospitals that provide inpatient newborn care are mostly staffed by pediatricians and family physicians, while critical access hospitals are staffed by family physicians. Hospitals with neonatal intensive care units are staffed by neonatologists, with telemedicine utilized in critical access hospitals. Hospitals with general pediatric admissions are staffed by pediatricians or family physicians, while critical access hospitals are staffed by family physicians. Hospitals with pediatric intensive care units are staffed by pediatric intensivists.

Conclusions: Despite workforce disparities and shortages, hospitals across Wisconsin, including many critical access hospitals, continue to provide inpatient pediatric services. Family physicians play a major role in the pediatric health care delivery in Wisconsin hospitals. Robust inpatient pediatric training of family physicians may enable rural health authorities to continue addressing the gaps that persist in inpatient pediatric care accessibility.

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INTRODUCTION

A retrospective study reviewing the availability of pediatric inpatient services in the United States from 2008 through 2018 showed an 11.8% decrease in pediatric inpatient unit beds, with rural areas experiencing a steeper decline than urban areas.[1] Hospitals in Wisconsin experienced the second greatest decline in the number of pediatric beds, behind Wyoming.[1] Another retrospective study from 2008 through 2016 determined that the capability for definitive hospital care for children at acute care hospitals had declined across the United States, especially at hospitals with low pediatric volumes and those serving rural populations. In addition, emergency department transfers for children increased at all acute care hospitals, with the exception of tertiary pediatric institutions.[2]

In Wisconsin, there are currently 58 critical access hospitals (CAH), which are rural acute care facilities designed by the Centers for Medicare and Medicaid Services (CMS) to improve access to essential health care.[3,4] Pilkey et al found that CAHs see few children and are challenged to remain proficient and capable of caring for pediatric patients.[5] However, prior studies continue to show that 50% to 70% of children are cared for in community and acute care hospitals nationwide, rather than tertiary children's centers.[6] It is unclear what the current state and accessibility of inpatient pediatric care is in Wisconsin, especially in its rural hospitals. As the national trends show declining inpatient pediatric capabilities at acute care and community hospitals, fur-

ther quantification of inpatient pediatric care in Wisconsin – particularly in rural areas – is necessary.

The newest proposed residency training guidelines from the Family Medicine Accreditation Council for Graduate Medical Education Review and Recognition Committee would exclude requirements for family medicine residency faculty to provide inpatient pediatric care.[7] However, family physicians historically have provided pediatric care in a variety of settings, including inpatient care. As of 2021, there are 110 areas in Wisconsin – both urban and rural – that have been designated as total primary care Health Professional Shortage Areas (HPSA), which include the specialties of general practice, family medicine, general internal medicine, pediatrics, and geriatrics.[8] A 2019 report by the Wisconsin Department of Health Services (DHS) notes that of Wisconsin's 72 counties, 33 were experiencing a shortage of primary care physicians; those counties with a higher proportion of rural areas were at greater risk of a severe shortage.[9]

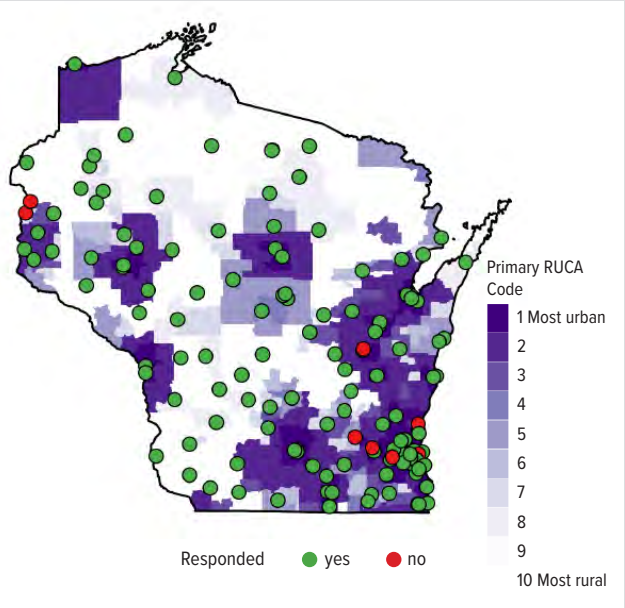
Approximately 24% of the Wisconsin population is considered rural, designated by an area with a population of less than 2,500 and 25 miles or more away from a population of greater than 50,000.[10] A 2021 report from the Wisconsin Council on Medical Education and Workforce demonstrated a longstanding maldistribution of the health care workforce, noting that 93% of physicians practice in urban areas, leaving 7% of physicians to cover Wisconsin's rural population.[11] The results of this study will help to better understand some of those needs and future directions of inpatient pediatric care across the state.

METHODS

With input from stakeholders, a cross-sectional Qualtrics electronic survey was designed and distributed to contacts at Wisconsin hospitals designated as general medical and surgical care or as a CAH from June through July 2022 (Figure 1). Hospitals that focused solely on rehabilitation, surgical, psychiatric, long-term acute, or veteran affairs were excluded. Nonresponding hospitals were contacted by phone and offered the opportunity to complete the survey via telephone interview. Four main categories of inpatient pediatric care were used to cover all types of pediatric care in hospitals, including inpatient newborns, inpatient pediatrics, neonatal intensive care unit (NICU), and pediatric intensive care unit (PICU). Options for physician management of pediatric care included pediatrician, family physician, pediatric hospitalist, neonatologist, pediatric intensivist, and "other" (Figure 2). Survey respondents also were asked open-ended questions about recent changes in their hospital system in the past 5 years or goals regarding inpatient pediatrics in the next 5 years.

Complete responses were received from 130 of 138 (94%) of Wisconsin's general medical surgical hospitals and 56 of 58 (97%) of Wisconsin hospitals designated as CAHs (Figure 1). Responses came from a variety of personnel, including chief nursing officers, chief medical officers, chiefs of staff, nurse managers, physicians, and other staff members. In addition to survey responses, hospital informatics data from DHS and the WHA Information Center was used to verify responses and supplement the information collected.[12] CAH designation was used in lieu of hospital rurality. Maps and figures were made using R version 4.1.3 (2022-03-10) and formatted using rural urban commuting area codes. Further data were analyzed using descriptive statistics. This study was not deemed to constitute human subject research and, therefore, was not subject to institutional review board review.

Figure 1. Map of Wisconsin With Hospitals Contacted for Survey Distribution



Abbreviations: RUCA, rural urban commuting area.

RESULTS

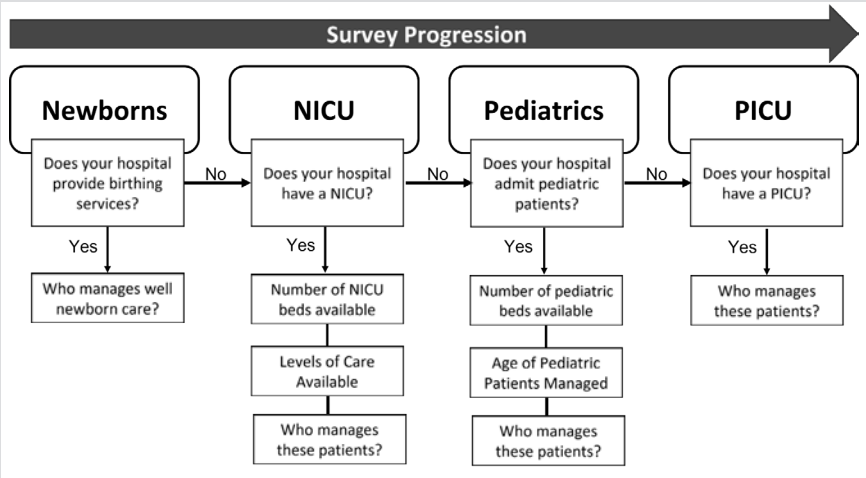
Inpatient Newborn Services

Survey results showed 87 (64%) Wisconsin hospitals currently provide inpatient newborn care, defined as the care of a newborn after delivery (Figure 3A). Of those hospitals, 28 (32%) are designated as CAHs. Hospitals providing inpatient newborn care were widespread throughout Wisconsin, with higher density in more urban areas.

Of the hospitals that provide inpatient newborn care, more than half utilize pediatricians (63%) or family physicians (55%) (Figure 4A). Other clinicians include neonatologists (8%), pediatric hospitalists (8%), nurse midwives (5%), neonatal nurse practitioners (3%), newborn hospitalists (2%), and telemedicine neonatologists (1%). Of note, 10 hospitals (11%) either did not report which clinicians provide inpatient newborn care or did not fill out the survey.

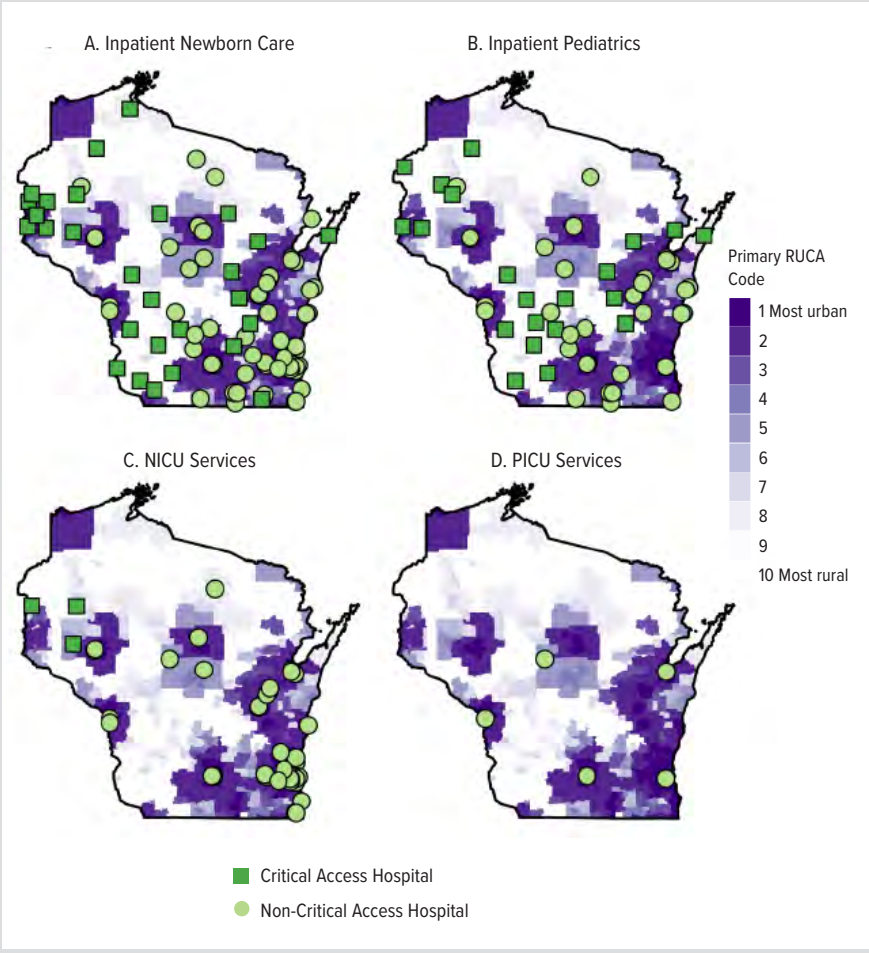
Of the CAHs, over three-fourths (79%) utilize family physicians for inpatient newborn care. Other less common clinicians

Figure 2. Electronic Survey Structure of Inpatient Newborn, NICU, Inpatient Pediatrics, and PICU Hospital Services



Abbreviations: NICU, neonatal intensive care unit; PICU, pediatric intensive care unit.
Respondents answered 1 to 3 additional questions if answered Yes, or move to the next category if selected No.

Figure 3. Maps of Wisconsin Hospitals that Provide Services of (A) Inpatient Newborn, (B) Inpatient Pediatric, (C) NICU, and (D) PICU Services



Abbreviations: NICU, neonatal intensive care unit; PICU, pediatric intensive care unit.

at CAHs include pediatricians (25%), nurse midwives (11%), telemedicine neonatologists (3%), and neonatal nurse practitioners (3%). These findings suggest that family physicians are the most common type of clinicians for inpatient newborn care in rural Wisconsin hospitals, while both pediatricians and family physicians comprise the majority who engage in inpatient newborn care at hospitals throughout Wisconsin.

Inpatient Pediatric Services

Fifty-six (41%) Wisconsin hospitals currently provide inpatient pediatric care, defined as admission of pediatric patients between the ages of 0-17 years old who do not need intensive care (Figure 3B). Of those hospitals, 21 (38%) are designated as CAHs. At all Wisconsin hospitals that admit pediatric patients, the median number of pediatric beds is 8, with the highest number of beds being 250. At the CAHs, the average number of pediatric beds is 7. Of the hospitals that admit pediatric patients, 46% do not have designated pediatric beds and rather admit pediatric patients to their general medical units. Overall, hospitals providing inpatient pediatric care are also widespread throughout Wisconsin but less dense than hospitals providing inpatient newborn care.

Of all Wisconsin hospitals that care for inpatient pediatric patients, more than half utilize pediatricians (59%) or family physicians (59%) (Figure 4B). Other clinicians include pediatric hospitalists (18%), hospitalists (13%), telemedicine pediatricians (4%), subspecialty physicians (2%), and acute care nurse practitioners (2%). Of the CAHs, almost three-fourths (71%) utilized family physicians for inpatient pediatric care. Other less common clinicians at CAHs include pediatricians (29%), hospitalists (24%), and telemedicine pediatricians (10%). One hospital did not report which clinicians provide inpatient newborn care. These findings suggest that family physicians are the most common type of clinician for inpatient pediatric care in rural Wisconsin hospitals, while both pedi-

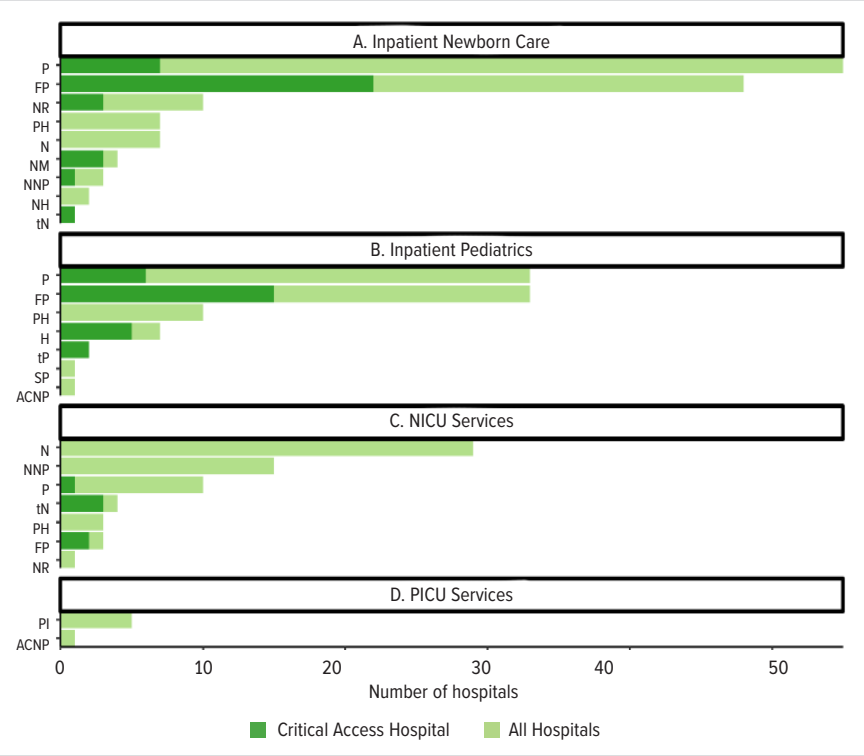
atricians and family physicians comprise the majority who engage in inpatient pediatric care at Wisconsin hospitals.

NICU Services

Forty-one (30%) Wisconsin hospitals currently have a NICU, varying from level 1 (lowest level of care need) to level 4 (highest level of care need) (Figure 3C). There are 6 level 1 NICUs, with an average of 2 beds available; 19 level 2 NICUs, with an average of 8 beds; 14 level 3 NICUs, with an average of 26 beds; and 2 level 4 NICUs, with an average of 75 beds. Of the Wisconsin hospitals with NICUs, 3 (7%) are designated as CAHs and all are level 1. Overall, hospitals with NICUs are clustered around more urban areas in Wisconsin, with the few designated NICUs in CAHs in the northwestern region of the state.

Of the 41 hospitals with NICUs, almost three-fourths utilize neonatologists (71%) (Figure 4C). Other clinicians include neonatal nurse practitioners (37%), pediatricians (24%), telemedicine neonatologists (10%), family physicians (7%), and pediatric hospitalists (7%). Of the CAHs, all (100%) utilize telemedicine neonatologists to care for neonates in NICUs. Other clinicians at CAHs include family physicians (67%) and pediatricians (33%). These findings suggest that neonatologists comprise the majority who care for neonates in Wisconsin NICUs, with telemedicine neonatologists being utilized to cover NICUs in CAHs.

Figure 4. Inpatient Pediatric Workforce of Wisconsin Hospitals That Provide (A) Inpatient Newborn, (B) Inpatient Pediatric, (C) NICU, and (D) PICU Services



Abbreviations: CAH, critical access hospital; NICU, neonatal intensive care unit; PICU, pediatric intensive care unit; ACNP, acute care nurse practitioner; FP, family physician; H, hospitalist; P, pediatrician; PH, pediatric hospitalist; PI, pediatric intensivist; N, neonatologist; NH, newborn hospitalist; NNP, neonatal nurse practitioner; NM, nurse midwife; SP, subspecialty physician; tN, telemedicine neonatologist; tP, telemedicine pediatrician; NP, not reported.

PICU Services

Five (4%) Wisconsin hospitals currently have a PICU, as designated by guidelines from the American Academy of Pediatrics (Figure 3D). Of these hospitals, 3 are designated as tertiary children's centers and none are CAHs. Hospitals with PICUs are clustered around more urban areas in central and southern Wisconsin; and all (100%) utilize pediatric intensivists and 1 (20%) utilizes pediatric acute care nurse practitioners (Figure 4D).

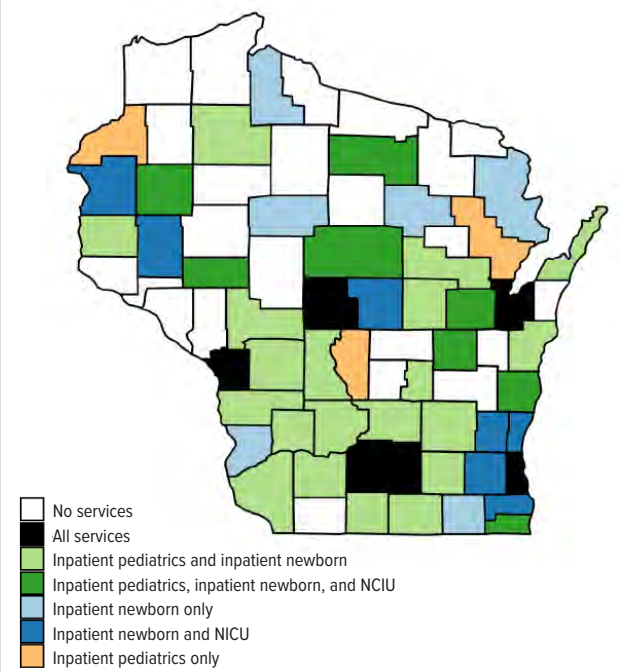
Overview of Inpatient Pediatric Services

Of Wisconsin's 72 counties, 5 have at least 1 hospital with all 4 pediatric services, including inpatient newborn, inpatient pediatrics, NICU, and PICU (Figure 5). Eight counties have hospitals that provide inpatient newborn, inpatient pediatrics, and NICU services. Eighteen counties have hospitals with inpatient newborn and inpatient pediatrics services, and 7 counties have hospitals with inpatient newborn and NICU services. Eight counties have hospitals that provide inpatient newborn services only, and 3 counties have hospitals that provide inpatient pediatrics services only. Notably, there are 23 counties with no type of pediatric services; many of these counties have a higher density of rural areas.

Information also was gathered on changes to the volume of inpatient pediatrics admissions and workforce at hospitals in Wisconsin over the past 5 years, with 37 non-CAH respondents and 22 CAH respondents. At non-CAHs, 7 hospitals closed their general inpatient pediatric units or services, 2 hospitals closed their inpatient newborn services, 41% of respondents now transfer all of their pediatric patients to different hospitals, and 24% continue to admit low acuity pediatric patients but transfer all others that need a higher level of care. Of the non-CAH respondents, 17% noted that shortages of nurses or providers or insufficient staff experience limit their ability to provide inpatient services. Three non-CAHs added an advanced practice practitioner (APP) program, 1 added a family medicine hospitalist program, and 1 closed its pediatric hospitalist program.

Among CAHs, 1 closed its general inpatient pediatric services, 5 closed their inpatient newborn services, 32% of respondents now transfer all of their pediatric patients to a different hospi-

Figure 5. Wisconsin Counties With Hospitals That Provide Inpatient Pediatric Services



Abbreviations: NICU, neonatal intensive care unit; PICU, pediatric intensive care unit.

tal, and 27% admit low acuity pediatric patients but transfer all others. One CAH added an APP program, 4 added telemedicine neonatologist or telemedicine pediatrician programs, and 1 added a family medicine hospitalist program. Many hospitals throughout Wisconsin—both CAH and non-CAH—noted that the COVID-19 pandemic limited their capability for pediatric admission.

Further information was gathered on hospitals' goals regarding their inpatient pediatric services in the next 5 to 10 years. Two hospitals indicated plans to expand their inpatient newborn, general inpatient pediatric, and PICU services, while 5 hospitals plan to expand their NICU services. Two hospitals plan to close their inpatient pediatric services; 2 hospitals hope to add APP programs; and 52 CAHs hope to add a pediatric hospitalist program or telemedicine neonatologists.

DISCUSSION

As inpatient pediatric availability has been declining nationwide, the current state of inpatient pediatric care in Wisconsin has been unclear. Wisconsin's rural areas have been at risk of or are already experiencing shortages of family physicians and pediatricians, compounding the state's historic physician workforce disparities in urban versus rural areas.[8,9] Despite these workforce disparities and shortages, some CAHs in Wisconsin continue to provide pediatric care, although many have low pediatric census and inadequate staffing, and some have closed their services altogether.

A 2018 study by the Wisconsin Office of Rural Health determined that 53% of CAHs in Wisconsin delivered babies, defined as having a stable number of births for the past 5 years.[13] The current cross-sectional study has now shown that 48% of the CAHs in Wisconsin provide inpatient newborn care and 32% provide inpatient pediatric care. Therefore, in the past 4 years, there may have been an approximate 5% decline in the number of CAHs that can provide inpatient newborn care. No recent study for comparison of inpatient pediatrics in Wisconsin could be found. Notably, several counties do not have any type of inpatient pediatric services, which may increase driving times to care and, therefore, limit accessibility for those who live in these regions. Further study is needed to help rural health authorities address the gaps that persist in inpatient pediatric care accessibility.

With Wisconsin mirroring the nationwide decline in inpatient pediatric care availability in rural areas, it remains important for both pediatric and family medicine residency training programs to provide a robust foundation in inpatient care. Both pediatricians and family physicians continue to play a major role in the pediatric health care delivery in Wisconsin hospitals, with a significant portion of rural Wisconsin hospitals utilizing primarily family physicians. Therefore, family medicine programs that have faculty providing inpatient pediatric care should be encouraged to continue providing this care, as residents may be more likely to continue practicing inpatient pediatric care if they have seen this modeled by their faculty.

Nationwide, inpatient coverage by pediatric hospitalists is becoming more common, even in smaller community hospitals.[14] Early career fellowship-trained pediatric hospitalists have self-reported a higher level of competency in core areas compared to their nonfellowship-trained peers.[15] Our findings suggest that non-CAHs in Wisconsin are starting to utilize pediatric hospitalists for inpatient pediatric services but to a much lesser extent than other specialties. As this field continues to develop and as the number of fellowship-trained physicians increases, there may be a shift in the inpatient pediatric physician workforce across the state in the future.

Another emerging field in medicine is the use of telemedicine for remote health care services without the need for direct contact with the patient. With the COVID-19 pandemic, telemedicine has been expanding rapidly across the country, with some physicians and hospital systems considering integrating telemedicine into their practice long-term.[16] In a 2021 study, neonatal telemedicine was shown to improve access to care and improve patient outcomes, especially in rural hospitals.[17] At both CAHs and non-CAHs across the state, telemedicine neonatologists and telemedicine pediatricians have been utilized for inpatient pediatric care.

There has been a recent push for regionalization of inpatient pediatric care, with children's centers now having a higher mean volume of inpatient pediatric patients than general hospitals.[6] Also nationwide, transfers out of community hospital emergency

departments to other hospitals that have the necessary level of inpatient pediatric capabilities and services also have increased, possibly contributing to the higher volume of patients seen at children's centers.[2] However, throughout the COVID-19 pandemic, many pediatric centers stated that they were "at or near capacity" and expressed concern they would not have enough beds or staff for quality care of their pediatric patients.[18] New studies have shown that telemedicine intensivists may have the potential to improve triage of pediatric patients and reduce pediatric emergency department transfers, especially in rural hospitals.[19] However, there are no known current telemedicine intensivists on staff in Wisconsin for inpatient pediatric care. There is opportunity for future implementation at some hospitals across the state to increase access to inpatient pediatric services, as admitting physicians may become more comfortable managing pediatric patients with a consistently higher volume of patients.

Study Limitations

The study was limited to a point-in-time analysis of Wisconsin hospitals and did not gather quantitative data for metrics on the definitive capability for each hospital to admit pediatric patients. Additionally, proportions of inpatient pediatric clinicians at each hospital (eg, number of family physicians vs pediatricians on staff) were not collected in this study and, therefore, do not reflect the total number of different clinicians at rural versus urban hospitals. A future study collecting this data would be beneficial to address specific gaps in the rural physician workforce. In addition, patient and provider satisfaction and quality metrics were not assessed in this study. Best practices in balancing competing demands of inpatient and outpatient coverage for pediatricians and family physicians who practice in both settings, ideal compensation structures, and measures to avoid burnout also were not explored. The generalizability of these findings to other US states is limited, as Wisconsin differs in its proportion of rural areas and population and health systems. However, primary care physician shortages are happening nationwide, with projected shortages between 17,800 and 48,000 for family medicine and general pediatric physicians.[20] Additionally, states surrounding Wisconsin have similar rural populations from 20.0% to 39.9%, including Minnesota, Michigan, and Iowa; therefore, similar trends to Wisconsin inpatient pediatric accessibility and workforce may be found in future studies in similar states.[21]

CONCLUSIONS

Inpatient pediatrics availability and capability for definitive care has been declining nationwide, including in Wisconsin. Physician shortages and rural workforce disparities in family practice and pediatrics have challenged rural hospitals in providing inpatient pediatric care. Family physicians and pediatricians are utilized for inpatient pediatric care in most of the CAHs in Wisconsin; therefore, residency programs should continue providing program faculty who can train in inpatient pediatric care. Despite workforce shortages, Wisconsin hospitals, including CAHs, continue to provide inpatient pediatric care to the rural population, although some have noted challenges with physician staffing and limited pediatric census to continue admitting pediatric patients. Notably, many Wisconsin counties do not have hospitals with inpatient pediatric care services available. Further investigation is needed to address these gaps in inpatient pediatric care accessibility.

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

Ryan Feldman, PharmD; Rachael Jaszczenski, PharmD

ABSTRACT

Introduction: There is controversy over the existence of a metronidazole-induced disulfiram-like reaction. Uncontrolled case reports suggest metronidazole can cause a severe disulfiram-like reaction in combination with ethanol. Criticism of these cases suggest the observed effects appear to be as likely caused by ethanol as by a drug interaction. Controlled experimental data refute these reports, demonstrating metronidazole does not increase acetaldehyde and cannot reliably produce disulfiram-like reactions. The purpose of this study is to retrospectively assess the incidence of clinical effects consistent with a disulfiram-like reaction in a population of patients with confirmed ethanol use who received metronidazole. As alcohol may also be responsible for the effects seen, the incidence of effects is assessed against a control group matched for age, sex, and ethanol concentration.

Methods: A retrospective chart review was performed from December 1, 2010, through December 31, 2020 on emergency department patients with ethanol use confirmed via detectable ethanol concentration who received metronidazole while ethanol was predicted to still be present in the serum. A matched comparator group with the same ethanol concentrations, as well as sex and age, was generated for comparison. The incidence of disulfiram-like reaction symptoms documented in the medical record was compared between groups.

Results: Thirty-six patients were included in the study: 18 in the metronidazole group and 18 in the ethanol concentration matched control group. The mean age in both groups was 46 years. The metronidazole group was 50% male, and the mean ethanol concentration was 0.21 g/dL. The control group was 44.4% male. There was significantly less hypertension in the metronidazole group compared to the control group (16.7% vs 61.1%, $P < 0.0001$). There were no other significant difference in disulfiram-like effects between the two groups. No patients who received metronidazole and had a detectable ethanol concentration had a suspected disulfiram-like reaction documented in the medical record.

Conclusions: This data set further supports the lack of a disulfiram-like reaction when metronidazole is used in patients with recent ethanol use in the acute care setting. Additionally, it highlights that the clinical effects of a disulfiram-like reactions may be present at baseline from ethanol ingestion or underlying disease regardless of metronidazole use. These findings are consistent with well-controlled human and animal data demonstrating no increase in acetaldehyde concentrations or disulfiram-like symptoms when metronidazole is co-administered with ethanol. In patients where metronidazole is indicated as the superior agent, its use should not be avoided due to concern about an interaction with ethanol.

INTRODUCTION

Use of alcoholic beverages (drinks containing ethanol) is extremely common among adults in the United States. Survey estimates suggest 86% of US adults have used alcohol at least once in their life.[1] In 2020, 1.8% of all emergency department (ED) visits in the US were related to alcohol.[2] This is only a minimum estimate of how often alcohol and acute health care intersect, as alcohol use is also commonly discovered in patients presenting for other reasons, such as traumatic injury.[3] Due to the frequency of alcohol use in patients intersecting with health care, it is important to understand when drugs have a significant interaction with alcohol.

The "disulfiram reaction" is an unpleasant syndrome of nausea, vomiting, flushing, tachycardia, hypertension, and dysphoria that occurs when ethanol is co-consumed with disulfiram.[4] Ethanol

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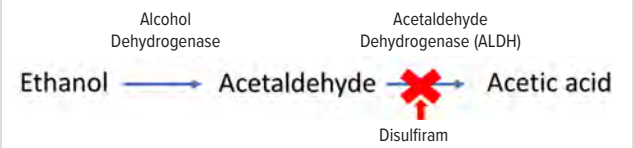
Figure 1. Mechanism of Disulfiram Reaction With Ethanol



The syndrome is caused by disulfiram inhibiting ALDH, halting metabolism at the acetaldehyde phase, and leading to build up of acetaldehyde.

normally undergoes metabolism via alcohol dehydrogenase to acetaldehyde, which is then metabolized via acetaldehyde dehydrogenase (ALDH). Disulfiram inhibits ALDH and causes a buildup of acetaldehyde, leading to the adverse effects seen in the disulfiram reaction (Figure 1). This is both a drug interaction and the basis of disulfiram's entire pharmacologic effect. Its utility as a deterrent from alcohol use lies in its ability to reliably inhibit ALDH and reproduce the unpleasant disulfiram reaction whenever alcohol is present.[4]

In 1964, an observational study evaluating side effects of metronidazole use reported a single patient who experienced a reduced urge to drink alcohol and potentially had a disulfiram-like reaction during 1 of the 3 times he was exposed to metronidazole.[5] This observation led to the suggestion that metronidazole may have a disulfiram-like effect on ALDH and can cause disulfiram-like reactions when combined with alcohol.[6]

Subsequent to this uncontrolled case report, a number of controlled studies assessed metronidazole's ability to induce disulfiram-like effects in patients administered alcohol.[6-10] While common metronidazole side effects such as nausea or a metallic taste were reported by participants, many studies reported no disulfiram-like effects in patients, and no study was able to reproduce a clear disulfiram-like reaction as had been reported in the index case (ie, flushing, dysphoria, vomiting, hypertension, tachycardia). An increase in acetaldehyde is fundamental to generating a disulfiram reaction. Controlled human and rodent studies verify that metronidazole does not inhibit ALDH and that systemic acetaldehyde concentrations do not rise when alcohol and metronidazole are coadministered.[6,10,11] These findings appear to objectively refute the existence of metronidazole's ability to cause a disulfiram-like reaction.

In spite of the controlled evidence refuting the interaction, the initial suggestion from the uncontrolled 1964 case report that metronidazole can cause this interaction persists. Case reports continue to be published asserting that metronidazole use with alcohol has led to severe and sometimes fatal disulfiram reactions.[12] Reviews of these cases are critical of their conclusions. A case report cannot demonstrate causation or differentiate if the effects reported are from metronidazole, ethanol itself, a concurrent illness, or a potential ethanol-metronidazole disulfiram-like reaction.[12] The symptoms of the disulfiram reaction are somewhat nonspecific and may be caused by a number of disease states or from ethanol itself (eg, flushing, nausea, vomiting, tachycardia). A clinician who has heard of this possible interaction with metronidazole and ethanol may recognize these symptoms in a patient who has them from another cause and misattribute them to a disulfiram-like reaction.

The persistent belief of this interaction in the face of contrary evidence appears controversial. Nevertheless, the numerous case reports have prompted warnings from the drug manufacturer to avoid coadministration of metronidazole and alcohol within 72 hours.[13] It is listed as a drug interaction of significant concern in most drug references.[14] Moreover, many pharmacies are required to label metronidazole prescriptions as "avoid with alcohol," and it is a common counseling point for most pharmacists.

Metronidazole is a frequently used drug, both inpatient and outpatient. It is used for intrabdominal infections, bacterial vaginosis, preoperatively for emergent abdominal surgery, and many other scenarios in which anaerobic organisms need to be targeted. In some cases, it is the only available treatment option (eg, trichomoniasis). Prescribers should know whether alcohol is, in fact, contraindicated when metronidazole is prescribed, and there is limited controlled data assessing this interaction in the acute care setting. The purpose of this study is to retrospectively assess the incidence of clinical effects consistent with a disulfiram reaction syndrome in a population of patients with analytically confirmed ethanol use who received metronidazole compared to a matched cohort of those with ethanol use who did not receive metronidazole.

METHODS

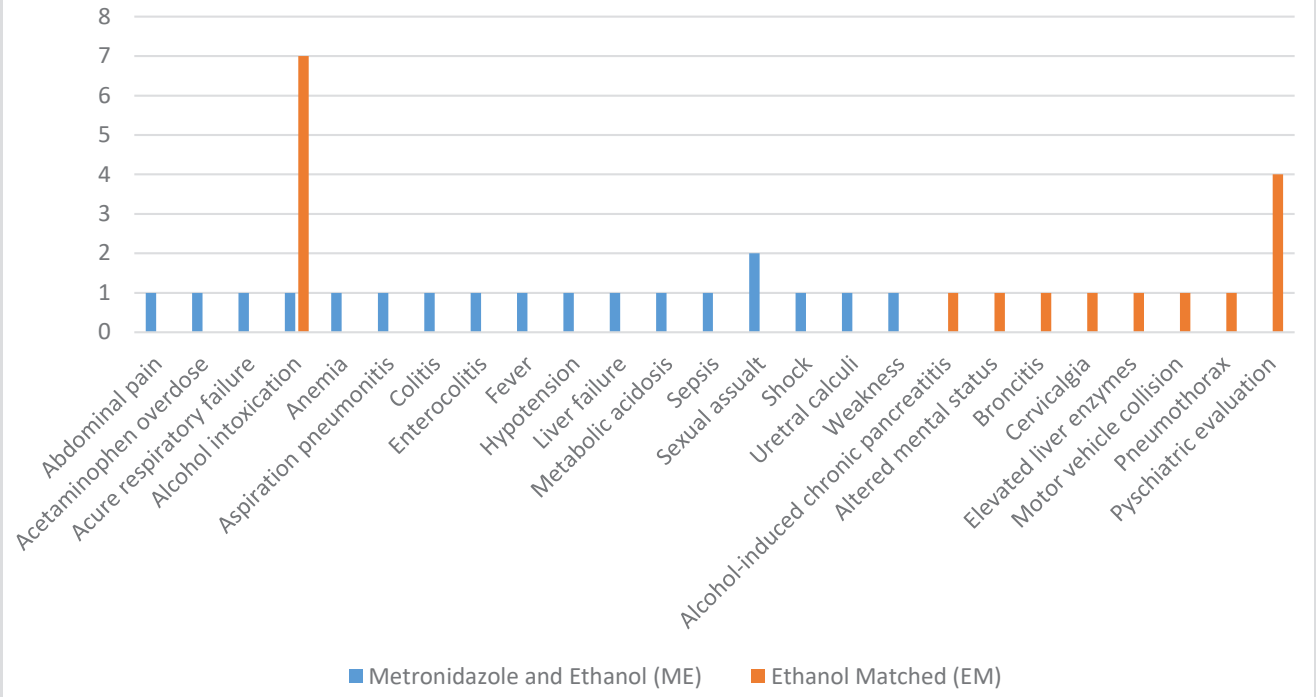
Study Setting and Design

This study was a cross-sectional case-control retrospective chart review of patients presenting to a single academic medical center ED from December 1, 2010, through December 31, 2020. Institutional review board approval with waiver of consent was obtained prior to conducting any research activities. The ED is located in an urban center in Milwaukee, Wisconsin and has approximately 72,000 visits annually.

Outcomes

The primary outcome was the incidence of disulfiram-like effects documented in the medical record in patients with detectable ethanol concentrations who had received metronidazole when ethanol was expected to still be present compared to patients with detectable ethanol concentrations who did not receive metronidazole. Disulfiram-like effects were defined as any documented occurrence of nausea, vomiting, flushing, tachycardia (heart rate > 100 beats per minute), hypertension (systolic blood pressure > 160 mmHg or diastolic blood pressure > 105 mmHg), hypotension (systolic blood pressure < 90 mmHg or mean arterial pressure < 65 mmHg) or use of an antiemetic medication. Antiemetics were

Figure 2. Admission Diagnosis



defined as serotonin receptor antagonists (eg, ondansetron) or dopamine antagonists (eg, metoclopramide, prochlorperazine, haloperidol, olanzapine). Steroids or benzodiazepines were included if the medical record specifically noted their indication was for nausea. Medical records were searched for the term "disulfiram." Rates of hospital admission, continued antibiotic use, and mortality data also were gathered.

Population

Patients were included if they were 18 years or older, had analytically confirmed ethanol concentrations, and had nursing documentation of metronidazole administration within the medication administration record. Only patients with nursing documentation of metronidazole administration in the medication administration record were included to avoid potential confounding by nonadherence with outpatient regimens. Patients were excluded if their medical record was incomplete, if they were pregnant, or if they were calculated to not have ethanol present at the time of metronidazole administration. Prediction of ethanol level was done utilizing zero order kinetics and a conservative estimated elimination rate of 0.015 g/dL/hour. This elimination rate was chosen due to its frequent use in forensic toxicology to extrapolate blood alcohol levels.[15]

The equation for predicted ethanol concentration at time of metronidazole administration was measured blood alcohol concentration – ([time of blood alcohol drawn – time of metronidazole given] *0.015).

A 10-year sample was selected as a convenience sample as well as the longest duration of time when complete patient records were expected to be available per the data acquisition team.

Generation of Matched Control

A demographic and ethanol concentration matched cohort was generated to compare the incidence of effects using demographic variables that may influence the incidence of disulfiram affects occurring at baseline (age, sex, ethanol concentration). After the list of patients with detectable ethanol levels who had received metronidazole was generated (case), a comparator (control) was selected from a list of all patients who had a detectable ethanol concentration. A patient of the same age, sex, and ethanol concentration was then selected from that list if available. If multiple candidates existed, the first candidate from the list was selected. If no exact match was available, the candidate closest in age with an exact ethanol match was chosen.

Data Collection

Data were collected within a predesigned data collection tool; all patients were collected in duplicate, and discrepancies were resolved by a third-party review. In the metronidazole group, the outcomes of interest (disulfiram effects) were recorded at any point after metronidazole administration. In the matched group, the effects were recorded if they occurred at any time during the ED visit.

Statistical Analysis

Assuming a 10% baseline incidence of disulfiram reaction symptoms in each group, a sample size of 16 patients in each group

Table. Demographics and Incidence of Disulfiram-like Reaction Effects in Patients Predicted to Have Detectable Ethanol Concentration at Time of Metronidazole Administration

	Metronidazole + Ethanol n = 18	Ethanol Alone n = 18	*P* value
Age (years) mean (SD, range)	46.2 (14.4, 22-76)	45.6 (12.6, 26-62)	0.912
Male, n (%)	9 (50%)	8 (44.4%)	1
Admission, n (%)	15 (83.3%)	1 (5.5%)	<0.00001
Ethanol level (g/dl) (mean SD)	0.21 (0.09, 0.047-0.375)	0.21 (0.09, 0.047-0.375)	1
Gastrointestinal-related diagnosis, n (%)	5 (27.7%)	2 (11.1%)	0.20
Tachycardia, n (%)	6 (33.3%)	9 (50%)	0.31
Nausea, n (%)	4 (22.0%)	2 (11.1%)	0.37
Vomiting, n (%)	2 (11.1%)	1 (5.5%)	0.55
Flushing, n (%)	0 (0.0%)	0 (0.0%)	1
Hypertension, n (%)	3 (16.7%)	11 (61.1%)	0.0153
Hypotension, n (%)	0 (0.0%)	1 (5.5%)	1
Antiemetic required, n (%)	6 (33.3%)	2 (11.1%)	0.22
Disulfiram-like reaction suspected, n (%)	0 (0.0%)	0 (0.0%)	1
Death, n %)	3 (16.6%)	0 (0.0%)	0.23

was calculated to detect a 60% difference in incidence of clinical effects using 80% power and an alpha of 0.05. With 18 in each group, the study was powered to detect a 46% difference in clinical outcome within either group. Data on incidence of clinical effects in alcohol-intoxicated patients compared to those experiencing a disulfiram effect while intoxicated is lacking; however, 1 study evaluated presenting ED patients on disulfiram and assessed their likelihood of experiencing a disulfiram reaction. Patients possibly experiencing disulfiram reactions had rates of many symptoms, including flushing, nausea, and vomiting, occurring at differences greater than 35% versus those not deemed to be having a reaction (flushing 89.5% vs 0%, nausea 71.3% vs 5.6%, vomiting 47.7% vs 8.3%, respectively). Ordinal variables were compared using Fisher exact test and continuous variables via a Mann-Whitney U test. Significance was defined as $P < 0.05$ (2-tailed).

RESULTS

A total of 24 patients met inclusion for detectable ethanol concentrations and receipt of metronidazole. After prediction formulas were applied for ethanol being present at time of metronidazole, 6 were excluded; no patients were excluded for any other reason. This left 18 patients who received metronidazole while ethanol was present in their blood (ME group). After generation of an ethanol-, age-, and sex-matched comparator group (EM group), 36 patients were included in the study: 18 in each group. Distribution of demographics and incidence of disulfiram-like effects are listed in Table. The mean age in the ME group was 46 years (SD ±14.4 years, range 22-76 years) and the mean ethanol concentration was 0.21 g/dL (SD ± 0.09 g/dL, range 0.047-0.375 g/dL). In the EM group, the mean age was 46 years (SD ±12.6, range 26-62 years). The ME group was 50% male, and the EM group was 44.4% male.

More patients in the ME group were admitted to the hospital and more continued receiving antibiotics (any antibiotic after first dose of metronidazole, including metronidazole itself) compared to the EM group (admission: ME n = 15, EM n = 1, $P < 0.00001$; antibiotics: ME n = 15, EM n = 0, $P < 0.0001$). There were more patients in the ME group who had a potentially confounding gastrointestinal-related diagnosis; however, this was not statistically significant (ME n = 5, EM n = 2, $P = 0.4$). See Figure 2 for the full list of admission diagnoses for each. Two patients in the ME group died; however, both had elevated lactate levels and hypotension prior to metronidazole administration. Their admitting diagnoses were unspecified hypotension and liver failure without hepatic coma.

No patients in the ME group had a suspected disulfiram-like reaction documented in the medical record. There was no significant difference in incidence of tachycardia, nausea, vomiting, flushing, hypotension, or antiemetic use between groups. There was significantly more hypertension in the EM group compared to the ME group (ME n = 3, EM n = 11, $P < 0.006$).

DISCUSSION

This small data set is consistent with past literature in supporting the safety of metronidazole use in patients with confirmed ethanol use. This study was not able to identify any patients where a disulfiram-like reaction was suspected after metronidazole administration, though it is limited by its retrospective design. Most patients in both groups had at least 1 symptom of a disulfiram-like reaction; however, the symptoms occurred at an equal frequency to the EM cohort who did not receive metronidazole. Our hypothesis was that if metronidazole were to cause this drug interaction, the ME group would demonstrate higher rates of any of these disulfiram-like symptoms. We were unable to reject our null hypothesis. The only symptom that occurred more often was hypertension, which occurred in the EM cohort. These data highlight that disulfiram-like effects are prevalent amongst ethanol-intoxicated patients regardless of metronidazole exposure. The symptoms also may be present due to baseline illness comorbidities (eg, liver disease-causing hypotension) or acute infection necessitating metronidazole.

While this study did control for confounding variables, such as ethanol use, some variables were not able to be matched. More patients who received metronidazole were admitted to the hospital and received ongoing antibiotics. While this highlights that the populations may have had baseline differences in demographics that could influence the prevalence of disulfiram-

like symptoms, it also biases the results toward observing disulfiram-like reactions more often in the ME group. This group was observed longer than the EM matched control and, thus, had more opportunity to document symptoms. Regardless, no disulfiram-like reactions were identified, and clinical effects were similar amongst both groups. Our data are consistent with past studies showing no observed disulfiram-like effects with metronidazole and, once again, call into question the existence of this reported interaction.

The first suggestion of a metronidazole-induced disulfiram-like interaction with alcohol was reported in 1964 by Jo Ann Taylor.[5] Reviewing this index report is valuable in understanding how the belief of metronidazole's interaction with ethanol came to exist and persist in the medical community. Taylor was completing a 3-year observational study on the side effects of metronidazole use and, from a cohort of 463 patients, highlighted a single case where a patient stopped drinking after using metronidazole. The patient drank alcohol daily and had been hospitalized multiple times for detoxification. His wife reported that while he was being treated with metronidazole for trichomoniasis, he did not finish his alcoholic beverage 3 different times. The wife remembered this effect and, at a later date when the patient had been binge drinking for 3 days and was described to be in a stupor, gave him a dose of metronidazole in hopes of ending the drinking binge. Twenty minutes later, he became more alert and accused his wife of giving him disulfiram, a drug he had previously taken and refused to take again due to the unpleasant reaction with alcohol. He had flushing, nausea, epigastric pain, and a feeling of impending doom. The symptoms worsened after another sip of alcohol but then resolved 4 hours later.

Several explanations could be considered for the observed syndrome of effects in this patient, including a psychosomatic reaction to believing his wife had given him disulfiram, abdominal pain from excess drinking, or acute withdrawal due to cessation of alcohol after a 3-day binge. Additionally, in the very same report, the author provided evidence that the reaction was not reproducible. The patient presented a year later to a hospital after a 10-day drinking binge, acutely intoxicated but beginning to experience delirium tremens. He was given metronidazole on arrival and instead of having a disulfiram reaction, the author asserted it significantly reduced his symptoms and led to the improvement of his liver function tests. The author reported a number of extraordinary conclusions from this case example: that metronidazole could reverse signs of liver disease, create aversions to alcohol, treat symptoms of withdrawal, and reduce cravings. The publication endorsed that 53 other patients within the 463 studied patients also reported alcohol aversions on metronidazole but provided no actual data or case details.

This uncontrolled index case report was popularized by lay media discussion (radio and television) and prompted a spree of research into metronidazole's role on alcohol use disorder.[15] An additional 20 studies were performed in the next 8 years.[6] The majority, however, evaluated the drug's ability to maintain abstinence and were not well-designed to assess for disulfiram reactions. None reported significant disulfiram reactions in patients who continued to drink, and only 4 of the subsequent trials assessed the ability of metronidazole to produce a disulfiram effect in a controlled setting.[15]

Only one of these controlled studies appears to provide any support to the proposed metronidazole disulfiram-like effect with ethanol. This study randomly assigned 41 volunteers to take metronidazole or a placebo. The participants then took part in a party where they could drink as many alcoholic beverages as desired. Participants given metronidazole reported a higher incidence of headache, nausea, and bitter taste compared to the placebo group. It should be noted that nausea and a bitter taste are potential side effect of metronidazole alone. There was no comparator group who took only metronidazole, so it is not clear if these symptoms would have occurred regardless of ethanol use. All of the reported effects were mild, and no participants reported severe symptoms consistent with disulfiram-like reaction.

Two additional studies placed abstinent patients on metronidazole for 2 weeks and challenged them with alcohol periodically.[8,9] During alcohol challenges, minor nonspecific symptoms were reported in some (change in taste of alcohol, coffee, and cigarettes; lack of desire to drink; headache; or feeling hot), while others reported increase in desire to drink and reduced tolerance. Once again, change in taste was noted, which is a known side effect of metronidazole. No patients reported disulfiram effects. A further study administered metronidazole for 10 days to abstinent patients with alcohol use disorder and then administered 2 ounces of whiskey. No disulfiram-like effects were seen.

While these controlled trials frequently reported metronidazole side effects (bitter metallic taste), it did not appear that disulfiram reaction symptoms could be reliably reproduced in a controlled setting. In fact, it was suggested after these studies that the metallic bitter taste induced by metronidazole was the mechanism for metronidazole producing an aversion to alcohol use as opposed to a disulfiram reaction. This prompted a study in 1972 to use a structurally related agent without a metallic taste (flundiazole) to assess if this also could induce an alcohol aversion.[6] In this small study of 11 healthy volunteers, flunidazole had no impact on producing aversion to ethanol. No one treated with flunidazole had disulfiram-like effects, and vital signs were not different than those treated with ethanol alone. Importantly, this study also measured acetaldehyde concentrations, the compound responsible for causing the clinical effects of the disulfiram reaction. There were no differences in acetaldehyde production between ethanol only or ethanol and flunidazole-treated groups (8.1 ng/ml vs 6.7 ng/ml). This study provided objective data that drugs within this class do not increase acetaldehyde production and do not cause a disulfiram-like reaction. However, it would

be nearly 30 years before these findings would be replicated with metronidazole in humans.

Several studies now exist assessing metronidazole's ability to increase acetaldehyde. In a 2000 study where rats were fed a 6-week diet of ethanol and metronidazole, metronidazole alone, or ethanol alone, it was demonstrated that metronidazole has no effect on blood acetaldehyde. Additionally, biochemical analysis in this study demonstrated metronidazole did not inhibit ALDH at all. This strongly supports the absence of a disulfiram-like reaction with metronidazole and ethanol. Notably, there was an increase in colonic acetaldehyde in metronidazole-treated rats. As metronidazole does not inhibit ALDH, the authors postulate this may be from metronidazole increasing the amount of alcohol dehydrogenase-producing aerobic bacteria in the gut, leading to more rapid acetaldehyde formation.[11] While chronic metronidazole use could theoretically increase systemic absorption of acetaldehyde, this was not observed after 6 weeks of use in the rodents.

A human study also corroborated these findings. In 2000, a randomized controlled trial assessed acetaldehyde production and incidence of disulfiram-like reaction effects (blood pressure, temperature, heart rate) in 6 participants who had been taking metronidazole 600 mg daily for 5 days and were then given a 0.4 mg/kg load of ethanol.[10] Both acetaldehyde production and disulfiram-like effects were compared to 6 participants who had been taking placebo for 5 days and received the same ethanol load. No disulfiram-like reactions were noted, and metronidazole had no impact on acetaldehyde production. In fact, there are data to support that metronidazole reduces acetaldehyde production. While it does not inhibit ALDH, at supratherapeutic concentrations, it can inhibit alcohol dehydrogenase, leading to a decrease in acetaldehyde.[16]

When examining the literature, no controlled experimental data appear to support the existence of this reaction. Yet, the persistence this single index case holds in the medical literature is exemplified by the case reports that continue to be published of this interaction each year.[12] As discussed previously, disulfiram-like effects are largely nonspecific (hypertension, flushing, nausea, tachycardia, headache) and may be caused by a number of confounding diseases for which metronidazole is warranted (infection) or ingestion of ethanol itself. In the studied population we report, some of the effects were even more common in those only exposed to ethanol (hypertension). Systematic reviews of these cases have drawn the same conclusions.[12,17] It is impossible to ascribe causality to a drug interaction within these reports as opposed to comorbid ethanol use, psychosomatic symptoms, or confounding medical conditions that may produce similar symptoms. Any clinician who has been informed of this interaction may be able to identify a consistent syndrome in patients who are suffering from infection or alcohol intoxication and believe they are observing it.

Despite the many limitations in supportive data, the drug manufacturer continues to warn of the interaction between metronidazole and ethanol. If there is an interaction, it objectively is not a disulfiram reaction. Our data confirm that metronidazole can be used safely in intoxicated patients for whom metronidazole is indicated. In some cases, metronidazole is the only agent available to manage certain infections (eg, trichomoniasis). Additionally, alcohol is a commonly encountered substance in the trauma population that may require emergent abdominal surgery and preoperative antibiotics with metronidazole. The presence of alcohol in a patient may cause a clinician to select an alternative agent that is potentially less optimal, which could cause undue harm—all in an effort to avoid an unsubstantiated interaction.

These data align with previous literature that demonstrates co-administration of metronidazole and ethanol does not cause a disulfiram-like reaction or any symptoms beyond regular metronidazole side effects. In patients who require metronidazole, it is likely safe to administer, regardless of concurrent ethanol use. This is consistent with the practice in our ED.

Limitations

This study is limited by its small sample size, which may have been inadequately powered to detect significant differences in specific disulfiram-like effects. Another significant limitation is the retrospective design, which makes it difficult to discern whether a patient is experiencing a disulfiram reaction. It is not possible to know if a disulfiram reaction was suspected if not documented in the chart or diagnosis code. Many patients did have multiple symptoms that are included in a disulfiram reaction syndrome, though these likely represent symptoms caused by alcohol or baseline illness. It is presumed if metronidazole does cause a disulfiram-like reaction, the ME group would consistently demonstrate higher rates of any symptoms, which it did not.

Confounding demographic factors may play a role in equalizing symptom incidence between groups. While age, sex, and ethanol concentration were matched, disease severity likely was not. This is exemplified by the fact that significantly more patients in the metronidazole group were admitted to the hospital. The need for antibiotics in the metronidazole group may have selected for a population with more complex medical needs. In the EM group, 55.5% of patients presented with a diagnosis of alcohol intoxication or isolated psychiatric problems. Future studies may consider propensity matching by admission status and receipt of antibiotics to better control for severity of illness. Additionally, a third control arm of patients receiving only metronidazole with no concurrent alcohol intoxication also may help differentiate between a disulfiram-like effect and metronidazole side effect profile.

CONCLUSIONS

There is significant controversy as to whether an interaction exists between metronidazole and ethanol. Its existence is purported by uncontrolled case reports yet refuted by controlled experimental data. This data set further supports the lack of a disulfiram-like reaction when metronidazole is used in patients with recent etha-

nol use in the acute care setting. Additionally, it highlights that the clinical effects of a disulfiram-like reaction may be present at baseline from ethanol ingestion or underlying disease, regardless of metronidazole use. This study was notably limited by a small sample size and inability to control for all confounding baseline variables. However, findings are consistent with well-controlled human and animal data demonstrating no increase in acetaldehyde concentrations or disulfiram-like symptoms when metronidazole is coadministered with ethanol. In patients where metronidazole is indicated as the superior agent, its use should not be avoided due to concerns about an interaction with ethanol.

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How Patients With Limited English Proficiency Make Health Care Decisions: Hmong Patients' Perspectives

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ABSTRACT

Introduction: Information about how the limited English proficiency immigrants make their decisions to seek health care is not well understood. With acculturation, immigrants tend to shift their beliefs and practices towards the practices of their host country. Yet, little is known whether this holds true for the Hmong's health care decision-making.

Methods: To understand the health care decision-making process of limited English proficiency Hmong, we conducted semistructured interviews with 11 Hmong adults with limited English proficiency. Interviews were audio-recorded, transcribed, and analyzed using directed and conventional content analysis.

Results: We identified several themes: participants sought advice and information from family members who were proficient in English and Hmong and/or who had a health background for a treatment that they perceived to be potentially life-threatening. However, participants were more reliant on their own decision-making in medical situations that were time sensitive. Participants without immediate family asked for health advice from community members or peers who had personal experience with the health condition or treatment.

Conclusions: Our findings suggest a cultural shift in Hmong health care decision-making processes from relying on clan leaders and elders to seeking out the advice of adult children and spouses. Understanding this change in cultural decision-making dynamics will help health care professionals provide more culturally competent care in areas where the Hmong community has a prominent presence.

INTRODUCTION

Efforts to reduce health disparities experienced by marginalized groups in the United States have not improved survival rates for minority patients compared to non-Hispanic White patients. One marginalized minority group often overlooked is the Hmong, a refugee group from Southeast Asia who first arrived in the US in the 1970s. The 2019 US Census estimates 327,000 Hmong living in the US, primarily concentrated in California, Minnesota, and Wisconsin, with growing communities across the country. Approximately 37% of the Hmong adult population speak English "less than well" or "not at all" (ie, limited English proficiency [LEP]).[1]

Multiple factors contribute to health disparities experienced by the Hmong: limited access to resources, low educational attainment, lower-income status, low health literacy, and LEP.[2] Moreover, LEP Hmong members' reluctance to seek care is often connected to poor health care experiences and poor-quality interpreter services.[3,4] These factors are associated with lower screening rates for cancer,[4] higher prevalence rates of type 2 diabetes,[5] and overall lower rates of preventive health care.[4]

Health disparities also arise because the Hmong health belief system[6] (based on shamanism where spirits influence health and well-being) often conflicts with the Western biomedical system. Consequently, the Hmong seek shamans to treat the soul and spirit before the physical body.[7,8] Thus, when they do seek Western

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health care, diseases are often at more advanced stages compared to non-Hispanic White patients.[9]

The Hmong organize in large, close-knit communities, known as clans. Traditionally, clan leaders and/or members of the clan (also called *kwv tij*)[10] assist members with their decision-making, including medical decisions.[7,11,12] As dictated by their culture, Hmong women consult their husbands before making final medical decisions.[7,13] However, as the Hmong acculturate, it is important to reevaluate if these decision-making patterns still exist. With acculturation, immigrants tend to shift their beliefs and practices towards the practices of their host country.[14,15] However, little is known whether this holds true for the Hmong's health care decision-making.

This study explored factors shaping the health care decision-making process of LEP Hmong. Our research questions were:

(1) When do LEP Hmong seek health advice?
(2) How do LEP Hmong make decisions to seek help?
(3) Who do LEP Hmong consult when making health care decisions?

METHODS

This qualitative study was part of a larger study exploring barriers and facilitators to preventive cancer screenings for Hmong and Spanish LEP patients in a large Midwest health care center. It was approved by the University of Wisconsin's Institutional Review Board.

Sample and Recruitment

We recruited a convenience sample of participants. Eligibility criteria included self-identifying as having LEP, being a native Hmong speaker, being eligible for preventive cancer screening (women ≥18 and men ≥50), having no previous cancer diagnosis, and having had at least one primary care visit in the past year.

Recruitment strategies employed were posting bilingual (Hmong and English) flyers in clinics and local community centers, sending bilingual letters to potential patients, and attending cultural events. Participants were encouraged to refer family and friends. A bilingual Hmong research assistant screened interested participants.

Data Collection

All participants reviewed study information and were interviewed at home. A semistructured interview guide ensured consistency across interviews. In this study, we asked about LEP Hmong participants' thought processes around health care decision-making, specifically who they turned to for health care advice and the factors that influenced their health care decisions. For example, we asked "When you make a decision about your health, do you consult with others or seek information outside the clinic? [Probe:] Who/What?" This guide was written in English and translated into Hmong by a bilingual study team member and then back-translated from Hmong into English by another bilingual study team member to ensure accuracy and capture the meaning rather than a literal translation. Any discrepancies were discussed until group consensus was reached. Interviews were conducted in Hmong with at least two bilingual study staff attending all interviews. Consistent with the Hmong collectivist culture, participants welcomed having more people in the conversation.[16] Interviews were collected from July to December 2013, lasted between 45 and 120 minutes, and were audio-recorded. All participants received a $50 honorarium.

Data Analysis

The audio files were transcribed verbatim in Hmong and translated into English using a group translation method to focus on meaning rather than literal interpretation for data validation.[17,18] Group translation involves people with cultural and linguistic skills working together to translate and review the materials with one adjudicator present to determine final translations.[17,18] We focused on capturing meaning because there are Hmong phrases and concepts with no English equivalent.[18] Disagreements in translation were resolved as a group, discussing all possible interpretations that most closely corresponded with what participants intended to convey.

We used directed and conventional content analysis[19] to analyze the data. Directed content analysis works well with predetermined categories of questions (eg, health care decision-making and barriers to seeking care). These predetermined categories were derived from empirical research.[4,8] Hence, we generated categories from prior research to guide the data analysis. For example, "I make my own health decisions" was coded as health care decision-making. Conventional content analysis was used for responses that did not fall within the predetermined categories. For example, "If I feel like I am going to die, I'm going to go to the doctor immediately" was coded as "making decision by self." Through an iterative process, codes were grouped into categories. Data saturation, when no new themes emerged,[20] occurred prior to the final interview. We used NVivo 10 (QSR International) to manage the data. Two study team members coded interviews separately, met to review codes, and added codes when they identified new content that did not fit within the predetermined categories. All codes and categories were brought to the larger interdisciplinary research team for confirmation. Discrepancies were discussed until consensus was reached. Data saturation was reached by the 8th interview, and we continued data collection until the 11th participant. Four themes resulted from our data analysis.

RESULTS

There were 11 Hmong participants (6 females, 5 males) with an average age of 55 (range 34 to 70 years). More than 80% of the participants had less than a high school education or none. Nine

participants were publicly insured and two were privately insured. All had been in the US from 8 to 33 years.

We identified 4 major factors playing a role in participants' decision-making processes: (1) the type of medical care, (2) the seriousness and/or urgency of the participant's health condition, (3) the participant's English language proficiency and health knowledge, and (4) the participant's personal experience with the illness.

Type of Medical Care

Most participants shared that their decision to seek advice depended on the type of medical care they needed: primary care visits versus surgical procedures. These categories were driving factors regarding whom they would allow to influence their medical decisions.

Primary care visits. Nine participants across both sexes reported that with routine primary care visits, they make their own medical decisions. One woman shared about her own decision-making that because others do not have enough medical experience to help make an informed decision, the decision ultimately depends on oneself: *"That, it depends on you only. They can't make the decision for you […] So I make the decision on my own."* Male participants conveyed similar sentiments about their health care decision-making: *"If you need to go, you don't talk to anyone."*

Surgical procedures. In contrast, some participants shared that for surgical procedures, they sought advice from their immediate family members—adult children, parents, siblings, and spouses. For surgical procedures that participants perceived to be invasive and/or life-threatening, seeking advice from family was a way to decide whether to proceed with the treatment and follow the physician's medical expertise. For instance, this participant expressed that she would talk to her family before making the decision to have surgery:

> [About] surgery […] I think that if [I] have an illness, I will first talk to my mother, father, brothers, husband, and children before I go […] If they say 'if you do this, then maybe it will be good too' then I will go do it. If you make your own decision, then you might make mistakes […]

Some participants shared that they also gathered information from extended family who had past experiences with the recommended medical treatment. They wanted to educate themselves about the experience and about any potential high risks associated with surgical interventions. For example, one man stated that requiring a bypass heart surgery necessitated him to seek medical advice from extended family members because his family would shoulder the burden if he became disabled or died:

> "To do something like that [surgery] to your heart, it is dangerous […] Something like this, you have to talk with your family so that they can help you make the decision to see which option is best."

Seriousness and/or Urgency of Health Condition

Participants shared that the seriousness and/or urgency of their perceived symptoms influenced whether or from whom they would seek medical advice. There were 2 qualifying conditions: (1) immediate life or death decision-making and (2) low urgency.

Immediate life or death decision-making. All participants reported that if they perceived their lives to be endangered and needed immediate medical care, they would make their own health care decisions. This is a default decision once cultural and spiritual healing practices failed to yield any medical improvements. For example, a participant shared that when she could no longer withstand the physical pain and believed herself to be very sick, she made her own decision:

> Because if you are super sick then you have to go. If you are super sick and you cannot talk with them [family], then you can go on your own and that's fine […] And if they say that if I don't do the surgery, I will die, then I will make the decision on my own.

Low urgency. In contrast, if Hmong participants perceived their medical conditions to be of low urgency, then they included immediate family members in their health care decision. One man replied that he and his wife made decisions together: *"After getting checked up and if they say 'oh, I see this and it's like this, we have to schedule another appointment for you to come back and we will treat it like this,' then you have to discuss it with your wife and family before you go."* Another female gave a similar statement about how she and her husband decided together for him to undergo a colonoscopy without involving other family members: *"Yeah, we were the two [participant and her husband] that made this decision for them [doctors] to take an x-ray inside the colon and the stomach to see if there is any illness in there."*

English Language Proficiency and Health Knowledge

All participants reported that because of language barriers and their unfamiliarity with Western medicine, they deferred their medical care needs to English-proficient family members, usually their adult children. Some also sought advice from family members whom they perceived to be knowledgeable about the health care system and/or involved in health-related professions. One female explained how she trusted her adult children's advice regarding her medical needs because of their English proficiency:

> I trust my family more. For example, it is my children and my husband. Because my husband, I trust him, but he doesn't know English. So even if I trust him, if it involves American people then he doesn't know English, so it's my children I trust.

One man also explained that his daughter helped with his medical decisions because she is bilingual and a nurse: *[…] the daughter has had some schooling in nursing […] She knows English better. Every medication, she knows. If they want me to take it, she knows how.*

Personal Medical Experience

Eight participants shared that community members were also key informants for medical-related decisions. Before a medical procedure, if no immediate family member could provide information, participants asked members of the community for their medical opinions. One man shared the importance of accessing health care advice from his peers who were familiar with medical procedures or know people who have been diagnosed with certain diseases. The information gained from his peers was more trustworthy than the medical advice from his provider: *"I talk to my friends and see what they say to me. If they say it's ok for me to go then I will go seek care and see how they [doctors] can help me, so that I can be happy."*

Another participant shared her personal experience with obstetric care with her friends and sister-in-law. She said they were pleased with the accurate descriptions of the entire process of routine prenatal care, including different types of medical procedures:

> "You have to think that it is a way to check up and protect yourself from getting sick and to help you know early and to help your child. This is something good for you." That's what I say to them, and they say "ok." After they go [for a] checkup, they say, "Oh yeah, it's like you said."

DISCUSSION

To the best of our knowledge, this study is the first to investigate factors motivating LEP Hmong in their health care decision-making processes. We found participants first identify their needs as surgical versus nonsurgical or dangerous versus nondangerous and then decide from whom to seek medical advice. Bilingual family members—especially those with a health background—are ranked as the most desirable, but only for decisions involving surgical interventions or dangerous treatments like chemotherapy. Extended family members become involved when the entire clan can be affected negatively if the participant has a high probability of becoming disabled or dying. Friends become relevant when family fails to provide medical information. Our finding regarding who participants consult about their health is consistent with existing research.[21] However, this ranking is irrelevant when participants perceive their symptoms as potentially harmful and life-threatening. Then participants are motivated to make their own decisions and trust their health care provider.

Interestingly, we found several instances where it appears that there may be a shift in Hmong health care decision-making. First, no participants mentioned seeking advice from clan leaders traditionally sought for medical advice.[7,10,11] Second, decision-making was shifted to spousal decision-making when traditional Hmong family structure dictates that men make decisions for all important matters, including health care.[7,10] We found that male participants valued their wives' opinions on their illnesses. All participants stated seeking spousal advice, especially for subsequent testing and procedures needed for diagnosis or treatment. This type of marital partnership does not conform to the patriarchal health decision model found in previous literature on the Hmong.[7,11,12] However, our most unexpected finding was that Hmong women expressed autonomy in health care decision-making instead of deferring to their husbands. Although we did not explore the impact of acculturation on Hmong people's health care decisions, it is plausible that it may have influenced this shift. Future research could explore to what extent acculturation affects health care decisions to better inform health care practices about the dynamic process of caring for their patients.

Our results demonstrate that for high-risk or invasive surgical procedures, LEP Hmong individuals sought medical advice instead of making the decision on their own. This is likely motivated by the Hmong's clan structure, whereby all members unite to provide social and financial support to individuals.[7,11,12] Therefore, the opinions and advice from extended family weigh heavily on Hmong individuals' decision-making processes. Including extended family members may mitigate any consequences from unexpected mortality or morbidity. Previous research supports this finding regarding family involvement when having to make decisions about important medical procedures.[7,12]

It is important to note the interesting dichotomy in the participants' decision-making processes. Health care advice from others is only relevant when the time-sensitive component is removed. For time-sensitive care, decision-making becomes self-dominant. This finding is consistent with a current hepatitis B screening study among Hmong who will make their own decisions in situations that they perceived to be emergencies.[22] This self-reliance regarding health decisions or reliance on others highlights complexities within health care decision-making processes that exist among LEP Hmong. Involving family members early in any health discussions may be key to helping LEP Hmong individuals receive appropriate and timely medical care. Future research also could study communication strategies that clinicians could use to be inclusive of Hmong family members in health care discussions, such as key Hmong phrases to support and empower family members' involvement.

Lastly, we learned our participants consulted with friends and peers in the Hmong community when family members were not available to provide medical advice. Their connections and/or personal experience with similar procedures provided insights into quality-of-life after medical intervention. Community members bring community buy-in, which may prevent delays in care thereby improving health outcomes. Multiple studies on social networks show that strong social support improves health outcomes.[23-25] A systematic review of shared health care decision-making in minority groups found that prior experiences of friends and family members significantly influenced the decision-making of patients to seek or forgo treatment.[26] Therefore, knowing key informants and the factors used to qualify who

patients ask for medical advice can lead to timely and effective medical interventions.

Lastly, our study uncovered a role reversal between parents and children regarding health care-related decisions. Participants sought medical advice from and expressed value in their adult children's opinions because of their English proficiency and health knowledge. This finding contradicts previous research findings that children/young adults do not participate in the health care decision-making processes of older Hmong adults.[28] Language barriers may account for this reliance on their children compared to English-proficient Hmong adults. Future research could explore Hmong families' navigation of this role reversal as another insight into acculturation into the American health care system. These cultural shifts in Hmong health care decision-making are similar to other immigrant groups acculturating into the dominant culture of their host country.[28,29] Our findings highlight the importance of understanding and appreciating evolving cultural norms and including family members and friends during medical encounters, which could facilitate better health care-seeking behaviors in the LEP Hmong population.

This study has some limitations. First, because health care decision-making was not the larger study's main focus, we may not have fully captured all the conditions informing LEP Hmong participants in their health care decision-making processes. In addition, we were unable to explore the impact of acculturation, religion, and immigration on health care decision-making among Hmong participants, because this study was focused on cancer screening. Because we used a convenience sample, there is some potential for bias to occur. Also, we were unable to explore situations where participants decided not to seek care. Lastly, because this study focused on LEP Hmong participants, our findings are applicable only to LEP patients. More research is needed in the area of medical anthropology to understand the shift and role of decision-making over time in the Hmong-American community.

CONCLUSIONS

We found that the process by which LEP Hmong adults decide when and from whom to seek advice is complex. They consult family, friends, and community, but whom they consult depended on the type of decision required: diagnostic testing, procedures, or high-risk surgeries. However, participants were more self-reliant if the treatment was time sensitive. These results suggest a shift regarding from whom medical advice was traditionally sought and have significant implications. Understanding the decision-making process among LEP Hmong can help clinicians provide more culturally competent care and develop strategies to increase medical compliance, thereby reducing health disparities in the LEP Hmong population.

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Database Tracking in Gender-Affirming Surgery: Are Patients Falling Through the Cracks?

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ABSTRACT

Background: This study sought to examine risk factors for venous thromboembolism in transfeminine vaginoplasty. Secondarily, the authors outline reasons why patients are not adequately classified for research purposes despite using relevant queried codes.

Methods: Transgender patients undergoing vaginoplasty were identified with diagnostic and procedure-specific codes using a national surgical database from 2010 through 2019.

Results: There were 457 transgender vaginoplasties performed, with 24 wound dehiscences, 17 unplanned reoperations, and 12 surgical site infections. With zero cases of venous thromboembolism, risk factor analysis was deferred.

Conclusions: Heterogeneity in coding practices for gender-affirming surgery led to an uncharacteristically small cohort of transfeminine vaginoplasty patients captured in the database. Current diagnostic and procedure-specific codes are nonspecific and unbundled, hindering accurate assessment of the incidence of standard surgical complications.

BACKGROUND

As of 2015, the transgender and gender nonconforming (TGNC) community is estimated to include 1.4 million people in the United States.[1] Transgender describes individuals whose gender identity or expression is incongruent with the sex they were assigned at birth.[1] This leads to gender dysphoria manifesting as extreme psychological and emotional distress from living in a body that is not their own.[2,3] Gender dysphoria contributes to a disproportionately high rate of mental health and social issues in the lesbian, gay, bisexual, transgender, queer (LGBTQ) population, including suicide, drug abuse, poverty, and homelessness.[4] National studies have found that LGBTQ disparities were due, in part, to limited access to health insurance, sexual orientation discrimination, and insufficient provider knowledge and research on LGBTQ health.[5] Surgical care – in coordination with a comprehensive multidisciplinary gender clinic – has been shown to improve these patients' quality of life 1-year postoperatively across metrics, including mental and emotional health and social functioning.[2] Gender-affirming surgery is categorized as transfeminine (feminizing) or transmasculine (masculinizing),[6] as gender identity exists in a spectrum and cannot be simplified to the traditional male/female binary. This is further differentiated into "top" surgery in the form of breast augmentation or mastectomy and "bottom" surgery in form of vaginoplasty or phalloplasty.[7]

Gender-affirming surgery (GAS) is among the fastest growing fields of plastic surgery and, as such, database research to better understand the risk profiles of these increasingly more common operations is needed. Most of these studies include only top surgery. One study utilizing the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database concluded that transmasculine patients undergoing mastectomies were not at an increased risk of 30-day all-cause postoperative complications compared to cisgender women and encouraged surgeons to offer gender mastectomy as a safe and integral aspect of gender-affirming care.[4] However, there has not been a published risk factor analysis of vaginoplasty utilizing national data. This operation is of special interest given the concern for

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increased incidence of thromboembolic events due to estrogen therapy, low lithotomy position with multiple hours under general anesthesia, and the necessary bedrest and activity restriction protocols postoperatively.[5] Given the complicated nature of these operations, we attempted to utilize the ACS-NSQIP database to examine the risk factors for deep vein thrombosis or pulmonary embolism within 30 days of vaginoplasty, with the goal of contributing to a more comprehensive and informed surgical approach to gender-affirming care.

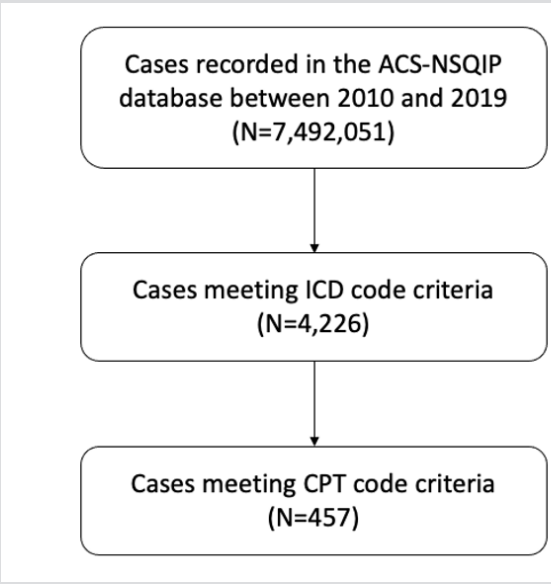
METHODS

Transgender patients undergoing vaginoplasty were identified by searching the ACS-NSQIP database from 2010 through 2019 for relevant International Classification of Diseases (ICD) and Current Procedural Terminology (CPT) codes. ICD diagnosis codes queried to isolate transgender patients were "gender dysphoria," "gender identity disorder" (ICD-9 codes 302.5, 302.50, 302.51, 302.52, 302.53, 302.85, 302.3; ICD-10 codes F64.0, F64.1, F64.2, F64.3, F64.4, F64.5, F64.6, F64.7, F64.8, F64.9) and "unspecified endocrine disorder" (ICD-9 code 259.9 and ICD-10 code E34.9). This cohort then underwent CPT code filtration with codes meant to isolate vaginoplasty patients: partial amputation of penis (54120), complete amputation of penis (54125), construction of artificial vagina with graft (57292), construction of artificial vagina without graft (57291), orchiectomy simple scrotal/inguinal approach (54520). If a patient possessed a queried ICD diagnosis code and any of these CPT codes as the "primary," "concurrent," or "other" code as part of their surgery, they were included. We then utilized this dataset to determine the incidence of 30-day complications as reported by the ACS-NSQIP database, including deep vein thrombosis.

RESULTS

Of the 7,492,051 cases recorded during 2010-2019 in the ACS-NSQIP, 4226 possessed relevant ICD diagnosis codes. After applying CPT code filters, 457 cases were identified as vaginoplasty patients (Figure). Within this cohort, there were zero cases of deep vein thrombosis or pulmonary embolism, 24 cases of wound dehiscence, 17 cases of unplanned reoperation, 7 cases of superficial surgical site infection, 3 cases of deep surgical site infection, and 2 cases of organ space surgical site infection. With no cases of deep vein thrombosis or pulmonary embolism--the primary outcome of interest--risk factor analysis was deferred.

Figure. Visual Overview of the Approach Utilized for Case Identification



Abbreviation: ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ICD, International Classification of Diseases; CPT, Current Procedural Terminology.

DISCUSSION

Lack of Standardization in Coding Fails to Capture All Patients

The standardized methodology we employed for patient identification yielded an extremely small cohort and undoubtedly did not capture the majority of vaginoplasty patients. Research suggests that roughly 35% of TGNC individuals undergo some form of GAS, with 5% to 13% of transfeminine patients reporting bottom surgery.[8] With 1.4 million self-identified transgender people in the United States,[1] it is fair to say that the 457 vaginoplasties identified is a small fraction of the number of cases performed in this 10-year span. One study found a total of 1859 gender-affirming top and bottom surgery cases from 2008 to 2017 using ACS-NSQIP.[7] In contrast, another group found 3200 operations that were performed nationally in 2016 alone, with 395 cases performed at their home institution in 2017, per their billing and electronic health records.[9] We believe that this highlights a problem in gender-affirming care: there is inconsistent use of ICD codes for gender dysphoria at the time of surgery, and the coding available to specifically describe gender-affirming operations is not specific, making it nearly impossible to accurately determine the incidence of standard surgical complications like deep vein thrombosis, pulmonary embolism, surgical site infections, or death.

There are multiple approaches to transfeminine bottom surgery, including vulvoplasty only, nongenital skin graft, penile inversion, and peritoneal pull-through vaginoplasty.[6] Penile inversion vaginoplasty is the most prevalent technique,[6] accomplished in a single operation encapsulating potentially 8 separate unbundled CPT codes (penectomy, orchiectomy, urethroplasty, vaginoplasty, clitoroplasty, labiaplasty, abdominal flap, and penile inversion flap). Additionally, some surgeons use the ICD diagnosis code of "unspecified endocrine disorder" for TGNC patients in lieu of "gender dysphoria," as "gender dysphoria," "gender identity disorder," and the antiquated code "transsexualism" are all psychiatric diagnoses. Also, many TGNC patients do not want these psychiatric diagnoses used in their care. As such, ICD filtration based on psychiatric diagnoses will miss these patients. Subsequent

CPT filtration will further dwindle the cohort, given not all vaginoplasty patients will undergo the same set of procedures as they are currently unbundled. This lack of standardization in coding presents a danger to TGNC patients as it inhibits quality improvement research from taking place, which occurred in our study.

Gender-Affirming Hormone Therapy and Thromboembolic Risk

Heterogeneity in coding practices hindered this study in capturing all patients undergoing transfeminine vaginoplasty. An estimated 75% of TGNC individuals are on some form of hormone therapy in the United States,[3] which prompted the authors to assess the incidence of standard surgical complications with special consideration to venous thromboembolism. Given their limited access to care, up to 70% of transgender women attain hormones secondhand through social networks and online markets.[5] Hormone use without guidance from a licensed provider brings significant concern in medical management, particularly with the increased risk of ischemic stroke, venous thromboembolism, and potential myocardial infarction.[5] Complicating factors include variable hormone doses, hormonal route of administration (transdermal and parenteral routes are superior to oral estradiol in preventing clots by bypassing first-pass hepatic metabolism), GAS, and comorbidities such as HIV infection, which disproportionately affects TGNC individuals.[5] Additionally, the impact of initiating hormone therapy on the cardiovascular risk of patients with preexisting comorbidities is unknown,[3] and there are concerns regarding estradiol interactions in transgender women undergoing antiretroviral therapy.[5] As such, most surgeons advise estrogen therapy cessation 2 to 4 weeks prior to vaginoplasty to minimize the theoretical thromboembolic risk.[5] However, the exact incidence of thromboembolic events in the postoperative period is unknown.

Gender-Affirming Surgery on the Rise

Such gaps in the knowledge of postoperative risks for procedures that are set to rise significantly in the coming years is concerning. With the passage of the Affordable Care Act, which included GAS as a covered benefit under Medicare, transfeminine and transmasculine operations increased by 109% and 392%, respectively, from 2015 to 2018.[7] For those under the age of 65, insurance coverage of GAS also has been increasing: 124 of 150 major insurance providers have begun offering GAS benefits as of 2019[1] and 25 states are now offering Medicaid coverage for GAS benefits.[10] The American Society of Plastic Surgeons noted this expansion and began offering formal education on TGNC patients in response to increased demand for GAS.[7] As more states expand coverage and more surgeons are trained to offer GAS as a result, the volume of bottom surgery in the United States is expected to rise. However, it is imperative that more information about the risks of GAS be elucidated through large database research, so we can provide comprehensive informed consent to this growing patient population.

CONCLUSIONS

Without an ICD code for "gender affirmation"—not the pathologic diagnosis of gender dysphoria—and surgery-specific CPT codes for each of the gender-affirming operations, it is difficult to accurately isolate patients for research purposes. The volume of TGNC patients receiving all forms of GAS is rising quickly, both in academic and private practice, yet ACS-NSQIP fails to collect data in the private sector despite its reach as a national academic database. Thus, we strongly suggest the optimization of coding practices for GAS, so surgeons may facilitate accurate use of standardized databases for research that seeks to keep TGNC patients safe.

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Description of Kratom Exposure Events in Wisconsin as Reported to the Wisconsin Poison Center, January 1, 2010 to September 1, 2022

Peter DeJonge, PhD; David Gummin, MD; Nicholas Titelbaum, MD; Jonathan Meiman, MD

ABSTRACT

Background: Consumption of kratom (*Mitragyna speciosa*), an herbal substance, can result in adverse health effects. We characterized kratom-associated adverse events in Wisconsin to provide pertinent recommendations for clinicians and public health practitioners.

Methods: Using Wisconsin Poison Center data, we searched for and summarized all records associated with exposure to "kratom," "electronic delivery device containing kratom," or "mitragyna" from January 1, 2010, to September 1, 2022.

Results: Kratom-associated exposure calls to the Wisconsin Poison Center increased 3.75 times during 2016–2020. Among all 59 calls, 26 (44.1%) reported concomitant use of another substance, agitation was the most common symptom reported (n=23, 39%), and 7 persons required critical care. Three unintentional ingestions were reported in children aged less than 2 years old.

Discussion: Kratom-associated exposure calls to the Wisconsin Poison Center generally have been increasing in frequency since 2011. Wisconsinites who choose to use kratom might benefit from education regarding health risks and safe storage practices to avoid unintentional pediatric exposure.

BACKGROUND

Kratom is an herbal substance derived from the leaves of *Mitragyna speciosa*, a tree native to Southeast Asia, and is commonly consumed in a tea or as a dried powder.[1] Two principal kratom alkaloids, mitragynine and 7-hydroxymitragynine, are responsible for kratom's psychotropic properties, which range from stimulant-like effects at low doses to opioid-like sedative effects at higher doses.[2] Kratom often is ingested for self-management of pain, anxiety, and depression and to stop or reduce opioid use or alleviate withdrawal symptoms.[3]

Although considered a "drug of concern" by the US Drug Enforcement Agency, kratom remains unscheduled by the US Controlled Substances Act, and its legality is determined on a state-by-state basis.[4] Wisconsin is 1 of 6 states where possession of kratom is illegal statewide and thus not subject to commercial regulation.[3] However, kratom use still occurs in Wisconsin and is, therefore, important to understand both clinically and from a public health perspective given the range of kratom-associated adverse events reported in literature.[1] We examined data from the Wisconsin Poison Center (WPC) during January 1, 2010 to September 1, 2022, to characterize kratom-associated adverse events in Wisconsin and provide pertinent recommendations for clinicians and public health practitioners.

METHODS

WPC data are shared with the National Poison Data System (NPDS), a collection of data logged by all poison centers in the United States and maintained by America's Poison Centers.[5] We queried NPDS for all Wisconsin-originated records associated with "kratom" (generic code: 0310130, product code: 7224390), "electronic delivery device containing kratom" (product code: 8306048), or "mitragyna" (product code: 4271683). We searched all records generated during January 1, 2010, to September 1, 2022.

We only considered calls associated with substance exposure (ie,

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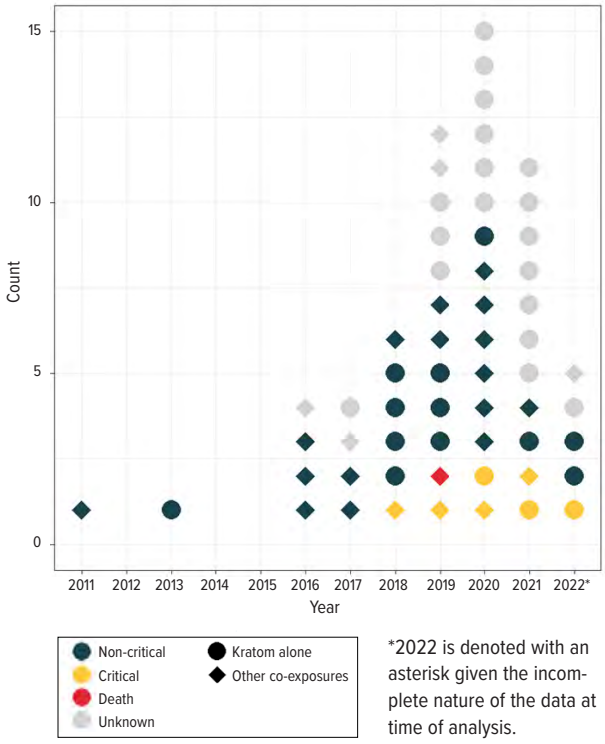
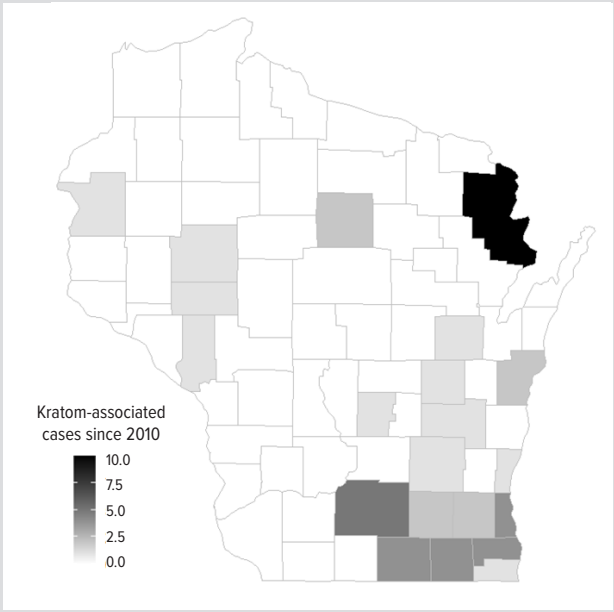
Figure 1. Timeline of Kratom-Associated Exposure Calls (N = 59) to the Wisconsin Poison Center, January 1, 2010–September 1, 2022



*2022 is denoted with an asterisk given the incomplete nature of the data at time of analysis.

Figure 2. Distribution of Kratom-Associated Exposure Calls with County Information (N = 54) Recorded by the Wisconsin Poison Center, January 1, 2010–September 1, 2022



calls for the purposes of drug identification or information-gathering were excluded). Kratom-exposure calls were characterized by year of exposure, county of caller, reason for call, demographic characteristics, single vs polysubstance exposure, reported symptoms, highest level of health care received, and overall medical outcome. These categories follow NPDS coding schemes developed by America's Poison Centers.[5] Fisher exact test was used for unadjusted comparisons of categorical variables. We also summarized narrative information from exposure calls associated with the most severe medical outcomes. R software version 4.1 was used to complete all data analyses and figures (R Core Team).[6] This activity was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy (eg, 45 CFR part 46, 21 CFR part 56; 42 USC §241(d); 5 USC §552a; 44 USC §3501 et seq).

RESULTS

During January 1, 2010 to September 1, 2022, WPC received 59 calls associated with kratom exposure (Table). Most exposed persons were self-reported male (37/59, 62.7%). One person reported being pregnant at time of exposure. Of 52 (88.1%) calls with age information available, the mean age of exposed persons was 35.3 years (range: 8 months–77 years). Three exposures occurred among children less than 18 years; all 3 were among infants less than 2 years and reported as unintentional ingestions. Each of these 3 pediatric exposures was recorded by WPC staff as associated with little-to-no medical outcome; however, 1 child (aged 8 months) was admitted to the pediatric intensive care unit for observation.

After zero calls reported in 2010, kratom exposure-associated calls increased from 1 call in 2011 to a peak of 15 calls in 2020 (Figure 1); based on visual inspection there were no obvious changes over time in the patterns of medical outcome or polysubstance exposure. Among exposures with county information (N = 54), the majority were concentrated in southeastern Wisconsin counties, containing the Madison and Milwaukee metropolitan areas (Figure 2). Marinette County in northeast Wisconsin reported the highest number of kratom exposures (10, 18.5%), which were distributed over time (1 in 2018, 4 in 2019, 2 in 2020, 2 in 2021, and 1 in 2022).

Approximately half of callers reported kratom as the only exposure substance (n = 33, 55.9%). Kratom exposure by itself, compared with polysubstance exposure, generally occurred in younger persons (mean age = 31.9 years vs 38.7 years, respectively). Among persons reporting polysubstance exposures, the most common co-substances were alcohol (n = 8, 30.8%) and benzodiazepines (n = 3, 11.5%). Fisher exact test for association indicated that compared with exposures of kratom alone, polysubstance exposure was not significantly associated with medical outcome reported (P = 0.22) nor level of health care received (P = 1.0), though these analyses are limited by small numbers.

Agitation (n = 23, 39.0%), tachycardia (n = 21, 35.6%), confusion (n = 4, 23.7%), and generalized central nervous system depression (n = 13; 22.0%) were the most commonly reported clinical findings. Among 50 calls with known medical outcome,

19 (38.0%) were reported with moderate or major medical outcomes. Among 36 calls with known levels of health care received, critical care was required for 7 persons (22.2%), although only 1 received laboratory confirmation of kratom exposure; 5 presented with marked agitation and required sedation therapy; and 3 required mechanical ventilation.

Among critical care admissions, 1 was an infant aged 8 months with suspected kratom exposure. The infant, presenting with tachycardia and vomiting, was kept overnight in the pediatric intensive care unit for monitoring; the child was reported normal at discharge the following day. Additionally, in different years and counties, 2 males in their early 30s were admitted to critical care. Both were active weightlifters, presented with agitation, and reported co-ingestion of phenibut, a central nervous system depressant unregulated in the United States and commonly marketed online as a dietary supplement.

WPC also recorded 2 critical care admissions among females aged 77 years. Both presented with tachycardia, confusion, and marked agitation. One of the women died in the hospital with sepsis complications, though postmortem toxicology identified kratom as contributory. During initial presentation at a local emergency department, a family member reported the patient's recent use of kratom for chronic pain—believed to be 1 or more 18 mg kratom capsules daily. A capsule source was not identified. A quantitative serum mitragynine level was obtained on hospital admission and returned at 26 ng/ml.

Table. Characteristics of All Kratom-Associated Exposure Calls (N = 59) to the Wisconsin Poison Center — January 1, 2010–September 1, 2022

Exposure characteristics	No. (%)
Female	22 (37.3)
Age in years, mean (sd)	35.3 (15.4)
Reason for call	
Adverse reaction to drug	8 (13.6)
Intentional — abuse, misuse, or unclear reason	38 (64.4)
Intentional — suspected suicide	6 (10.2)
Withdrawal symptoms	2 (3.4)
Unintentional	3 (5.1)
Unknown or missing	2 (3.4)
Symptom reported[a]	
Agitation	23 (39.0)
Tachycardia	21 (35.6)
Confusion	14 (23.7)
Central nervous system depression	13 (22.0)
Hypertension	9 (15.3)
Medical outcome[b]	
No effect	7 (11.9)
Mild effect	28 (47.5)
Moderate effect	16 (27.1)
Major effect	3 (5.1)
Death	1 (1.7)
Unable to assess, lost to follow-up	4 (6.8)
Highest level of health care facility care	
Unknown or refused treatment	23 (39.0)
Admit, treat and release	17 (28.8)
Admit, noncritical[c]	12 (20.3)
Critical care admission	7 (11.9)

[a]Multiple symptoms were able to be reported by exposed persons. Here, the 5 most frequently reported symptoms are presented.

[b]Defined by the National Poison Data System (NPDS) as the "Medical outcome of the patient following exposure based on all available information." No effect reflects a combination of 2 NPDS outcome categories: "No effect" and "Unrelated effect, the exposure was probably not responsible for the effect(s)." A mild effect was defined as "the patient exhibited some symptoms as a result of the exposure, but they were minimally bothersome to the patient." A moderate effect was defined as "the patient exhibited symptoms as a result of the exposure which are more pronounced, more prolonged or of a more systemic nature than minor symptoms." A major effect was defined as "the patient exhibited symptoms as a result of the exposure which were life-threatening or resulted in significant residual disability or disfigurement."

[c]Includes 1 exposed person who was recorded as "admitted to psychiatric facility."

DISCUSSION

In Wisconsin, kratom-associated exposure calls to WPC generally have been increasing in frequency during the past decade—similar to the trend nationwide.[7] Though the number of studies on kratom use is increasing also, the literature still lacks a consensus as to the substance's health benefits and risks.[8] For one, analyses of US kratom use are challenged by the limitations of passive surveillance systems,[7,9] which likely undercount kratom-associated adverse events. Neither traditional drug tests nor forensic toxicology assays generally screen for mitragynine.[8] Secondly, in the absence of governmental or commercial kratom regulation, research is often unable to categorize the potency, quality, or actual substance being consumed.[10]

An additional complication in our understanding of kratom-associated outcomes is the considerable prevalence of polysubstance exposure—recorded in approximately half of WPC calls in our project. Clinicians and public health practitioners may consider cautioning people against use of kratom concomitant with other substances due to unknown possible harmful drug interactions.[2,7] This message is perhaps particularly relevant among older adults, such as the 2 persons aged 77 years in WPC data, who are more at risk for adverse drug interaction outcomes because of their high prevalence of prescription medication use.

Kratom use education also may consider prioritizing messaging among adults with children or expectant parents. WPC recorded 1 woman being pregnant at time of exposure. Though national incidence of prenatal kratom use is unknown, 5 peer-reviewed case reports describe maternal and infant kratom withdrawal symptoms; 2 cases involved infants who were only exposed to kratom during the prenatal period, and both required treatment with a morphine weaning protocol to manage symptoms of neonatal abstinence syndrome.[11] WPC also received 3 calls related to unintentional kratom ingestion in children less than 2 years old. As with any other psychoactive substance, public health messaging and clinical guidance to adults who use kratom should consider including information

about safe storage practices to avoid unintentional ingestion or misuse by children.

As a final point, we consider the high prevalence of agitation among persons admitted to critical care worth noting. Again, extricating the role of kratom among these call data is challenging given small numbers in our dataset and the concomitant use of other substances in 5 of 7 critical care admissions. However, clinicians and toxicologists should recognize that although kratom does have sedative, opioid-like properties at higher doses, it also can act as a significant stimulant at lower doses,[2,3] which is perhaps evidenced by prevalent agitation reported in WPC calls.

CONCLUSIONS

During January 1, 2010, to September 1, 2022, in Wisconsin, kratom-associated exposure calls to the WPC increased in frequency, were commonly reported as polysubstance exposures, and occasionally indicated intensive care unit admission. Continued research may help to more fully define kratom's risk-benefit profile. Meanwhile, Wisconsin clinicians and public health experts can (1) be aware of its increasing prevalence, (2) expand the collection of data specific to kratom use and exposure among patients—during the clinical documentation of patient history for example, and (3) utilize available scientific literature to promote education materials for adults who choose to use kratom, particularly if they do so alongside other substances.

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Functional Assessment of Concussion Tool Application in a Pediatric Concussion Clinic

Katherine Lumetta, MD; Sam Halama, BA; Shayne Fehr, MD; Jennifer Apps, PhD; Danny G. Thomas, MD, MPH

ABSTRACT

Background: Traditional concussion symptom scales do not assess function. We piloted a mobile app-based assessment that aims to measure the functional impact of symptoms.

Methods: Patients with concussion completed the Functional Assessment of Concussion Tool and traditional symptom scales postinjury.

Results: Linear regression assessed the predictive value of the Functional Assessment of Concussion Tool symptom number and function rating compared to scores on 2 traditional symptom scales across 4 symptom domains. The mobile app symptom number predicted scores on traditional symptom scales across domains. The rating score predicted traditional scale scores in 2 domains. The mobile health tool did not predict recovery.

Discussion: This mobile health concussion symptom assessment may measure the functional impact of symptoms, though further study is needed.

BACKGROUND

Mild traumatic brain injury (mTBI), also known as concussion, affects nearly 2 million youth annually, and 70% to 90% of traumatic brain injuries are mTBIs.[1,2] The standard recommended rest period post-concussion is 24 to 48 hours followed by symptom-guided return to activity, and evidence suggests prolonged delays in resuming physical activity are associated with delays in recovery. Patients who have a longer rest period post-injury may spend more time perseverating on their symptoms and less time being physically active.[3] While evidence has moved away from prolonged rest after injury, symptom-sensitive patients may inadvertently subject themselves to prolonged activity restriction. Traditional symptom scales ask patients to rate the intensity of a wide range of symptoms, which can lead to both under- and overreporting of symptoms. Overreporting could result in a more cautious treatment approach and longer period of activity restriction as symptoms guide return to normal activity. Underreporting could result in premature return to activity.

Mobile health (mHealth) is a tool to monitor mTBI patients' symptoms and activity levels. mHealth is the use of mobile devices for remote patient monitoring to help improve health outcomes and conduct health research.[4] Ninety-one percent of Americans own a cell phone,[5] and adolescents, in particular, rely on texting to communicate.[6] mHealth can take advantage of technology to provide a convenient way for patients to communicate with health care providers and has been used to assess patient outcomes for other conditions.[7,8]

This study developed and tested an mHealth tool, the Functional Assessment of Concussion Tool (FACT), to measure longitudinal outcomes and recovery following mTBI. The FACT was developed to be easy to use to facilitate remote pediatric patient monitoring. It takes less than 5 minutes to complete and uses a simplified scale to measure the impact of concussion symptoms on daily activities. Traditional symptom assessments ask patients to rate the severity of more than 25 individual symptoms. In contrast, the FACT assessment asks patients to rate how their symptoms affect daily activities using an age-appropriate functional scale modeled on a stoplight (red = symptoms "stopped" me from normal routine; yellow = symptoms "slowed me down;" green = "good to go," did not impact normal routine).

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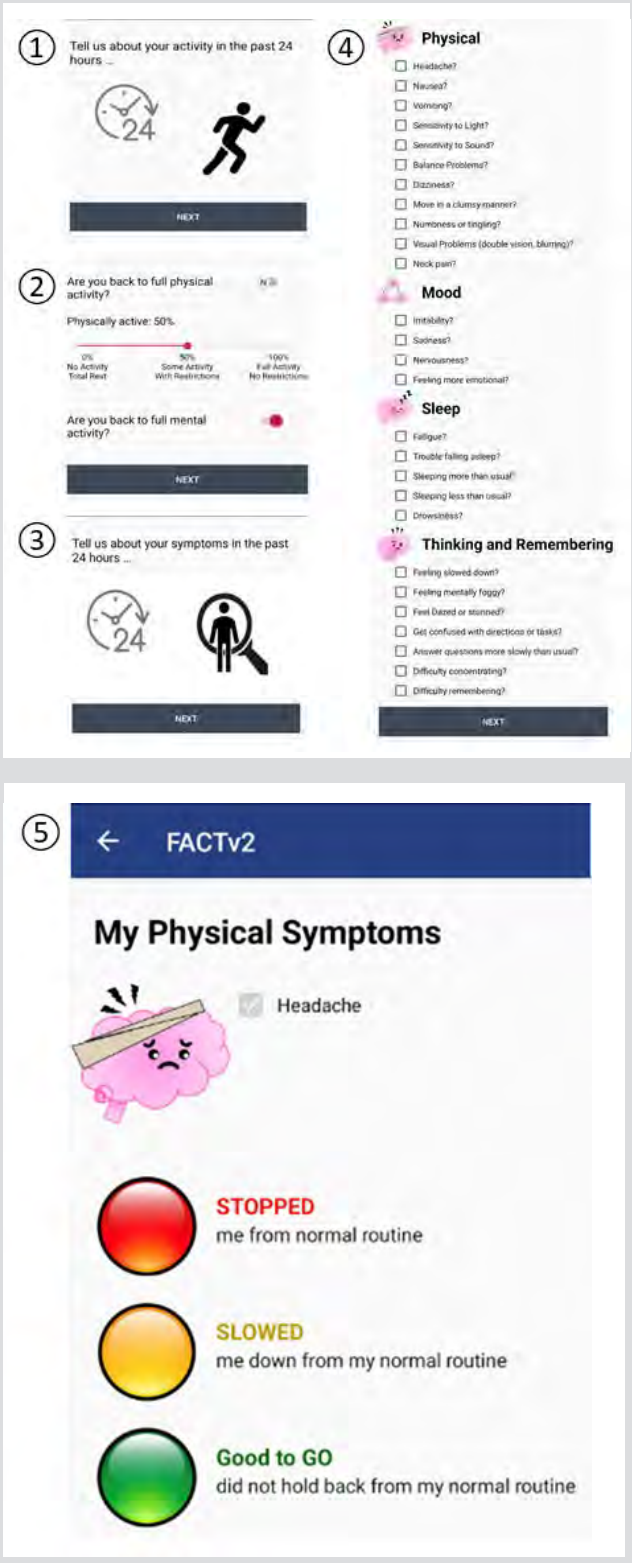
Figure 1. FACT App Screen Shots



(1) Subject is asked about physical and mental activity, which they answer using (2) radio buttons and a slider to report percentage of activity. (3) Subject is then asked to report symptoms and (4) selects symptom they experienced from a checklist of 27 post concussion symptoms. Finally, subject is asked to rate symptoms by each domain (eg, My Physical symptoms) using a stoplight paradigm to determine functional impact of concussion symptoms.

This assessment paradigm is intended to shift patients' focus from symptom counting to symptom reflecting.

This study aims to determine FACT's ability to assess functional outcomes in pediatric patients following acute mTBI and to determine if FACT is better correlated with recovery times compared to traditional symptom scales. We hypothesized that FACT scores would demonstrate a strong correlation with the Sport Concussion Assessment Tool (SCAT)[9,10] and the Post-Concussion Symptom Scale (PCSS)[11] and that FACT scores would have better correlation with recovery by 14 days than the traditional PCSS.

METHODS

We recruited patients aged 8 to 18 years during their first visit to Children's Hospital of Wisconsin/Medical College of Wisconsin Concussion Clinic after a diagnosis of mTBI. Exclusion criteria included (1) history of brain surgery or moderate to severe traumatic bran injury (Glasgow Coma Score < 14), (2) history of substance abuse, (3) history of major psychiatric disorder, (4) special education, or (5) no access to a smartphone. After obtaining informed consent, patients completed a SCAT3/Child SCAT3, Post-Concussion Symptom Scale (PCSS), and FACT app assessment in the concussion clinic.

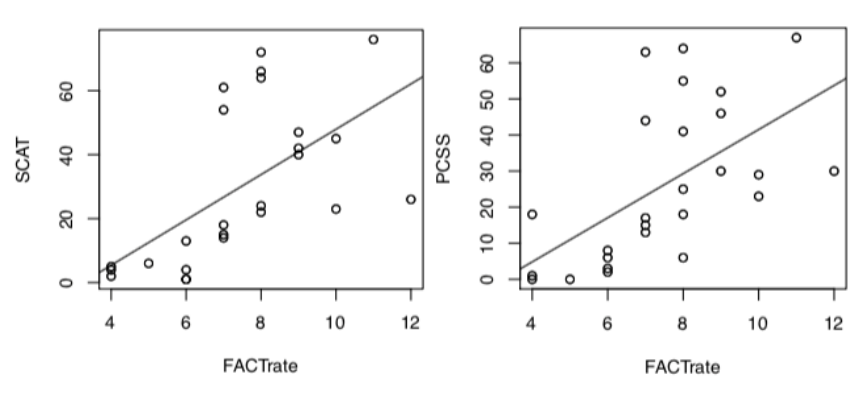
The FACT app asked patients to report their physical and mental activity levels, the symptoms they experienced in the last 24 hours, and how their symptoms affected their normal activity. Symptoms were divided into 4 domains: physical, mood, sleep, and thinking and remembering. Patients selected the symptoms they were experiencing in each domain and rated how the symptom domain affected their normal activity using a stoplight scale displayed in Figure 1. The FACT app prompted patients to complete a FACT survey every day for the first 21 days, then every 3 days until 3 months post-injury or achieving FACT recovery. FACT recovery was defined as self-reported return to full activity and "Green" rating in all 4 domains for at least 2 consecutive assessments. Clinical recovery was defined as time from first clinic visit to clearance by sport medicine clinician and was determined by chart review. Parental input on the ease of use of the app was collected on the first 20 patients to optimize usability. For analysis, FACT app rating scores were converted to numeric values (red = 3, yellow = 2, green = 1, respectively). We analyzed both the FACT number of symptoms and FACT ratings of symptoms.

A linear regression model (simple and multiple) was used to determine whether the number of initial FACT symptoms reported and FACT rating across all 4 domains could predict initial SCAT3 and PCSS scores. We used a Cox proportional hazards model to evaluate predictive values of initial SCAT3, PCSS, FACT, and FACT ratings adjusted for gender effect on time to recovery (FACT and clinical).

RESULTS

We recruited 27 patients. Two-thirds were female and the mean age was 14.56 years. Sports were the most common mechanism of injury (16/27 patients), and median time from injury to first clinic visit was 11 days (interquartile range 6.5-17.5). Mean time to FACT recovery was 31.27 days (n=11), and mean time to clinical recovery was 46.67 days (n=24; 11 cleared during last clinic visit, 13 cleared in phone follow-up after last visit). Mean initial PCSS score was 26 (n=26; one did not complete), and mean SCAT3 score was 29.8 (n=25; two did not complete). Mean total FACT rating on the initial FACT assessment was 7.48 (n=27). The most common symptoms reported on the initial FACT assessment were in the physical and thinking and remembering domains, with more than two-thirds of patients reporting a headache and difficulty concentrating.

Figure 2. Comparison of Total Functional Assessment of Concussion Tool Rating Score to Traditional Symptom Scales Scores Obtained at Initial Clinic Visit



Total Functional Assessment of Concussion Tool rating score (for all 4 domains: physical, mood, sleep, and thinking and remembering) was predictive of Total Sport Concussion Assessment Tool (SCAT) and Post-Concussion Symptom Scale (PCSS) scores ($P<0.01$).

The total number of initial FACT symptoms reported was predictive of the total initial SCAT and PCSS scores and SCAT and PCSS scores in the physical, mood, sleep, and thinking and remembering domains ($P<0.03$). The total FACT rating score was predictive of total SCAT and PCSS scores ($P<0.01$) (Figure 2) and SCAT and PCSS scores in the mood and thinking and remembering domains ($P<0.02$) using simple linear regression (Figure 3).

Multiple linear regression models were used to evaluate if the total number of FACT symptoms was predictive of initial SCAT or PCSS scores after adjusting for the FACT rating. The number of initial FACT symptoms was a significant predictor of the total initial SCAT and PCSS scores; the initial SCAT scores in the physical, mood, sleep, and thinking and remembering domains ($P<0.01$); and in the initial PCSS scores in the physical, mood, and thinking and remembering domains ($P<0.01$). However, the FACT rating score was not a statistically significant predictor of any SCAT or PCSS scores in the multiple linear regression models.

We have compared predictive properties of initial SCAT, FACT, FACT rating, and PCSS for each of their domains and the total scores. For the times to event (time to FACT recovery and time to clinical recovery), gender was the only significant predictor. Initial FACT symptom scores and clinical PCSS scores were not significant predictors of recovery when adjusted for gender using Cox proportional hazards models.

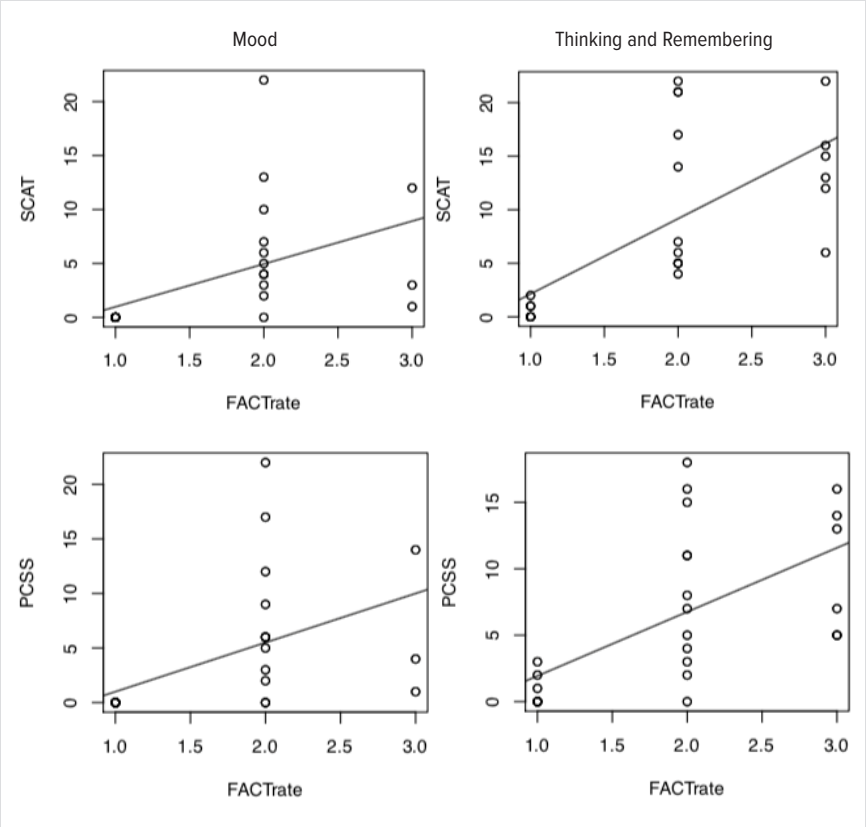
DISCUSSION

This is the first study to utilize the FACT assessment paradigm. This preliminary data suggest that FACT symptoms corresponded to traditional symptom scales, as the number of FACT symptoms are correlated with SCAT and PCSS scores across all symptom domains. As the PCSS and SCAT are weighted toward symptom capture, it is not surprising that the number of symptoms on FACT is correlated. Though FACT assessed similar symptoms as the SCAT and PCSS, it uniquely assigned a rating score to the symptoms based on how the symptoms affected daily function. Our findings suggest that as the FACT rating system consolidates symptoms by domain and asks for a functional rating, it measures different components of symptoms compared to traditional symptom scales. This explains why the FACT rating score is a significant predictor of SCAT scores and PCSS across only 2 of 4 domains. The 15-day difference in FACT recovery and clinical recovery may reflect differences in subjective perception versus clinical assessment of recovery or time delays related to scheduling clinic visits for formal concussion clearance.

The PCSS is a standard symptom scale, but it has a number of limitations, including its subjective nature and variable results.[12] As a self-reported scale, some elements of the PCSS, including symptom severity reported on a 0 to 6 scale, may be interpreted differently by individual patients.[13] Additionally, patients without concussion may report concussion symptoms that are due to an unrelated condition, as 1 study showed that patients without concussion endorse symptoms on the PCSS.[13] Many factors influence the number of baseline symptoms reported, including diagnosis of learning disabilities, history of headaches or previous concussion, and others.[13] One study found that athletes with a high number of baseline symptoms on the PCSS had no difference in PCSS scores at 2 to 7 days post-injury.[13] Therefore, knowledge of a patient's baseline and how symptoms affect daily function would be important for interpreting PCSS results, especially when considering symptoms as a guide for recovery.

The FACT's structure may address some of the limitations of the PCSS. While also subject to biases inherent to self-

Figure 3. Comparison of Functional Assessment of Concussion Tool Rating Score by Domain to Traditional Symptom Scales Scores by Different Symptom Domains



Functional Assessment of Concussion Tool rating score was predictive of Sport Concussion Assessment Tool (SCAT) and Post-Concussion Symptom Scale (PCSS) scores in the "Mood" and "Thinking and Remembering" domains ($P < 0.02$ for both SCAT and PCSS).

reported measures, the FACT uses a functional scale focusing on how symptoms affect normal daily activities, which potentially can minimize variability in reporting compared to the PCSS. FACT also accounts for patients who experience symptoms at their baseline, as these regularly experienced symptoms would be present when participating in their normal daily activities. This contrasts with the PCSS, which may capture baseline symptoms that were present before concussion. The initial data in this study support that FACT rating measures a different aspect of symptoms, possibly reflecting the functional effects of concussion symptoms, which is not accounted for in standard symptom scales.

While not replacing other symptom scales, we propose that FACT could be used as a remote monitoring tool that is a more convenient assessment of the patients' symptoms compared to traditional symptoms scales. It allows providers to understand how concussion is affecting a patient. This information could assist providers with management decisions, such as determining follow-up intervals and return-to-activity plans, as well as providing additional information (ie, functional impact of symptoms) on recovery status, though by itself it is not a significant predictor of recovery. Future iterations of the FACT app will allow for patients to serially track scores, display recovery progress, and share concussion symptom history with clinicians and school personnel.

The primary limitation of this study is sample size. We recognize that while FACT may address a different component of symptom reporting, the scale is still self-reported and subject to under-/overreporting like the traditional symptom scales. Another important limitation is that while most patients have access to a mobile device,[5] not all children or families in the community do, which may exacerbate health disparities. We do not know how often parents assisted in survey completion or how many families were excluded because they did not have a smartphone. Finally, significant limitations in methodology exist, including temporal comparisons of FACT and traditional symptoms scales. FACT data were obtained daily to every 3 days, while traditional symptom scale data were collected inconsistently at subsequent clinic visits, which limited the ability for comparison of repeated measures. Despite these limitations, the FACT app appears to be a promising means to provide remote patient monitoring for pediatric concussion recovery. Further investigation with a larger sample is needed to assess the FACT's strength in measuring the functional component of symptoms and its predictive value in concussion recovery

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Pediatric Acute Q Fever in Rural Wisconsin: A Case Report

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ABSTRACT

Introduction: Q fever is a zoonotic disease with a variable clinical presentation and potentially fatal complications. While rare, it is more common in rural areas due to its transmission from animals, including cattle.

Case Presentation: A 3-year-old boy presented in December 2020 with intermittent fevers, headache, rash, and lymphadenopathy. After several months of symptoms, he was diagnosed with acute Q fever.

Discussion: This case demonstrates the importance of considering Q fever in the differential diagnosis when a patient presents with nonspecific infectious symptoms and an epidemiological link that places them at risk.

Conclusions: While rare, Q fever is a potentially serious infection that can affect people living in Wisconsin's rural farming communities.

INTRODUCTION

Q fever is a zoonotic disease caused by the bacterium *Coxiella burnetii.* Humans typically become infected by inhaling air that has been contaminated by waste products of infected animals. It most commonly presents as a febrile influenza-like illness, often with headache; it also may cause pneumonia and hepatitis. Signs and symptoms are often variable and nonspecific, making it difficult to diagnose. Approximately 50% of infections are asymptomatic, leading to significant underreporting.[1] Persistent localized Q fever, previously classified as chronic Q fever, is estimated to occur in less than 5% of persons who are initially infected and may occur after symptomatic or asymptomatic infections. Here, we present a child with a prolonged course of relapsing febrile illness eventually diagnosed as acute Q fever.

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CASE PRESENTATION

In December 2020, a 3-year-old boy with no pertinent past medical history presented to the clinic with a 1-day history of submandibular lymphadenopathy, fatigue, and subjective fever. Exam was notable for bilateral cervical lymphadenopathy but otherwise normal. He tested negative for SARS-CoV-2 and group A streptococcal pharyngitis and was presumed to have a nonspecific viral infection. Two weeks later, he was seen in the emergency department (ED) for persistent symptoms of fever and submandibular lymphadenopathy. Exam revealed a prominent right-sided submandibular lymph node but was otherwise unremarkable. A neck ultrasound revealed multiple enlarged lymph nodes with normal echotexture and no evidence of a fluid collection or abscess. A complete blood cell count (CBC) was normal, except for a mild normocytic anemia. A urinalysis was normal. A heterophile antibody for infectious mononucleosis and *Bartonella henselae* titer were negative. He was diagnosed with lymphadenitis and treated with a 7-day course of amoxicillin-clavulanate.

Over the next 6 weeks, the patient was seen multiple times in the ED and his primary care clinic with recurrent fevers, lymphadenopathy, headache, malaise, and a diffuse erythematous maculopapular rash on extremities and trunk. Further workup included uric acid, lactate dehydrogenase, CBC, complete met

Figure. Centers for Disease Control and Prevention Surveillance Case Definition and Case Classification for Acute and Persistent Localized Q Fever

	Acute Q fever	Chronic Q fever
Clinical evidence of infection	Fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzymes	Newly recognized culture-negative endocarditis (particularly in a patient with previous valvulopathy or compromised immune system), suspected infection of a vascular aneurysm or vascular prosthesis, or chronic hepatitis, osteomyelitis, or pneumonitis in the absence of other known etiology
Laboratory criteria[a,b]	**Laboratory confirmed (one or more of the following):** • Fourfold change in IgG antibody titer to *Coxiella burnetii* phase II antigen by IFA between paired sera • Detection of *C burnetii* DNA in a clinical specimen by PCR • Demonstration of *C burnetii* in a clinical specimen by IHC • Isolation of *C burnetii* from a clinical specimen by culture	**Laboratory confirmed (one or more of the following):** • IgG titer ≥1:800[c] to *C burnetii* phase I antigen by IFA • Detection of *C burnetii* DNA in a clinical specimen by PCR • Demonstration of *C burnetii* in a clinical specimen by IHC • Isolation of *C burnetii* from a clinical specimen by culture
	Laboratory supportive (one or more of the following): • Single IgG titer ≥1:128 to *C burnetii* phase II antigen by IFA (phase I titers may be elevated as well) or • Elevated phase II IgG or IgM antibody reactive with *C burnetii* antigen by ELISA, dot-ELISA, or latex agglutination	**Laboratory supportive:** • IFA IgG titer ≥1:128 and <1:800[c] to *C burnetii* phase I antigen
Case classification	**Confirmed acute Q fever:** Laboratory-confirmation with clinical evidence of infection or an epidemiological link to a laboratory-confirmed case	**Confirmed chronic Q fever:** Clinical evidence of infection with laboratory confirmation
	Probable acute Q fever: Clinical evidence of infection with laboratory-supportive results	**Probable chronic Q fever** Clinical evidence of infection with laboratory-supportive results

Abbreviations: ELISA, enzyme-linked immunosorbent assay; IFA, indirect immunofluorescence antibody assay; IgG, immunoglobulin G; IgM, immunoglobulin M; IHC, immunohistochemistry; PCR, polymerase chain reaction.

[a]CDC prefers simultaneous testing of paired samples. IgM tests are not strongly supportive of serodiagnosis because the response might be persistent (making it unreliable as an indicator of recent infection) or nonspecific (resulting in false positives). ELISA tests are not quantitative and cannot be used to measure changes in antibody titer; thus, they can only be used for classification of probable cases. Performing laboratories determine the appropriate cutoff titers for ELISA. Serologic test results should be interpreted with caution because baseline antibodies acquired as a result of previous exposure to Q fever might exist, especially in patients with rural or farming backgrounds.

[b]Patients with suspected chronic Q fever should be evaluated for titers both to phase I and phase II antigens. Serologic test results should be interpreted with caution because baseline antibodies acquired as a result of previous exposure to Q fever might exist, especially in patients with rural or farming backgrounds.

[c]US laboratories use a twofold dilution scheme that does not result in a titer equaling 800; in this document, a titer of 1024 is used as the replacement.

Reprinted from the Centers for Disease Control and Prevention: Diagnosis and Management of Q Fever — United States, 2013 Recommendations from CDC and the Q Fever Working Group, Table 3.[1]

abolic panel, C-reactive protein, and erythrocyte sedimentation rate, along with Epstein–Barr virus and cytomegalovirus serologies. Findings included a white blood cell count of 15.6 K/μL and platelets of 452 K/μL, with all other results normal.

The patient's social history was significant for living on a dairy farm with his parents. His mother reported handling of placenta and birth fluids during calving season prior to the development of her son's signs and symptoms. She said he was present in the maternity pen while cattle were birthing. The family also regularly consumed unpasteurized cow's milk from their farm.

The patient's mother discussed her son's symptoms with their veterinarian, who mentioned that another local dairy farmer recently had been diagnosed with Q fever after presenting with similar nonspecific signs and symptoms. Given this new information, our patient was subsequently tested for Q fever by obtaining phase I and phase II IgG antibody titers. While awaiting those results, he continued to have intermittent fever, rash, and lymphadenopathy. Pediatric infectious disease was consulted. Additional serologies for *Toxoplasma, Brucella,* parvovirus B19, and tularemia were negative. The patient's Q fever IgG titers revealed a phase I titer of 1:256 and a phase II titer of 1:2048, and he was diagnosed with acute Q fever. He was treated with a 14-day course of doxycycline, and his case was reported to both the local and state public health departments. His symptoms quickly resolved. Repeat titers at 1 and 3 months posttreatment remained stable without evidence of an increasing phase I titer. His 12-month titers were decreased at 1:128 for phase I and 1:256 for phase II. He had a normal echocardiogram in March 2022.

In February 2021, the patient's mother presented with headaches, neck pain, abdominal pain, and nausea, and had positive serology testing with phase I titer of 1:128 and phase II titer of 1:512. Given her signs and symptoms, positive serology, and similar exposure history as our patient, it was presumed that she had acute Q fever, and she received treatment with doxycycline. She had rapid resolution of her symptoms, and her titer nor-

malized on recheck 3 months later. Then, 4 months later, the patient's father and another worker on the farm were both diagnosed with and treated for Q fever.

DISCUSSION

Q fever is a reportable disease in the United States, although it is likely underreported due to misdiagnosis or asymptomatic and mild disease not prompting medical evaluation. Over the last 3 years, an average of 2 acute Q fever cases per year and 0 to 2 persistent localized Q fever cases were reported in Wisconsin (Wisconsin Department of Health Services, unpublished data). In 2019, 178 cases were reported to the Centers for Disease Control and Prevention.[2]

Coxiella burnetii, the causative organism of Q fever, is an intracellular gram-negative bacterium that is extremely hearty and virulent; a single organism is considered sufficient to cause disease and, thus, is considered a potential bioterrorism agent.[1] Transmission is typically via inhalation of contaminated aerosols. Animal reservoirs include ruminants, such as cattle, sheep, and goats, which frequently manifest with reproductive difficulties, such as low birth weight and abortions—especially at late gestation.[3] Human infection may be either from direct exposure to animal birth products, urine, or feces; consumption of unpasteurized milk of infected animals; or indirectly from contaminated dust in barns or birthing stalls.[3] Rarely, tickborne transmission has been reported.[4] In this case, our patient regularly consumed unpasteurized milk and was exposed to birthing cattle.

Coxiella burnetii has an incubation period of 2 to 3 weeks in humans, although the incubation period can be variable based on the inoculum dose. Of the 50% who manifest signs and symptoms, acute Q fever is most commonly a self-limited influenza-like illness of high fever, chills, myalgias, and headaches. Fevers can be acute or may last for weeks, as in this case. A generally mild, viral-pattern pneumonia also may develop and rarely can progress to more severe respiratory failure. Hepatitis without jaundice may present with fever and transaminase elevations. Rarely, immune-mediated endocarditis may occur, and persistent infection can result in chronic or subacute endocarditis. The mortality rate of untreated acute Q fever is 1% to 2%, as many cases are self-limited.[1]

Children have lower rates of symptomatic acute Q fever compared to adults, and their symptomatic infections tend to be milder.[1] Children commonly present with a febrile illness and headache, as in our patient. They are more likely than adults to have gastrointestinal and dermatologic presentations. While most acute Q fever cases in children are self-limited, there are cases of recurrent, relapsing febrile illnesses, similar to our case presentation.

Persistent localized Q fever may develop months to years after either symptomatic acute Q fever or asymptomatic infection. It typically manifests as endocarditis, vascular infections (aneurysms), and osteomyelitis/septic arthritis, particularly of prosthetic joints.[1] Untreated persistent localized Q fever has high fatality. A separate phenomenon, known as post-Q fever fatigue syndrome, is possible in any infected individual. This syndrome is also nonspecific and can present with fatigue, nausea, insomnia, short-term memory loss, headaches, myalgias, and arthralgias.[1]

Criteria for the diagnosis of Q fever include appropriate history, physical exam, and laboratory evidence (polymerase chain reaction [PCR] or serology) of infection (Table). Additional laboratory abnormalities to support acute Q fever are nonspecific and frequently include mild transaminase elevations, thrombocytopenia, and either leukopenia or leukocytosis. The antibody response to Coxiella burnetii infection occurs in 2 antigenic phases: phase I and phase II. Therefore, the patient's serum is collected and tested against phase I and phase II IgG antibodies. A fourfold rise in a patient's phase II titer between an acute and convalescent sample is confirmatory for acute Q fever, and a phase II titer of 1:128 or greater is strongly indicative of acute Q fever. In acute Q fever, the phase II antibody titer is higher than the phase I. A phase I titer of 1:1028 or greater, along with an identifiable source of infection (eg, endocarditis, osteoarticular arthritis, osteomyelitis, vascular infection, chronic hepatitis, pneumonitis), is diagnostic of persistent localized Q fever (Table). Phase I and II titers may be falsely negative in the first 1 to 2 weeks of symptom onset, thereby highlighting the importance of acute and convalescent titers. During these first 2 weeks, if there is high suspicion or known exposure, diagnosis via PCR is possible.[1] If PCR is not available and a high clinical suspicion exists, antibiotic treatment should be initiated while awaiting serologic results.

As mentioned above, many cases of acute Q fever are self-limited and resolve without antibiotic treatment. However, symptomatic patients should be treated with antibiotics to decrease the duration of illness, severity of symptoms, and risk of progression to persistent localized Q fever. The recommended treatment for symptomatic acute Q fever is oral doxycycline for 14 days. Children with acute Q fever should also be treated with doxycycline, which has a low incidence of severe side effects if administered for less than 21 days. Asymptomatic pregnant patients, identified by screening for high-risk exposures or occupations, also should be treated due to the risk of severe maternal complications and poor fetal outcomes. Pregnant patients are treated with trimethoprim-sulfamethoxazole (TMP-SMX) throughout pregnancy. Additional folic acid supplementation is administered to reduce the theoretical risk of congenital abnormalities. TMP-SMX, minocycline, clarithromycin, and ciprofloxacin are alternatives if allergies or other contraindications to doxycycline exist. Patients with a history of cardiac valvular stenosis, prosthetic valve, cardiomyopathy, or aortic aneurysms are at higher risk for developing persistent localized disease and need longer

treatment courses with 12 months of doxycycline and hydroxychloroquine. Patients with invasive or persistent localized disease need longer treatment regimens and adjunctive hydroxychloroquine for 18 to 24 months. There is limited data about the most effective treatment for persistent localized Q fever in children.

Follow-up titers are typically recommended after completion of therapy for acute Q fever. The timing for obtaining titers depends on the patient's risk of progressing to persistent localized Q fever. Titers are generally repeated 6 months after diagnosis in healthy, low-risk individuals and every 3 to 6 months for 2 years after diagnosis in high-risk patients (eg, pregnant patients or those with cardiovascular risk factors).[1] In this case, our patient had titers repeated 3 months and 12 months after completion of therapy, which were stable and decreasing, respectively. Persistently elevated or increasing IgG titers, along with clinical suspicion, warrant further evaluation for persistent localized infection. Our patient's decreasing titers at 12 months and normal echocardiogram were both reassuring against persistent localized infection.

Patients undergoing prolonged therapy (ie, greater than 2 weeks) should have titers followed during and after treatment.[1] Consultation with an infectious disease specialist can be helpful during the diagnosis and treatment of a patient with suspected Q fever to assist in the timing and interpretation of Q fever antibody titers. In addition, their involvement is essential in the management of pregnant patients with Q fever and persistent localized Q fever in children. In our case, the primary care and pediatric infectious disease teams worked closely in the treatment and management of our patient.

Once *Coxiella burnetii* is in the environment, it is very difficult to eliminate. While a vaccine for Q fever is available in Australia for agricultural workers, it is not used routinely in the United States.[1] Instead, other prevention measures are recommended, such as educating farmers about Q fever, avoiding consumption of unpasteurized milk on farms with any known cases, routine animal testing for Q fever, and standard biosafety measures. It is recommended that disposable gloves, protective clothing (washable or disposable coveralls and rubber boots), eye protection, and properly fitted N95 or higher respirator mask be used when calving cattle.[1,2]

CONCLUSIONS

Q fever is a rare zoonotic disease with variable and nonspecific symptomatology that makes it difficult to diagnose. Farmers and others who work with animals are at higher risk, and clinicians should consider acute Q fever in such patients who present with a persisting, nonspecific febrile illness. Serologic testing is used to confirm Q fever cases, and antibiotic therapy can reduce symptom duration and decrease the risk of complications. Persistent localized Q fever and post-Q fever fatigue syndrome are potential complications that should be considered in any person with a history of prior Q fever infection or occupational exposure.

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Disseminated Coccidioidomycosis With Fungemia and Possible *Strongyloides* Co-infection

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ABSTRACT

Introduction: Coccidioidomycosis is most often an asymptomatic or mild self-limited respiratory infection, but in rare cases it can become disseminated and cause severe disease.

Case Presentation: A 29-year-old man who was originally from Thailand and had been living in Arizona for 2 years presented with intermittent fevers, fatigue, and other nonspecific symptoms, including abdominal pain, nonbloody diarrhea, and pruritic rash. Initial laboratory values showed significant peripheral eosinophilia. Extensive evaluation revealed possible *Strongyloides* species infection. Shortly after, *Coccidioidies* species fungemia was found. Fevers and symptoms resolved after adequate treatment.

Discussion: Disseminated coccidioidomycosis with fungemia is very rare in immunocompetent individuals. Co-infection with *Stronglyloides* species is only reported in two other case reports.

Conclusions: We report this case to raise awareness of a rare infection. In adequate epidemiological circumstances, co-infections *Coccidioides* and *Strongyloides* species should be considered in presence of fever and eosinophilia.

INTRODUCTION

Coccidioidomycosis is caused by the dimorphic fungus *Coccidioides immitis (C immitis)* or *Coccidiodes posadasii.* Infection with either species has a similar clinical presentation. *C immitis* is most found in soil in the southwestern United States, parts of Mexico, and South America. Highly endemic areas include southern Arizona and California's southern San Joaquin Valley.[1] *Coccidioides* grows as a mold with septate hyphae that develop arthroconidia in the soil, which can then become aerosolized and inhaled. Once inhaled, the warm environment of the lungs triggers a morphological change into spherules. The spherules then rupture and release endospores.[2] Sixty percent of coccidiomycosis infections are asymptomatic or present as a mild self-limited respiratory infection, and less than 1% become disseminated.[3] Extrapulmonary coccidioidomycosis most commonly involves the skin, bone, and meninges and less commonly involves the liver, spleen, lymph nodes, kidney, eye, and endocrine glands.[3] Risk factors for disseminated disease include immunocompromised status (HIV infection, steroid use, therapy with immunobiological modulation, malignancy), pregnancy, male sex, and ethnicity (Filipino, Asian, and/or African).[4] *Coccidioides* species fungemia is an even rarer event and almost universally found in immunosuppressed patients.[3,5]

We present a case of coccidiomycosis fungemia in an immunocompetent, Asian male patient with possible *Strongyloides* coinfection. There are only two other case reports identified in the medical literature of *Strongyloides* and coccidioidomycosis coinfection.[6]

CASE PRESENTATION

The patient is a 29-year-old man originally from Thailand. He had a 3-week history of intermittent fever, chills, night sweats, increasing fatigue, intermittent nonlocalizing headache, generalized arthralgias, left-sided cramping abdominal pain, and watery nonbloody diarrhea associated with pruritic nodular erythematous rash on his arms and legs. He reported having a very similar epi-

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sode about 5 years before admission when he lived in Thailand; however, it was not treated and the symptoms at that time fully resolved. He did not have any visual symptoms, rhinorrhea, chest pain, dyspnea, cough, hemoptysis, nausea, vomiting, neurologic symptoms, dysuria, urgency, or frequency.

His past medical history included untreated hypertension with no pertinent prior surgical history. He was not taking any medications and did not report any allergies. His family history was unremarkable. He was born and raised in Thailand, but he immigrated to the United States 2 years prior and had been living in Arizona. In the few weeks before admission, he moved to Omaha, Nebraska. He reported social alcohol use and occasionally smoked marijuana. He denied tobacco use, illicit drug use, or any recent sexual activity. He had tattoos done professionally in Thailand. He was not employed. Bacille Calmette-Guerin vaccination status was unknown.

Evaluation at admission revealed a blood pressure of 163/75 mmHg, heart rate of 110 beats per minute, and a temperature of 38.7 °C. Exam showed an alert, cooperative patient with normal white conjunctiva and oral mucosa without lesions. Lungs were clear with good bilateral breath sounds without wheezes, crackles, or rhonchi. Cardiac exam revealed tachycardia without murmur. Abdominal exam showed hepatosplenomegaly with mild diffuse abdominal tenderness. Dermatologic examination was relevant for a patchy erythematous rash on arms, dorsum of hands, and inner upper thighs (Figure 1). Musculoskeletal exam was normal without muscle tenderness, swelling, or arthritis. His neurological exam was unremarkable without nuchal rigidity. No cervical, axillary, or inguinal lymphadenopathy was identified.

Initial laboratory evaluation revealed an elevated white blood cell count (WBC) 20.8 K/µL (range 4-12 K/µL) with eosinophilia at 34% and absolute eosinophil count (AEC) 7.1 K/µL (range 0-0.4 K/µL), hemoglobin (Hg) 11.9 mg/dl (range 13.5-17.5), platelets 363 K/µL (range 140-440 K/µL), normal creatinine, aspartate aminotransferase (AST) 21 IU/L (range 10-40 IU/L), and alanine aminotransferase (ALT) 53 IU/L (12-78 IU/L). Computed tomography (CT) of abdomen and pelvis with contrast showed hepatosplenomegaly. A chest x-ray was normal. He was empirically started on ceftriaxone and doxycycline. Further workup was obtained as detailed later.

Over the initial 4 to 7 days of hospitalization, the patient continued to experience fevers up to 39.6 °C. Leukocytosis remained persistent and peaked at 30.1 k/µL on day 4 with an AEC up to 11.4 k/µL. His liver enzymes, creatinine, hemoglobin, and platelets remained normal. On day 4, a fungal blood culture was obtained, cultured on Sabouraud agar, inhibitory mold agar, and mycosel agar, and incubated at 30 °C ambient air.

With persistent fevers and eosinophilia, fluconazole 400mg/ daily was added on day 4. On day 5, ceftriaxone was changed to meropenem and albendazole was added. On day 8, the patient underwent a lumbar puncture with overall unremarkable findings: blood cell count 0 WBC, 0 RBC, glucose 52 mg/dL, protein 38 mg/dL, and opening pressure 9 cm H_20. Further workup showed negative HIV screening, malaria testing, and many other negative/ unremarkable results shown in Table 1. He also underwent esophagogastroduodenoscopy that showed duodenum with mild villous blunting with increased lymphoplasmacytic infiltrate within the lamina propria and colonoscopy with no architectural distortion, granulomas, or features of chronicity identified. The lamina propria contained an appropriate amount of eosinophils.

Blood flow cytometry showed small, atypical T cell popu-

Figure 1. Images of (A) Patient's Right Hand and (B) Left Inner Upper Thigh

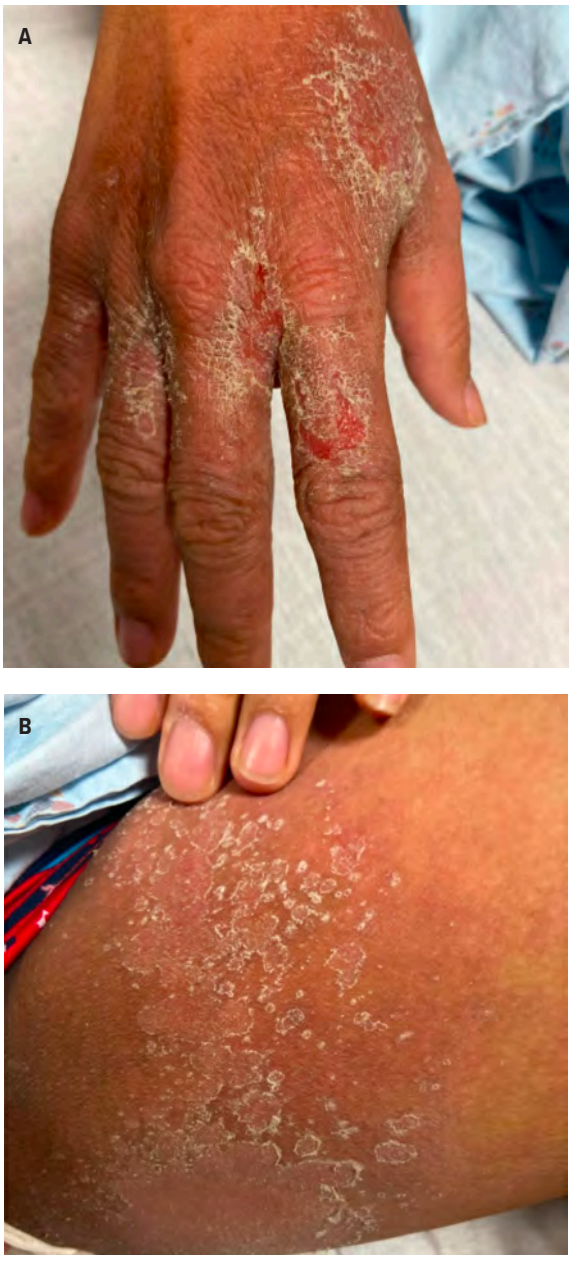

Figure 2. Four-Day-Old Fungal Blood Culture of *Coccidioides* species on Sabouraud Dextrose Agar Showing White Cottony Colonies

Figure 3. Lactophenol Cotton Blue Preparation at 400x Magnification Showing Hyphae of *Coccidioides* Species With Arthroconidia (arrow).

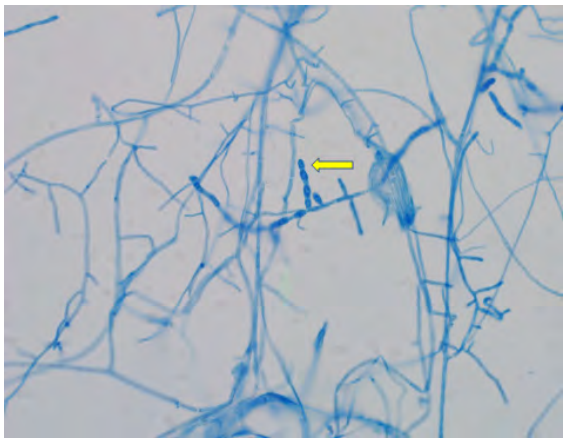

Table 1. Additional Evaluation

Test Name[a]	Hospital Day Resulted
Blood cultures	Day 1 (finalized day 5)
Thyroid stimulating hormone	Day 1
Mononucleosis spot test	Day 1
COVID-19 PCR (nasal swab)	Day 1
Urinalysis (urine)	Day 1
Hepatitis A IgM, Hepatitis C antibody, Hepatitis B core IgM	Day 1
Gastrointestinal pathogen panel by PCR (stool)	Day 2
Legionella pneumophilia serotype 1 antigen (urine)	Day 2
1st malaria thick/thin smear	Day 2
HIV 4th generation screen	Day 2
1st ova and parasite (O and P) (stool)	Day 4
2nd malaria thick/thin smear	Day 4
Toxoplasma IgG/IgM	Day 5
3rd malaria thick/thin smear	Day 5
Repeat blood cultures	Day 5 (finalized Day 10)
Coxiella burnetii IgG	Day 6
Interferon gamma release assay for *Mycobacterium tuberculosis*	Day 6
Echinococcus IgG/IgM	Day 7
Leptospira IgM by dot blot	Day 7
Cryptococcus antigen	Day 7
Bartonella quintana/henselae IgG/IgM	Day 7
Plasmodium species PCR	Day 7
Antinuclear antibodies	Day 7
Brucella IgG/IgM	Day 8
Celiac panel	Day 8
2nd O and P (stool)	Day 8
Meningitis/encephalitis PCR panel[b] (CSF)	Day 8
3rd O and P (stool)	Day 11
Francisella tularensis IgG/IgM	Day 11
Antineutrophil cytoplasmic antibodies	Day 11
Tropheryma whippleii PCR	Day 12
Trichinella IgG	Day 14

Abbreviations: PCR, polymerase chain reaction; Ig, immunoglobulin; CSF, cerebrospinal fluid.
[a]All studies performed on blood/serum unless otherwise indicated
[b]Cerebrospinal fluid culture, fungal culture, and mycobacterial culture all without growth.

lation, left-shifted myeloid maturation pattern and increased eosinophils. IgE was elevated at 9300 IU/ml (range 0-158 IU/ml), normal IgG subclasses, positive cytomegalovirus IgG, serologies consistent with prior Epstein-Barr virus infection. *Coccidioides* IgG was positive at 10.7 (positive >1.4) by enzyme-linked immunosorbent assay (ELISA), IgM was indeterminate at 1 (negative <1; indeterminate 1.0-1.4). With high levels of IgE, positive *Coccidiode*s IgG and *Strongyloides* IgG, albendazole was changed to ivermectin.

By day 9, the patient's fevers decreased, and the leukocytosis and absolute eosinophil counts started to normalize. On day 11, the Sabouraud agar grew white cottony colonies (Figure 2). On the same day, a lactophenol cotton blue wet preparation from these colonies was performed and demonstrated arthroconidia (Figure 3). On day 12, he was initiated on liposomal amphotericin-B 350 mg intravenous every 24 hours. On day 21, identification of *Coccidioides immitis* was confirmed by matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry at a reference lab. Stool ova and parasite exam was negative.

Hence, disseminated *Coccidiodes immitis* infection with fungemia was diagnosed with possible *Strongyloides* species co-infection. The possible *Strongyloides* infection was treated with an 8-day course of ivermectin 200 mcg/kg/day (15,000 mcg/day). After 3 days of amphotericin-B, the patient was discharged home on day 15 on oral fluconazole 800 mg once daily for 3 months. The leukocytosis improved to 14,000 K/µL, with AEC

3.1 K/μL on the day of discharge. At the end of treatment, his WBC and eosinophil counts normalized.

DISCUSSION

Fungemia is a rare manifestation of disseminated coccidioidomycosis with a very poor prognosis.[5,7] Overall mortality at 30 days is 62% (70/113; mean survival, 11.4 days).[3,4,8]

Between 1998 and 2008, there were only 113 reported cases of fungemia with *Coccidiodes* species. Forty-three patients (38%) were living with HIV, 20 (18%) were on corticosteroids, 11 (10%) were solid organ transplant recipients, and 5 (4%) were pregnant. Sites of extrapulmonary dissemination were reported for 97 patients (86%), with the most common sites being the liver (26/97 [27%]), spleen (21/97 [22%]), and meninges/central nervous system (17/97 [18%]). The 113 cases thoroughly reviewed by Keckich et al[8] included those by Ampel et al[5] and Rempe et al.[7] Since then, there have been only a handful of other case reports of *Coccidiodies* species fungemia (Table 2).[9-11] Fungemia is rare and even moreso in patients considered immunocompetent.

Table 2. Review of *Coccidiodies* Species Fungemia

Author/Year	No. of Patients	Average Age (Years)	Male Sex (%)	Immunosuppression (% of Total)
Ampel et al, 1986[5]	15	47	93	Cancer (40%), HIV (20%); CS use (66%)
Rempe et al, 2007[7]	33	37	94	HIV (87%)
Keckich et al, 2010[8]	113[a]	42	80	HIV (38%), CS use (18%), SOT (10%)
Blodget et al, 2012[9]	3	43	100	SOT (100%)
Langelier et al, 2014[10]	1	54	100	N/A (immunocompetent)
Valdez et al, 2019[11]	1	33	100	HIV (100%)

Abbreviations CS, corticosteroid; SOT, solid organ transplant; N/A, not applicable.
[a]107 by review + 6 from the single center.

Diagnosis of coccidioidomycosis can be done by histology, cultures, urine, and/or cerebrospinal fluid antigen detection, IgM and IgG detection by enzyme-linked immunosorbent assay (ELISA), immunodiffusion, and complement fixation (CF).[3,12,13] The gold standard diagnosis remains growth in culture.[12] For the mold phase, specimens are cultured on Sabouraud dextrose agar or potato dextrose agar and incubated at 25 °C. Incubation at 37 °C can be attempted to recover the yeast phase of most dimorphic organisms. The immunodiffusion and CF tests remain the most reliable methods for the serologic diagnosis of coccidioidomycosis. A less labor-consuming ELISA immune assay was developed as a screening test after which confirmatory tests are performed.[3,12,13]

Our patient was diagnosed with *Coccidiodes* infection by recovering the fungus from the blood culture in the setting of a compatible clinical presentation and laboratory findings. He did not have a focus of infection per se. However, we did not think he had developed a focal organ disease, as at the end of the treatment his WBC and AEC were normal. While basic testing for immunodeficiency (HIV, flow cytometry, etc) was completed, extensive testing with functional immune assays was not done given his condition improved significantly once appropriate treatment was started.

Strongyloides species co-infection was suspected based on marked eosinophilia; the presence of a pruritic, erythematous cutaneous eruption consistent with those seen in *Strongyloides* infections; and his epidemiologic association with country of origin where the disease remains prevalent. Lab testing noted positive *Strongyloides* IgG indicating either acute or prior infection. Stool ova and parasite exams were negative. It was not known if he had previously been treated for *Strongyloides* in Thailand. He was not in a refugee camp, and we could not know if he was screened and treated prior to admission to the United States. Per the Centers for Disease Control and Prevention, "most refugees receive overseas pre-departure treatment with ivermectin … unless contraindicated [due to] confirmed or suspected concomitant infection with *Loa lo*a … [or] may be presumptively treated on arrival, or screened ("test and treat").[14] As such, the possibility of *Strongyloides* co-infection could not be confirmed or ruled out. Stool nucleic acid amplification test for *Strongyloides* was not performed.

While the patient did have risk factors of being male and of Asian ethnicity and epidemiologic risk factors including living in Arizona and Thailand, our case is a rare presentation of disseminated *Coccidiodes* with fungemia in an otherwise healthy patient without any immunocompromising conditions with possible *Strongyloides* coinfection – the third to be reported.[6]

Treatment of *Coccidiodes* species includes fluconazole, itraconazole, voriconazole, isavuconazole, posaconazole and amphotericin B. Treatment is tailored to the presentation, patient immune status, and extent and/or severity of the disease.[15]

CONCLUSIONS

We report this case to raise awareness of a rare infection. In adequate epidemiological circumstances, co-infections *Coccidioides* and *Strongyloides* species should be considered in presence of fever and very high eosinophil count.

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Leprosy in the Upper Midwest

Kathy Bach, MD; Molly A. Hinshaw, MD; Bridget E. Shields, MD

ABSTRACT

Introduction: Leprosy is a life-threatening infection caused by *Mycobacterium leprae* with an average 5-year long incubation period. It is curable when treated early. Early diagnosis requires knowledge of its myriad clinical features as risk factors may not be readily apparent.

Case Presentation: We report the case of a male patient from Wisconsin who tested positive for leprosy without a known exposure or recent travel to endemic areas.

Discussion: The clinical presentation of leprosy exists on a spectrum and correlates with cell immunity levels. The Ridley-Jopling and World Health Organization classifications are used to define leprosy subtypes and guide treatment. Histopathologic examination may aid in diagnosis of suspicious presentations.

Conclusions: Leprosy may present with nonspecific clinical features and elevated inflammatory markers leading to a misdiagnosis. It should be considered in the differential diagnosis for suspicious presentations and appropriately worked up with various diagnostic modalities. A multidisciplinary approach to treatment may prevent spread and permanent damage.

INTRODUCTION

Leprosy is a curable infectious disease that primarily affects the skin, peripheral nerves, upper respiratory tract, and eyes.[1] Endemic to over 140 countries, leprosy continues to spread through human transmission and travel.[1] In the United States, armadillos also serve as a reservoir for zoonotic transmission.[2-4] However, there have been reports of autochthonous leprosy (human-to-human transmission) in the United States between Americans with no history of foreign exposure.[5] With multiple variables affecting an individual's susceptibility for contracting the disease and a long incubation period of several years, leprosy can be difficult to diagnose in the absence of obvious risk factors for infection and classic clinical features. We present a case to highlight the diagnostic pathway that leads to leprosy in a patient without identifiable risk factors for infection.

CASE PRESENTATION

A Wisconsinite in his 70s was sent to dermatology in consultation for presumed connective tissue disease in the setting of a 3-month history of asymptomatic plaques and nodules on the trunk and extremities, an elevated rheumatoid factor (19), and antinuclear antibody (1:320). The lesions began on his arms and spread to involve his chest, abdomen, and back. He noted concomitant edema of the hands, feet, and lower legs; fatigue; arthralgias; nasal congestion; epistaxis; decreased visual acuity; increased cold sensitivity; anorexia; and acute onset left foot drop. Treatment with compression stockings, hydrochlorothiazide, and diclofenac sodium 1% cream had been ineffective.

Physical examination revealed numerous pink to violaceous indurated plaques without ulceration on the upper arms, chest, abdomen, flanks, and back (Figure 1). Punch biopsies of the right upper arm and left flank revealed a dermal and focally subcutaneous infiltrate of histiocytes arranged in multinucleate collections and sheets with minimal associated lymphocytic inflammation (Figure 2). Within histiocyte cytoplasms were innumerable acid-fast bacilli- and Fite-positive organisms diagnostic of an atypical mycobacterial infection (Figure 3). In context of the clinical presentation, tissue was sent for nontuberculous myco-

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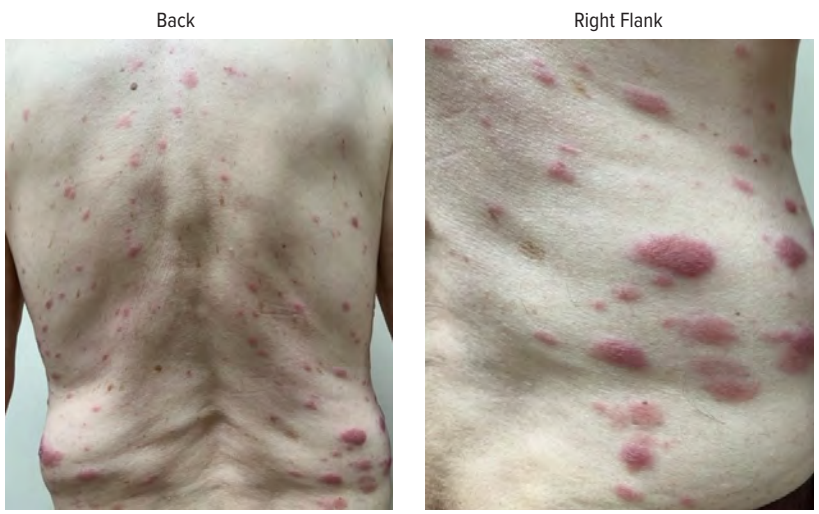
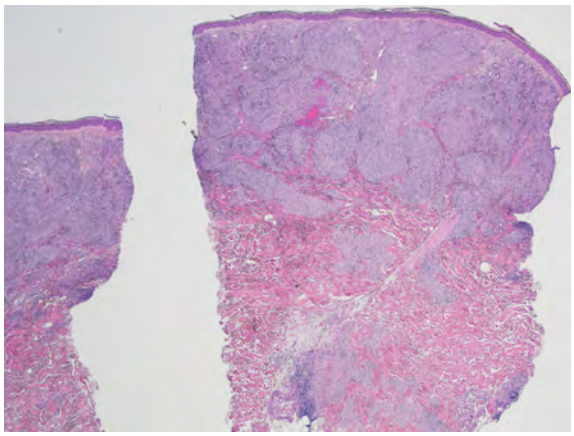
Figure 1. Skin Lesions

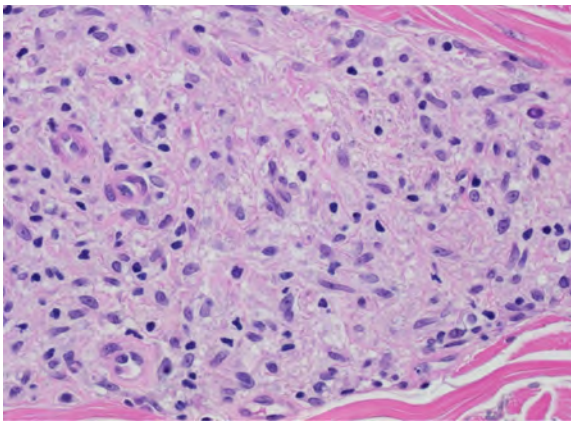


Numerous pink to violaceous indurated plaques without ulceration on the back and flanks.

Figure 2. Dermatopathology



x20 hematoxylin and eosin stain



x400 hematoxylin and eosin stain

Throughout the dermis is a nodular, vaguely linear, and sheet-like infiltrate of histiocytes forming multinucleated collections with minimal associated lymphocytic inflammation.

bacterial testing by polymerase chain reaction (PCR), and *Mycobacterium leprae (M leprae)* was detected using 16s and rpoB primer sets. These combined clinical and pathologic features correspond to the diagnosis of borderline lepromatous leprosy. Recommendations were given by the National Hansen's Disease Program (NHDP) to initiate prednisone, methotrexate, folic acid, vitamin D, rifampin, moxifloxacin, and minocycline.

On further history taking, the patient denied a history of immunodeficiency, prior unusual infections, or known exposure to leprosy. He denied pet or animal exposures, including to armadillos. He had an extensive travel history over the preceding 20 years, including to Central America, Caribbean islands, South America, the Mediterranean, and Eastern Europe. His travel in the southern United States included the Carolinas and New Orleans within the last 5 years.

The source of our patient's *M leprae* is unclear, but he is improving slowly with treatment co-managed by dermatology and infectious disease.

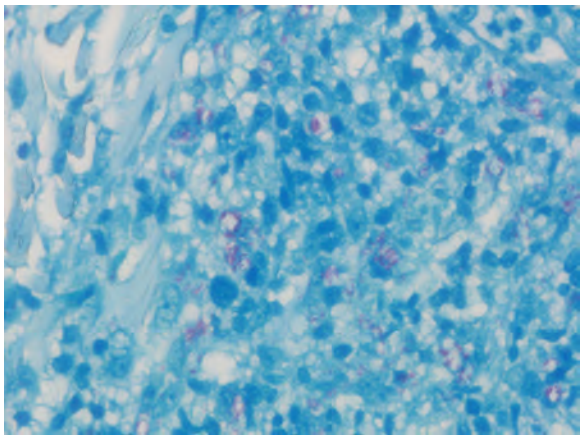
DISCUSSION

The highest incidence of leprosy in 2016 was recorded in Southeast Asia at 75% of the global total; however, the Americas recorded a significant 15% of the global total.[1] In 2020, there were 159 new cases of leprosy reported in the United States.[6] Most cases in the United States occur in Arkansas, California, Florida, Hawaii, Louisiana, and New York.[1]

M leprae is an obligate intracellular organism with low pathogenicity that requires a genetically or immunologically susceptible host to have prolonged contact with an untreated carrier of leprosy, especially with multibacillary lepromatous leprosy.[1] Risk factors for infection include armadillo exposure and ages 5 to 15 years or over 30 years at time of exposure.[1] An average incubation period of 5 years makes it difficult to find the source of infection. The skin, peripheral nerves, upper respiratory tract, and eyes are most affected. The Ridley-Jopling and World Health Organization (WHO) classifications are used to define leprosy subtypes and guide treatment.[1]

Clinical presentation exists on a spectrum – when cell-mediated immunity is high, tuberculoid leprosy exhibits one to a few well-defined, anesthetic, paucibacillary plaques. When cell-mediated immunity is low, lepromatous leprosy exhibits innumerable infiltrative, multibacillary papules and nodules. Borderline tuberculoid leprosy presents clinically as a few, less-defined anesthetic macules and plaques, while borderline lepromatous leprosy presents clini-

Figure 3. Fite Stain, x600



Special staining, with appropriate controls, shows innumerable Fite-positive acid-fast bacilli.

cally as numerous macules, plaques, and nodules with sensation mostly intact.[1] Accompanying features may include painless ulcerations, madarosis, and early nerve damage.[1]

Immunologic reactions may occur at any time during the disease course regardless of multidrug therapy and include reversal reaction (type 1), erythema nodosum leprosum (ENL) (type 2), and Lucio phenomenon.[7] Reversal reactions may cause significant nerve damage, ENL may cause inflammation to multiple organ systems, and Lucio phenomenon may cause necrotic ulcers.[7] Between 30% and 50% of patients with leprosy develop immunologic reactions, most commonly in patients with lepromatous and borderline subtypes.[8] As these are the most common subtypes occurring in the United States, it is important to identify these reactions early and to treat emergently to prevent further morbidity.[8]

Our patient's presentation emphasizes that leprosy may present with nonspecific findings of elevated inflammatory markers and with features suggesting a rheumatologic disorder. The diagnosis of leprosy relies on exposure identification, travel history, and clinical features, including anesthetic, hypopigmented skin lesions and motor neuropathy.[1] Our patient did not have a recent travel history, which emphasizes the indolent nature of this infection. It is important to include leprosy in the differential diagnosis when one or more of these risk factors and findings are noted.

Skin biopsy in leprosy is a readily accessible piece of diagnostic information that should be utilized when this infection is suspected. Histopathologic examination and PCR testing are the most used diagnostic modalities in the United States.[9] While expensive and labor-intensive in most endemic countries, PCR is free of charge at the NHDP and, therefore, commonly used in the United States to support a leprosy diagnosis. Treatment with multidrug therapy is subtype dependent, and the WHO and the NHDP provide separate recommendations on specific antibiotics and treatment durations.[1,3,8,9]

CONCLUSIONS

Cases of leprosy in developed countries remain low but still persist, including in the United States. We present this case of leprosy in a Wisconsinite with remote history of risk factors to highlight the key clinical, histologic, current molecular, and therapeutic features of this rare but life-threatening infection to aid clinicians and patients in its early diagnosis.

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Ocular Findings Aid in Diagnosis of West Nile Virus

Brandon K. Winward, MD; Justin L. Gottlieb, MD; Jonathan S. Chang, MD; E. Luke Bradbury, MD; Nenita Maganti, MD; Chintan Pathak, MD; Benjamin J. Fowler, MD, PhD

ABSTRACT

Introduction: West Nile virus disease, which is endemic to the United States, is a rarely reported systemic infection that can be difficult to diagnose. Chorioretinitis is an uncommon manifestation of West Nile virus but has pathognomonic ocular findings that can aid in diagnosis.

Case Presentation: A 69-year-old man presented with acute onset fever, chills, and dyspnea. He underwent an extensive but nondiagnostic workup during hospitalization. New visual complaints prompted ophthalmology consultation. Funduscopic examination showed macular hemorrhages and midperipheral chorioretinal lesions. Fluorescein angiography revealed target-like lesions in a radial distribution, which is pathognomonic for West Nile virus chorioretinitis. Serology confirmed the diagnosis of West Nile virus disease. Systemic and ocular symptoms improved with supportive care.

Discussion: West Nile virus disease has many nonspecific manifestations. History of recent mosquito exposure is not always readily elicited. In patients with visual symptoms, eye examination can help in its diagnosis.

Conclusions: West Nile virus should be considered in patients with acute febrile or neurological illness during mosquito season.

INTRODUCTION

West Nile virus (WNV), originally isolated in 1937 in Uganda, is a zoonotic pathogen within the *Flaviviridae* family that is transmitted to humans from infected wild birds via mosquito vectors.[1-3] Since WNV first appeared in the United States in 1999, the Centers for Disease Control and Prevention (CDC) has documented approximately 55,000 human cases throughout all 50 states.[3] WNV is considered endemic to the United States.[2,3] While periodic outbreaks can occur, human incidence is low in many areas. In Wisconsin, from 2016 through 2020, an average of only 21 human cases were reported each year.[4]

Approximately 80% of persons infected with WNV are asymptomatic.[3] Fever, headache, weakness, myalgia, and gastrointestinal upset are common though nonspecific symptoms.[2,3,5] The incubation period for WNV disease can be up to 14 days in immunocompetent patients and longer in immunocompromised hosts,[3] making the diagnosis difficult when a history of recent vector exposure is not readily available. Severe headache, neck stiffness, altered mental status, convulsions, paralysis, and vision loss may indicate neuroinvasive disease.[3] Chorioretinitis is the most common manifestation of ocular WNV infection and has been found in over 85% of cases with ocular involvement. The chorioretinitis is pathognomonic and evident on funduscopic examination and ancillary ocular imaging, particularly fluorescein angiography.[2,6-10]

We highlight a case of WNV disease in Wisconsin that presented with nonspecific symptoms. A history of mosquito exposure was not elicited initially. The patient underwent an extensive laboratory and imaging workup. Diagnosis was delayed until symptoms of chorioretinitis developed and prompted ophthalmic investigation, including fluorescein angiography. Understanding the risk factors, manifestations, and seasonal presence of WNV within the region can lead to more timely and cost-efficient diagnosis.

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CASE PRESENTATION

A 69-year-old man with past medical history of hypertension, cerebral vascular accident, dysphagia, urinary incontinence, major depressive disorder, and lumbar stenosis presented to the emergency department (ED) in September, 2021, with 1 day of progressive fever, chills, and dyspnea. Emergency medical services were called as the chills progressed to rigors. In the ED, he was febrile (103.1 ºF), tachycardic (120 beats/min), and hypoxemic (requiring 2L of supplemental oxygen via nasal cannula to maintain normal oxygen saturation). He was consistently normotensive. Basic metabolic panel, complete blood cell count, and urinalysis were unremarkable. Influenza and COVID-19 assays were negative. Chest radiograph showed opacities in the right lower lobe. Intravenous ceftriaxone and azithromycin were started, and the patient was admitted for presumed community-acquired pneumonia.

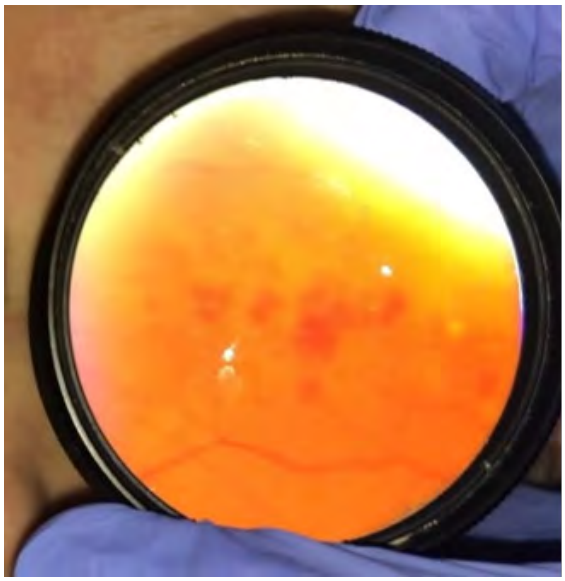
The patient received acetaminophen for intermittent fevers. His hypoxemia and fever slowly improved. Blood cultures drawn earlier in the ED resulted negative. The antibiotic regimen was transitioned to oral amoxicillin/clavulanate. He was discharged after hospital day 3 following a 24-hour period without fever or supplemental oxygen requirement.

The patient returned to the ED 3 days later with recurrent fever, chills, dyspnea, frontal headache, mild abdominal pain, and diarrhea. He confirmed adherence to his outpatient antibiotic regimen. He was febrile (102.7 °F) and hypertensive (174/92 mm Hg) upon arrival and soon became hypoxemic, requiring 1 liter of supplemental oxygen via nasal cannula. His pulse was 90 beats per minute. Intravenous isotonic fluids, vancomycin, and cefepime were administered. He was admitted to the hospital under the working diagnosis of acute hypoxic respiratory failure due to community-acquired pneumonia, presumably refractory to outpatient antibiotics.

Complete blood cell count with differential showed a white blood cell count of 11,700 cells/microliter with 81% neutrophils. Peripheral blood smear showed 20% to 40% band cells. Additional laboratory workup, including comprehensive metabolic panel, urinalysis, bacterial and fungal blood cultures, cardiac troponins, erythrocyte sedimentation rate, procalcitonin, thyroid stimulating hormone, respiratory viral panel, *Legionella* urine antigen, *Streptococcus pneumoniae* urine antigen, and *Bordetella* species and common allergens, was unremarkable. Repeat chest radiograph showed largely unchanged opacities of the right lower lung fields. Computed tomography (CT) of the abdomen and pelvis was normal.

During admission, persistent headache and language fluency difficulties were noted. Neurological examination and CT of the head were normal. The neurology consult service recommended magnetic resonance imaging and angiography of the head and neck, which likewise showed no abnormalities. Headache and speech difficulties were consequently attributed to recrudescence of prior ischemic medullary stroke in the context of acute illness. The patient did not undergo a lumbar puncture.

Figure 1. Funduscopy

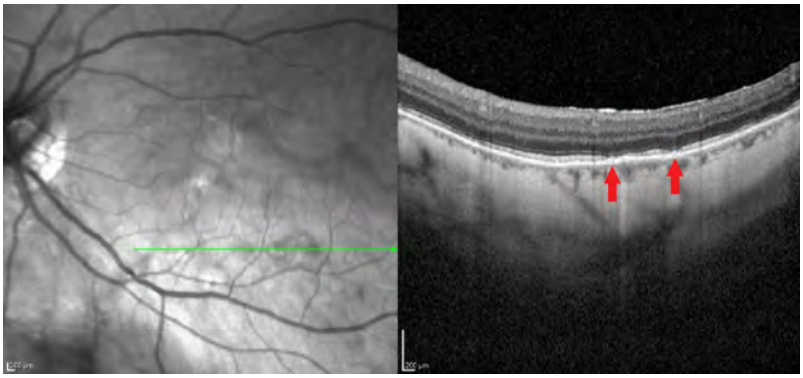


Retinal hemorrhages in the macula of the left eye visualized through a 20-diopter handheld lens at the patient bedside.

On the 10th day of hospitalization, the ophthalmology service was consulted for new onset blurry vision and floaters in the patient's left eye. Pupils were equal, round, and reactive, without afferent pupillary defect. Best-corrected visual acuity (BCVA) was 20/30 and 20/70 in the right and left eye, respectively. Intraocular pressure was within normal limits in both eyes. Slit lamp biomicroscopy revealed early nuclear sclerotic cataracts in both eyes and mild vitreous haze in the left eye only. Dilated fundus exam of the right eye at presentation was normal; the left eye had retinal hemorrhages in the macula (Figure 1) and peripheral round chorioretinal lesions.

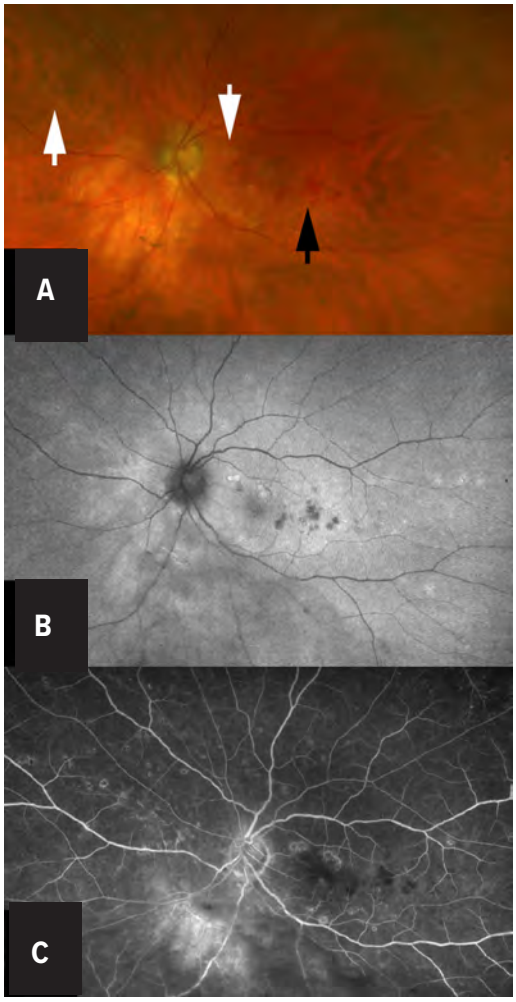
The patient's respiratory status improved, and he was discharged to a skilled nursing facility on the 14th day of hospitalization with same-day outpatient ophthalmology follow-up and multimodal ophthalmic imaging. Optical coherence tomography showed a few foci of outer retinal disruption in the macula of the left eye (Figure 2). Fundus photography and autofluorescence imaging revealed resolving macular hemorrhages and numerous round chorioretinal lesions (Figure 3A-B). Fluorescein angiography of the left eye highlighted many circular lesions with target-like rings of hyperfluorescence in a radial distribution (Figure 3C), which is pathognomonic for WNV chorioretinitis. Additional history revealed that the patient was an avid photographer and frequently exposed to mosquitos in forested areas at dusk. He was started on a 3-week taper of ophthalmic predniso-

Figure 2. Optical Coherence Tomography



Outer retinal disruption (red arrows) in the macula of the left eye.

Figure 3. Multimodal Fundus Imaging



A. Fundus photography of the left eye showing macular hemorrhages (black arrow) and scattered chorioretinal lesions (white arrows). B. Fundus autofluorescence of the left eye showing circular hyper-autofluorescent chorioretinal lesions. C. Fluorescein angiography of the left eye showing numerous target-like lesions with hyperfluorescent rings, radiating in a curvilinear pattern from the optic disc and throughout the fundus.

lone acetate in the left eye, and confirmatory serum studies were ordered. The index value for WNV-specific immunoglobulin G and M resulted 2.81 (normal <1.29) and 5.25 (normal <0.89), respectively. Supportive care was recommended for his systemic manifestations of WNV disease.

Six weeks later, the patient's systemic symptoms had resolved. BCVA improved to his baseline (20/30). The vitreous haze and macular hemorrhages resolved. Chorioretinal scarring was appreciated in areas of prior macular hemorrhage, and peripheral chorioretinal lesions had significantly faded. At 4-month follow-up, his ocular condition was stable.

DISCUSSION

WNV diagnoses occur in areas of increased mosquito activity. In Wisconsin, WNV cases typically occur between June and October, with a peak in cases in August.[4] WNV is the most common epidemic viral encephalitis in the United States;[11] clinicians should be aware of WNV disease, especially given the at-risk aging population and increased numbers of immunocompromised individuals in the United States. Moreover, the seasonal duration and burden of WNV is predicted to increase with rising global temperatures.[12] Acute WNV disease has a wide range of nonspecific manifestations;[1,3,5,6,13] it can be difficult to diagnose, and patients may undergo extensive workup before WNV is considered.[2] History of recent mosquito exposure is not always available and, as in our case, might be gathered only after a diagnosis is made from objective findings.[2,14]

Ocular symptoms are uncommon with WNV infection.[2,6,7,9,10,13,15,16] Risk factors for ocular involvement include advanced age, immunosuppression, male sex, and diabetes.[2,9] Ocular involvement of WNV may be asymptomatic or present with symptoms of decreased vision, floaters, photophobia, retrobulbar pain, or diplopia.[2,6,7,9,10,13,16] Ocular manifestations of WNV include chorioretinitis, vitritis, retinal vasculitis, optic neuritis, and nystagmus.[7,9] Table 1 summarizes a literature review of the reported ocular manifestations of WNV disease; chorioretinitis is the most common.[2,9] In a cohort study of 111 patients with a history of WNV infection, 24% of patients had chorioretinal scars; if the patient had encephalitis, the prevalence of chorioretinal lesions was 49%.[15]

Chorioretinal lesions in acute WNV chorioretinitis are classically described as deep, round, cream-colored lesions.[2,6,8-10] Fluorescein angiography usually shows pathognomonic "target-like" lesions (central hypofluorescence with a hyperfluorescent rim) radiating from the optic disc in a curvilinear fashion.[2,6,8,9] It is

Table. Reported Ocular Manifestations of West Nile Virus Disease

Reference/Description	Reported Ocular Manifestation of West Nile Virus Disease							
	Sample Size	Multifocal Linear Chorioretinal Lesions	Vitritis (%)	Optic Disc Edema or Pallor (%)	Intraretinal Hemorrhages (%) [a]	Retinal Vasculitis (%)	Retinal Occlusive Vasculitis (%)	Misc (%)
Cross-sectional study of patients w history of WNV infection who underwent dilated fundus exam[15]	111 patients	27 (24%))	N/A	N/A	N/A	N/A	N/A	
Clinic patients w/ocular inflammation and fever who tested positive for WNV[17] [b]	51 eyes (37 patients)	7 eyes (14%)	37 eyes (73%)	7 eyes (14%)	22 eyes (43%)	Arteritis: 18 eyes (35%) Phlebitis: 15 eyes (29%)	8 eyes (16%)	
Patients hospitalized w/ WNV disease and ocular symptoms[18] [b]	27 patients	0	0	11 (41%)	N/A	9 (33%)	2 (7%)	Peripapillary retinitis: 6 patients (22%)
Patients w/ WNV disease and neurological symptoms[19]	29 patients	23 (79%)	23 (79%)	2 (7%)	21 (72%)	9 (31%)	N/A	Sixth nerve palsy: 1 patient, Nystagmus: 1 patient
Retrospective chart review of patients w/ ocular WNV[7]	14 eyes (7 patients)	12 eyes (86%)	6 eyes (43%)	6 eyes 43%)	7 eyes (50%)	4 eyes (29%)	2 eyes (14%)	Sixth nerve palsy: 1 patient
Case series of patients w/ WNV chorioretinitis[2]	3 patients	3 (100%)	3 (100%)	0	1 (33%)	0	0	

Abbreviation: N/A, not available; WNV, West Nile virus.

[a] Some of the intraretinal hemorrhages may represent diabetic retinopathy.

[b] There may be some shared patients between these studies, which overlap in time at the same eye institute.

Data were obtained from a literature review of ocular manifestations of patients with serology/polymerase chain reaction-confirmed West Nile virus disease. Only case series with 3 or more patients were included. Search criteria included multiple PubMed searches using the keywords "West Nile virus," "ocular," "eye," "ocular manifestation," "WNV," and "chorioretinitis." If both eyes were affected, ocular manifestations are reported as positive if either eye had the manifestation. In some studies, only the number of eyes was available, which is noted above.

thought that the curvilinear distribution of retinal lesions is related to the contiguous spread of virus from the central nervous system to the retina along nerve fiber layers, although there also might be hematogenous spread through the choroidal circulation.[2] Fundus autofluorescence and indocyanine green angiography – additional ancillary tests commonly ordered in the evaluation of chorioretinitis – also highlight this characteristic finding and help differentiate WNV from other forms of chorioretinitis.[8,9] Optical coherence tomography may reveal multifocal disruption of the outer retina.[2,8] Our patient manifested these classic ocular findings (Figures 1-3).

When systemic manifestations are also present, a laboratory diagnosis of WNV disease is often made prior to the diagnosis of WNV chorioretinitis.[2,6,8-10,14] In one such case when serologies for WNV were positive but there was insufficient volume of cerebrospinal fluid (CSF) for WNV testing, the presence of chorioretinitis was interpreted as an indication of neuroinvasive disease.[6] However, in our case and a case described by Learned et al in 2014,[2] the diagnosis of WNV infection was primarily driven by ocular findings. Still, serum antibody testing (and CSF analysis when there is suspicion for neuroinvasive disease) is the recommended initial procedure when considering a diagnosis of WNV disease. In our patient, chorioretinitis and mental status changes were suggestive of central nervous system involvement, although he did not have more worrisome signs of neuroinvasive disease, such as ventral spinal root involvement, which can cause flaccid paralysis. It is possible that the lack of serious neurologic symptoms and prior diagnosis of community-acquired pneumonia before the onset of ocular symptoms delayed a workup for WNV, which is often a component of encephalitis viral panels. Nevertheless, regardless of severity of WNV infection, treatment is largely supportive.

WNV infection is reportable to local and national public health services in the United States;[3] in Wisconsin, these services are the Wisconsin Department of Health Services and the CDC. Various medications and vaccines have been evaluated in clinical studies for use in preventing or treating WNV, but none have shown substantial clinical benefit in humans.[3,9] Supportive therapy is the only recommended treatment for WNV disease.[3,9] Community-level mosquito control programs and personal protective wear are effective preventive measures.[3]

Ocular disease typically is self-limited, but topical steroids and cycloplegics can be given for inflammation and pain.[2,9] We prescribed a short course of tapered topical steroids in this case. Persistent visual loss, though rare, may occur in instances of retinal

scarring, choroidal neovascularization, nonclearing vitreous hemorrhage, and macular edema.[7,9,16]

CONCLUSIONS

Acute WNV disease can be difficult to diagnose but should be considered, in addition to other arboviruses, in patients with an acute febrile or neurological illness. Common symptoms include headache, myalgia, arthralgia, gastrointestinal distress, and transient maculopapular rash.[3] Eliciting a history of mosquito exposure can be helpful in making the diagnosis, keeping in mind the incubation period is typically 2 to 6 days but can be longer.[3] Laboratory serology testing is recommended when there is suspicion for WNV disease. Ophthalmology consultation may be useful in the diagnosis and reporting of WNV disease in patients with ocular symptoms

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An Unlikely Guest With an Overstayed Welcome: *Cyclospora*-Induced Postinfectious Irritable Bowel Syndrome

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ABSTRACT

Introduction: Postinfectious irritable bowel syndrome is a phenomenon that can occur following bouts of acute gastroenteritis. While bacterial pathogens are typically implicated in the development of postinfectious irritable bowel syndrome, viral and parasitic infections should also be considered as inciting pathogens.

Case Presentation: An immunocompetent, 65-year-old woman presented with several weeks of watery diarrhea, which polymerase chain reaction testing confirmed to be a *Cyclospora* infection. Resolution of diarrhea was achieved with antibiotic treatment, however, months later she presented to the gastroenterology service with persistence of loose stools and abdominal cramping consistent with a diagnosis of postinfectious irritable bowel syndrome.

Discussion: Postinfectious irritable bowel syndrome has a similar presentation to sporadic irritable bowel syndrome, with diagnosis aided by the identification of an inciting pathogen. To our knowledge, this is the first documented case of *Cyclospora*-induced postinfectious irritable bowel syndrome. While parasitic infections typically are not implicated in cases of postinfectious irritable bowel syndrome, this case highlights the value of considering this condition as a cause of protracted diarrhea in patients previously diagnosed with *Cyclospora*.

INTRODUCTION

Some patients may experience symptoms of irritable bowel syndrome (IBS) following an exposure to acute gastroenteritis. This phenomenon, known as postinfectious IBS (PI-IBS), is the persistence of diarrhea, abdominal discomfort, and bloating that can continue despite clearance of the inciting pathogen.[1] Risk factors for development of PI-IBS can include severity of enteric infection, host immunity factors, and identity of the infectious pathogen.[2] PI-IBS typically is associated with bacterial pathogens, with other studies showing a possible pathogenetic link between IBS and parasites.[2,3] However, there are no documented cases of *Cyclospora*-induced PI-IBS.[2,3]

CASE PRESENTATION

A 65-year-old woman with a history of fatty liver and Gilbert syndrome presented with 3 weeks of persistent, nonbloody, nonmucoid diarrhea. She denied recent travel, sick contacts, or changes in eating habits prior to the onset of her symptoms. Her illness began with a subjective fever followed by watery diarrhea, which prompted her to seek treatment twice in the emergency department. Workup at these encounters included testing for *Clostridium difficile*, SARS-CoV-2, and stool cultures, which were all negative. Computed tomography of the abdomen was also unremarkable. Symptomatic management with hydration and antidiarrheal medication was recommended before she was sent home.

Conservative treatments were ineffective, and the patient was admitted to the hospital with ongoing diarrhea 11 days after the initial onset of symptoms. Her vital signs were stable, physical exam was pertinent for diffuse abdominal tenderness, and her complete blood cell count did not show leukocytosis. Gastroenterology service was consulted and recommended repeat stool culture, fecal leukocytes, ova and parasites, *Clostridioides difficile* testing, fecal elastase, calprotectin, and celiac antibody testing, which were all negative. A colonoscopy was performed with no acute findings. She was discharged 5 days later on ciprofloxacin, which she discontinued due to myalgias.

Four days later, the patient was readmitted to the hospital with persistence of symptoms. The infectious disease service was con-

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sulted, and it was discovered she had eaten a bag of lettuce prior to the onset of her diarrhea, raising suspicion for *Cyclospora* infection. An acid-fast smear for *Cyclospora* was negative. Additional testing for HIV, norovirus, rotavirus, cryptosporidium, and giardia were negative. The clinical suspicion for *Cyclospora* remained high, so polymerase chain reaction (PCR) testing was sent out and she was started on trimethoprim-sulfamethoxazole empirically while results were pending. PCR testing confirmed *Cyclospora*. Given that her diarrhea had improved by the time she was discharged, it is highly unlikely that the PCR was falsely positive.[4]

During a virtual visit with gastroenterology 2 months later, the patient complained of an increase in the number of her daily bowel movements and reported that they were associated with abdominal cramping. The cramping was thought to be due to adhesions from a prior hysterectomy, so she was recommended a high-fiber diet and to follow up if symptoms persisted. Nearly 6 months later at a follow-up visit with gastroenterology, she reported ongoing soft stools, a frequent urge to defecate, and lower abdominal cramping sensations consistent with IBS. She was considered to have PI-IBS due to her *Cyclospora* infection and prescribed methyl cellulose for symptomatic management.

DISCUSSION

Here we present a rare case of *Cyclospora*-induced PI-IBS in an immunocompetent host. The mechanisms of development of PI-IBS are thought to be multifactorial, although they are not fully understood. It is proposed that due to persistent subclinical inflammation from an infectious pathogen, alterations take place in intestinal permeability and gut flora.[1] Some studies also have indicated a possible genetic susceptibility, which causes decreased epithelial and mucosal barrier function exacerbated by acute bouts of gastroenteritis.[1] Incidence and prevalence of PI-IBS can be variable, with global numbers ranging from 5% to 32%, and no apparent endemic geographic or environmental predispositions.[1] Similar to cases of sporadic IBS, there appears to be a higher risk of developing PI-IBS in females than males.[1] The proposed explanation for a higher incidence of PI-IBS in females could be due to higher rates of psychological distress, as preexisting psychiatric diagnoses have been implicated as risk factors for PI-IBS. The severity of initial infection and duration of diarrhea also can be risk factors for the development and severity of PI-IBS.[1] Additional symptoms, such as abdominal cramping, bloody stools, and weight loss from the inciting gastroenteritis, can indicate higher risk for developing PI-IBS. There is limited evidence to link the severity of PI-IBS with the identity of infectious pathogens; however, bacteria remain the most common inciting factor.[2]

The diagnosis of PI-IBS remains a diagnosis of exclusion. As evidenced by our patient, the diagnosis can be aided by a clear onset of symptoms combined with positive identification of an infectious pathogen.[1] Diarrhea remains the predominant symptom in cases of PI-IBS. However, such as in this case, PI-IBS also can include abdominal discomfort and bloating. PI-IBS typically has a favorable prognosis, with resolution of symptoms occurring in up to 50% of patients at the 5- to 6-year mark after acute gastroenteritis.

Treatment of PI-IBS is similar to treatment of sporadic IBS, which typically is centered around nonspecific alleviation of symptoms.[1] Supplements, such as probiotics that have been shown to be effective in treating acute gastroenteritis, may be indicated, but no specific interventions for modulating gut flora have been studied for PI-IBS. Treatment with antimicrobials can be indicated when infectious pathogens have been identified.[1] Literature is limited regarding the incidence of viral and parasitic causes of PI-IBS, and there appears to be no documented cases of *Cyclospora*-induced PI-IBS.[2]

Cyclospora cayetanensis is a protozoan responsible for the diarrheal illness cyclosporiasis.[5] *Cyclospora* infection is usually self-limited in immunocompetent hosts, but it can be more severe in immunocompromised patients.[5] The presentation of illness is typically large-volume watery diarrhea with a variable duration. Additional presenting symptoms can include anorexia, nausea, flatulence, low-grade fever, and weight loss.[6] Less common complications of *Cyclospora* infection include cardiac arrest,[7] biliary disease and acalculous cholecystitis in AIDS patients,[8-10] Guillain-Barré syndrome,[11] and reactive arthritis syndrome.[12] Treatment usually consists of a 7- to 10-day course of trimethoprim-sulfamethoxazole, with longer treatments required in the setting of immunosuppression.[5]

Clinicians should have a higher clinical suspicion for *Cyclospora* infection in patients who have recently visited tropical and subtropical areas.[13] Most outbreaks of *Cyclospora cayetanensis* in nonendemic areas can be traced to consumption of contaminated produce, which is what appears to have occurred in this case.[5] Since oocysts that are shed in the feces of infected humans sporulate outside their host, direct person-to-person transmission is rare.[13] Diagnostic testing for *Cyclospora* is not routinely performed in the US and is not commonly included in PCR panels.[13] Patients also can shed an insufficient amount of oocysts in stool even when symptomatic, further making diagnosis more difficult.[13] When there is a high suspicion for *Cyclospora*, patients can be asked to provide multiple samples collected on different days to ensure adequate sampling.[13] When a diagnosis is confirmed, clinicians should be aware of their local guidelines for reporting purposes. The state of Wisconsin lists cyclosporiasis as a category 2 reportable communicable disease that requires reporting in writing within 72 hours upon recognition of a case or suspected case.[14] In some instances, clinicians also can enlist the help of infection preventionists to obtain the relevant history and information to prevent additional infections.

CONCLUSIONS

Here we present a rare and, to our knowledge, the first documented case of *Cyclospora*-induced PI-IBS. This case highlights the value of maintaining clinical suspicion for PI-IBS as a potential cause for protracted diarrhea. While bacterial infection is commonly considered to be the inciting factor for PI-IBS, viral and parasitic cases should also remain on the list of differential diagnoses. When clinical presentation is typical, such as in this case, *Cyclospora cayetanensis* can be considered as a potential cause of parasitic infection in patients with PI-IBS.

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Imagining Eco-Wellness: A Scoping Review of Interventions Aimed at Changing Individual Behaviors to Promote Personal Health and Environmental Sustainability

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ABSTRACT

Introduction: Climate change poses enormous threats to humanity and much of life on earth. Many of the behavioral patterns that drive climate change also contribute to the epidemics of obesity, diabetes, and cardiovascular disease.

Objectives: The primary objective of this study was to compile and categorize the literature on interventions aimed at modifying individual behaviors to promote both personal health and environmental sustainability. Secondary objectives were to help define the emerging field of behavioral eco-wellness and to discuss future directions, including the need for assessment tools and analytic strategies.

Methods: A scoping review was conducted to locate, categorize, and interpret current scientific studies of interventions aimed at changing individual behaviors to promote both personal health and environmental sustainability.

Results: Other than a pilot study that this team previously conducted, nothing was found that strictly fit the inclusion criteria. However, we did find 16 relevant studies that fit neatly within 4 broad topical areas: dietary intake, active transportation, indoor air quality, and green space immersion.

Discussion: While this systematic scoping review found little meeting original criteria, we did find that 4 separate fields of study are converging on a scientific area that we are calling behavioral eco-wellness, defined as the simultaneous pursuit of both personal health and environmental sustainability. The emerging field could provide a conceptual framework and methodological toolkit for those seeking to enhance sustainability while supporting health behaviors, including dietary intake. This, in turn, could help to inform and motivate the urgent action needed to confront both climate change and the epidemics of obesity, diabetes, metabolic syndrome, and cardiovascular disease.

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INTRODUCTION

Agencies, governments, organizations, and experts across the world have highlighted the potential devastation of climate instability and the urgency of actions needed.[1] Many individuals and groups are engaged in researching policies, technologies, and interventions to reduce greenhouse gas emissions to mitigate the magnitude of and destructive effects of climate change. Most climate action recommendations are rooted in science from studies analyzing the large-scale impact of technologies, policies, or lifestyle changes. However, little is known about interventions designed to help individuals modify their behaviors to reduce their carbon footprint.

While the climate crisis has been declared the largest single threat to global health in the foreseeable future,[2-4] the epidemics of obesity, diabetes, metabolic syndrome, and cardiovascular disease also are jeopardizing the health of countless people across the globe. A number of authors have noted that many of the same behaviors that reduce carbon footprint also help ameliorate these disease burdens.[5-7] For example, walking, running, or bicycling rather than driving an automobile provide "co-benefits" of better health and a lower carbon footprint.[8-10] Similarly, replacing meat and dairy with plant-derived foods, such as whole grains, nuts, legumes, and vegetables, will lead to both a lowered carbon footprint and improved health.[11-13] Moreover, it is possible that health and sustainability motivations may be mutually reinforcing. Individuals may be more apt to consider taking action for

our climate when educated on the positive health benefits of said actions.[14] Or, knowing that they will be contributing to sustainability, people may be more likely to adopt recommended health practices.[15] Interventions aimed at eco-wellness, defined as the simultaneous pursuit of both personal health and environmental sustainability, may be more effective than those aimed at only one of these targets.

The concept of eco-wellness is particularly apt for the field of nutrition. Because of positive effects for both physiological health and environmental sustainability, the reduction of meat and dairy in the diet has been widely discussed in the literature.[7,11,12,16-18] It is well known that animal-based foods disproportionally contribute to land and water use, air and water pollution, and carbon footprint. Globally, at least 26% and perhaps as much as 35% of anthropogenic greenhouse gases come from food production.[19,20] A recent comprehensive life cycle analysis found that worldwide meat production leads to twice the total greenhouse gas emissions as plant foods, despite the fact that meat represents less than 10% of global calories.[19] One systematic review found that for some affluent areas, reduction in greenhouse gas emissions of 50% or more could be achieved by dietary changes alone.[21]

At the same time, due to high calories and unfavorable fat profiles, animal-based foods are contributors to the global epidemics of obesity, dyslipidemia, and cardiovascular disease, substantively contributing to morbidity and mortality.[22,23] Supporting this conclusion, recent studies have found linear dose-response relationships between red meat consumption and premature death, with an estimated 10% increase in mortality associated with an increase of 100 g of daily meat consumption.[24-26] Nevertheless, despite the well-known health and environmental benefits of transitioning away from meat and dairy and towards a plant-based diet, very few interventions have been developed and tested towards these ends.

Over the past few years, our team developed and piloted the Mindful Climate Action behavioral change program, a mindfulness-based approach aimed at the simultaneous pursuit of both personal health and environmental sustainability.[27-29] Outcomes assessed in our pilot studies include miles and minutes spent walking, bicycling, and driving; household consumption of gas, electricity, and water; and proportion of diet from animal-based versus plant-based sources, assessed using the Automated Self-Administered 24-hour Dietary Assessment Tool (ASA24). Our team also developed a new dietary intake environmental impact calculator to help support this work. The Multi-factor Dietary Impact on the Environment Tool (miDIET) takes self-report data from the ASA24 and then applies environmental impact factors to produce individual-level sustainability metrics, including carbon footprint.[30] This pilot work also included data from validated self-report instruments assessing mental and physical health, self-efficacy, perceived stress, depressive symptoms, presenteeism at work, and happiness.

Experience with this previous work prompted us to look for other studies examining interventions aimed at influencing eco-wellness behaviors. The basis of our definition of intervention was influenced by the National Institutes of Health definition. We sought to find prospective studies involving the manipulation of a human subject's environment to evaluate the effect of the intervention on the study participants' health (either health-related biomedical or behavioral outcome) and on some form of sustainability. Examples of strategies to change health and sustainability-related behaviors include cognitive therapy, motivational interviewing, diet, exercise, or development of new habits.[31]

An initial literature search found no previously published systematic or scoping reviews of individual-level interventions aimed at behavioral eco-wellness. Therefore, our group launched such a review, reported here.

The primary objective of this study was to compile and categorize the literature on interventions aimed at modifying individual behaviors to promote both personal health and environmental sustainability. Secondary objectives were to help define the emerging field of behavioral eco-wellness and to discuss future directions, including the need for fit-for-purpose methods, including assessment tools and analytic strategies for evaluating the efficacy and effectiveness of these interventions for both individual and environmental health.

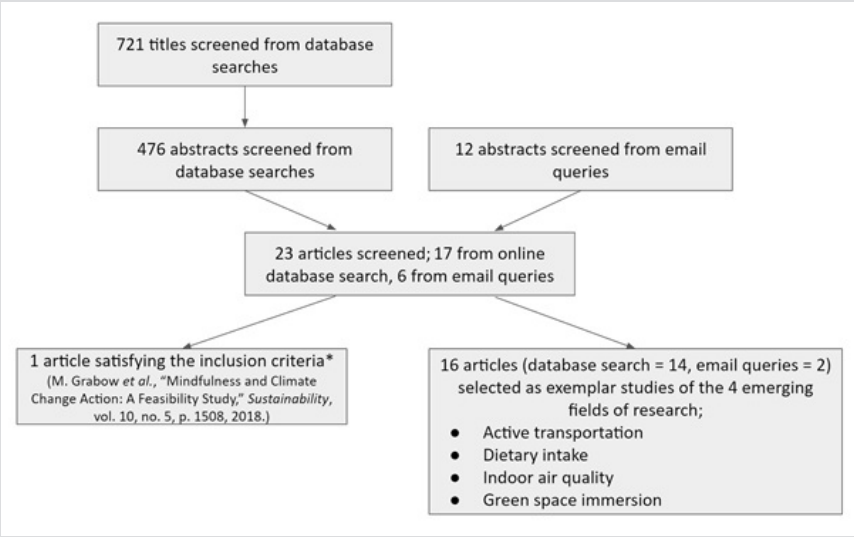
METHODS

To meet the primary objective, we first sought published empirical studies that: (1) conducted an intervention aimed at changing behaviors, (2) were delivered at the individual or group level, with pre- and post-intervention assessments including (3) at least 1 measure assessing a mental or physical health attribute, and (4) at least 1 measure directly related to environmental sustainability (eg, reduced waste, energy use, or carbon footprint; improvement of air or water quality). Our search strategy was limited to English language publications that included terminology regarding both sustainability (environment, climate) AND health (physical, mental, well-being, health behavior). We relied heavily on the term "co-benefit," as this encompasses the intersection of human health and the environment. See supplemental material for specific search terms and strategy.

The scoping review process was guided by the PRISMA Scoping Review guidelines[32] and is summarized in the Figure. The search strategy was developed with health sciences academic librarians, including coauthor MH. We used 3 databases—PubMed, Agricultural and Environmental Science Collection, and Scopus—aiming to identify articles that fulfilled our search criteria. There were no publication date restrictions. The original search was completed by MH on March 6, 2020, then repeated on July 27. The final search was done on January 15, 2021, with the condition that the publication date was limited to the year 2020.

Results were compiled, and duplicate items were removed

Figure. Flow Diagram Showing Review Strategy



*Inclusion criteria were empiric studies that: (1) conducted an intervention aimed at changing behaviors, (2) were delivered at the individual or group level, followed by post-intervention assessments including (3) at least 1 measure assessing a mental or physical health attribute, and (4) at least 1 measure directly related to environmental sustainability.

using Endnote X9, resulting in 572 article titles from the original search, a number that increased to 721 titles after the January 2021 search was completed (see Figure). Team members SR and SW screened all titles for inclusion criteria, resulting in a total of 476 abstracts being reviewed (431 abstracts from the original search). Abstracts were read initially by team members SR and SW, who selected 111 abstracts for indepth review by the full team. The titles and abstracts rejected at the first 2 stages did not describe empirical studies of small group or individual-level interventions aimed at behavior change. The 111 resulting abstracts were read by team members BB, BK, and SW, applying the entire set of inclusion criteria. In case of discrepancy, team member MG reviewed the abstract. Group consensus was achieved by discussion. Database searches resulted in 17 publications that were read in full by at least 2 team members.

To complement the online database search, senior author BB sent email queries to 41 published experts asking for studies that matched our inclusion criteria. The list of experts queried was based on having published relevant literature. This resulted in 12 additional abstracts, which were then reviewed by at least 2 team members (BB, BK, and/or SW), resulting in 6 publications recommended by experts being read in full.

These 2 search processes resulted in 23 papers (17 from the first online database search, none from the second and third online database search, and 6 from authors contacted by email), which were read in full by at least 2 team members (BB, BK, MG, and/or SW) and analyzed for eligibility based on the inclusion criteria described above.

RESULTS

After full-text reviews, we found no studies that strictly fit the inclusion criteria, with the exception of our own Mindful Climate Action pilot study.[27] Reasons for exclusion varied. Many papers were based on theory or models and did not include empirical outcome data from a prospective study design. A number of papers did not include at least 1 health and 1 sustainability outcome measure. Some did not describe discrete interventions, and some were not aimed at addressing individual behaviors. Other than our own work, not a single paper described an empirical study describing an intervention aimed at changing individual behaviors to impact health and sustainability co-benefits.

Nevertheless, despite this null finding, we did identify 4 broad categories of literature relevant to the goal of assessing and influencing both personal health and environmental sustainability: (1) dietary intake, (2) active transportation, (3) indoor air quality, and (4) green space immersion. The emergence of these 4 categories occurred after reading the 23 papers but was strongly informed by reviewing the 721 titles and 476 abstracts. Of the 23 papers, 16 fit within these categories and serve here as exemplars of the potential of behavioral eco-wellness as a burgeoning field. (See Tables 1-4.) The 16 papers included 3 papers involving dietary change, 3 papers focusing on active transportation, 7 papers investigating indoor air quality, and 3 papers looking at green space immersion. All of these were published after 2010. Thirteen of the 16 studies were published after 2015. While this paper highlights research on dietary intake for health and sustainability co-benefits, we also summarize what we found in the other 3 areas.

Dietary Intake

This scoping review did not find any reports of empirical testing of behavioral interventions aimed at changing individual diets to achieve both health and environmental benefits. However, we did discover an emerging stream of literature pointing in this direction. There were large-scale analyses of potential co-benefits of dietary change.[11,21] There were several regional studies looking at health and sustainability correlates of dietary intake patterns.[33-35] There were discussions and analyses of how people might be persuaded to modify their diets towards health and sustainability.[16,36,37] Nevertheless, as far we could find, there were no empirical studies testing interventions aimed at changing dietary intake that included outcome measures relating to both personal health and environmental sustainability.

Table 1. Dietary Intake: Analysis of Major Criteria and Sample Size of Final Review Studies Within the Dietary Intake Category

Studies	Presence of Inclusion Criteria	Study Design	Population	Sample Size	Type of Intervention	Mental/Physical Health Outcome	Environmental Sustainability Outcome
Aston et al, 2012[38]	C, D	Modelling	British general public	N_I=1724	None (consumption of red and processed meat	Risk of coronary heart disease, diabetes, colorectal cancer	Greenhouse gas emissions from dietary intake
Behrens et al, 2017[39]	D	Modelling	NA	NA	None (Nation-specific nationally recommended diets)	None	Impact of diets on greenhouse gases, eutrophiction, land use
Bharucha et al, 2020[40]	C	Cross-sectional study	Participants of local food initiatives in the United Kingdom	Local food initiatives (N_I = 302), general population (N_I = 157)	None (local food project participants)	Psychological need satisfaction, diet, nature-connectedness, physical activity	None

Inclusion criteria were empiric studies that: (A) conducted an intervention aimed at changing behaviors, 9B) were delivered at the individual or small group level, followed by post-intervention assessments including (C) at least 1 measure assessing a mental or physical health attribute, and (D) at least 1 measure directly related to environmental sustainability.

N_I indicates the number of individual participants.

Table 2. Active Transportation: Analysis of Major Criteria and Sample Size of Final Review Studies Within the Active Transportation Category

Studies	Presence of Inclusion Criteria	Study Design	Population	Sample Size	Type of Intervention	Mental/Physical Health Outcome	Environmental Sustainability Outcome
Chapman et al, 2018[43]	A, C, D	Prospective cohort	Community households in 4 New Zealand cities	Interventional (N_H = 1120) control (N_H = 1020)	Incorporation of walking, cycling programs	Disability adjusted life years	Transport-related carbon emissions
Frank et al, 2010[45]	C, D	Cross-sectional study	Participants >16 years old in Atlanta, Georgia region	N_I = 10,148	None (Built environment's impact on transportation)	Kilocalories burned from walking	Kilocalories burned from motorized transport (ie, CO_2 emissions)
Keall et al, 2015[44]	A	Prospective cohort	Community households in New Zealand cities	Interventional (N_H = 1120), control (N_H = 1020)	Incorporation of walking and cycling programs	Rates of active travel[a]	Rates of active travel[a]

Inclusion criteria were empiric studies that: (A) conducted an intervention aimed at changing behaviors, (B) were delivered at the individual or small group level, followed by post-intervention assessments including (C) at least 1 measure assessing a mental or physical health attribute, and (D) at least 1 measure directly related to environmental sustainability.

N_H indicates the number of households, and N_I indicates the number of individual participants.

[a]Indicates outcome measurement not adequate to meet inclusion criteria.

The 3 studies that we chose to include as exemplars are shown in Table 1.[38-40] Two of these utilized a modeling method, while the third conducted a cross-sectional study. Two papers studied populations in the United Kingdom, while the other looked at diets from a global perspective. Studies variously focused on reduced meat consumption, the environmental impact of nationally recommended diets, and the impact of local food initiatives. Two studies estimated greenhouse gas emissions as an environmental outcome, with one also including eutrophication and land use. One study measured health outcomes (coronary artery disease, diabetes, and colorectal cancer), and another assessed psychological need satisfaction, fruit and vegetable intake, nature connectedness, and physical activity.

Active Transportation

Modifying transportation infrastructure and supporting active transportation has been discussed at length in the literature as a major potential source of health and sustainability co-benefits.[6,41,42] Nevertheless, very few empirical studies aimed at supporting active transportation have been conducted. The majority of the papers

Table 3. Indoor Air Quality Analysis of Major Criteria and Sample Size of Final Review Studies Within the Indoor Air Quality Category

Studies	Presence of Inclusion Criteria	Study Design	Population	Sample Size	Type of Intervention	Mental/Physical Health Outcome	Environmental Sustainability Outcome
Anderman et al, 2015[49]	C	Cohort	Households in southern India	NH=199	None (Biogas cook stove vs traditional stove)	Dietary diversity	Subjective firewood utilization[a]
Aung et al, 2018[50]	A, B, C	Randomized control trial	Women >25 years in India	Control N_I=111 and intervention N_I=111	Rocket cook stove vs traditional stove	Systolic/diastolic blood pressure, self-reported eye symptoms	Fine particle (PM 2.5) mass and absorbance around cooking area[a]
Barn et al, 2018[54]	A, B, C	Randomized control trial	Nonsmoking pregant women in Mongolia	Control N_I=253 and intervention N_I=259	HEPA filter air cleaners vs no air cleaners	Blood cadmium and hair nicotine from second-hand smoke exposure	Indoor and outdoor PM 2.5[a]
Champion and Grieshop, 2019[51]	A, B, C	Cohort	Households in Rwanda	Pellet stove (N_H=14), (N_H=4), and charcoal stove (N_H=4)	Pellet cook stove vs wood/charcoal wood stove	Carbon monoxide exposure stoves	Estimated tons of CO_2 equivalent per year of cook stove use and indoor PM 2.5[a]
Patange et al, 2015[52]	C	Cross-sectional study	Households in India	Forced draft stove N_H=10 stove N_H=12	None (forced-draft cook stove vs and traditional	Black carbon exposure traditional stove)	Black carbon around cooking area[a]
Wathore et al, 2017[53]	C	Cross-sectional study	Households in Malawi	Households N_H=22	None (Alternative cook stoves [ceramic forced-draft, institutional models] vs traditional cook stoves)	Carbon monoxide exposure	Indoor PM 2.5[a]
Zhou et al, 2014[55]	A, B, C	Cohort	Participants >40 years in southern China	N_I=996	Household biogas digester for clean fuel usage and kitchen ventilation	FEV1 and risk of COPD	Indoor SO_2, CO, CO_2, NO_2, and PM <10

Abbreviations: PM, particulate matter; FEV1, forced expiratory volume in 1 second; COPD, chronic obstructive pulmonary disease; SO_2, sulfur dioxide; CO_2, carbon dioxide; CO, carbon monoxide; NO_2, nitrogen dioxide.

Inclusion criteria were empiric studies that: (A) conducted an intervention aimed at changing behaviors, (B) were delivered at the individual or small group level, followed by post-intervention assessments including (C) at least 1 measure assessing a mental or physical health attribute, and (D) at least 1 measure directly related to environmental sustainability.

N_H indicates the number of households, and N_I indicates the number of individual participants.

[a]Indicates outcome measurement not adequate to meet inclusion criteria.

we found described modeling studies. Here we will mention 3 empirical studies, 2 studies using a prospective cohort design in New Zealand, and the other using a cross-sectional design in the United States (Table 2).[43-45] All of these studies looked at the impacts of the built environment and socioeconomic factors on active transportation. The environmental outcome measurement was related to motorized vehicle emissions in 2 of the 3 studies. The health outcomes measure varied, including disability-adjusted life years in one study and kilocalories burned during active transportation in another. One of the studies looked generally at rates of active travel and the likely impact on health and environmental outcomes.

Indoor Air Quality

Our scoping review yielded dozens of studies assessing the use of new or upgraded cook stoves and other technological approaches to improve indoor air quality. This is unsurprising given the well-known effects of air pollution—especially fine particulates—on human health.[46-48] Nevertheless, while some studies assessed both health and environmental outcomes, none of these were aimed at changing individual behaviors. Of the 7 exemplar studies, 3 studies used randomized controlled trial methods, 2 studies utilized a cross-sectional design, and 2 studies used a prospective cohort design (Table 3).[49-55] Five studies were conducted in Asia (3 in India, 1 in Mongolia, 1 in China), and 2 studies were conducted in Africa (Rwanda and Malawi). Six studies investigated "cleaner" cooking stoves, and 1 study researched HEPA air filters. Four studies measured indoor fine particulate matter (PM2.5) as an environmental outcome. Other studies measured black carbon

Table 4. Green Space Immersion: Analysis of Major Criteria and Sample Size of Final Review Studies Within the Green Space Immersion Category

Studies	Presence of Inclusion Criteria	Study Design	Population	Sample Size	Type of Intervention	Mental/Physical Health Outcome	Environmental Sustainability Outcome
Coventry et al, 2019[61]	C, D	Cross-sectional study	Conservation volunteers in the UK	N_I=45	None (guided walks, practical conservation or citizen science in urban or semi-urban green spaced)	Mood and stress	Engagement in conservation and sustainable urban development
Raymond et al, 2019[62]	C, D	Semistructured qualitative interviews	Home gardeners in Winnipeg, Canada	N_I=50	None (gardening for biodiversity)	Subjective psychological, physiological, cognitive, and social benefits	Subjective environmental benefits of conservation of native habitat
Reeves et al, 2019[63]	B, C	Self-controlled case series	Healthy participants in London, England	N_I=36	Exposure to urban green spaces	EEG measurements and self-reportedd stress, anxiety, depression	None

Abbreviations: EEG. electroencephalogram.

Inclusion criteria were empiric studies that: (A) conducted an intervention aimed at changing behaviors, (B) were delivered at the individual or small group level, followed by post-intervention assessments including (C) at least 1 measure assessing a mental or physical health attribute, and (D) at least 1 measure directly related to environmental sustainability.

N_I indicates the number of individual participants.

[a]Indicates outcome measurement not adequate to meet inclusion criteria.

concentration, fuel use, and other indoor air pollutants, including CO_2. The studies investigated health outcomes, including blood pressure, eye symptoms, cardiopulmonary and cardiovascular disease mortality, hair nicotine and blood cadmium levels, lung function, incidence of chronic obstructive pulmonary disease, and carbon monoxide exposure. One nonrandomized study from India (n = 199 households) found that households using clean biogas cook stoves reported greater dietary diversity than comparison households.[36]

Green Space Immersion

Experiencing nature (ie, green space immersion, forest bathing, shinrin-yoku, nature immersion, etc) has emerged as a potential avenue toward better mental and physical health and also as a way to foster ecological values.[56-60] Included here as 3 exemplars, 2 green space immersion studies implemented a qualitative approach, while a third study utilized a cross-sectional design (Table 4).[61-63] The studies included short-term exposure to urban green spaces, guided walks/practical conservation tasks/citizen science in urban and semi-urban green spaces, and home gardening for biodiversity. All 3 studies assessed general indicators of physical and psychosocial wellness; one also included measures of stress response, self-reported mood, and heart rate. We did not find green space immersion studies that specifically looked at potential relationships with food production or dietary intake.

DISCUSSION

Although we found no investigations other than our pilot study that matched the specific inclusion criteria, we did find emerging literatures regarding 2 sets of eco-wellness behaviors with well-known health and sustainability co-benefits (active transportation and food choice), as well as research in 2 areas where co-benefits from behavior change have received less attention (indoor air quality and green space immersion). The findings of this scoping review provided new insights into the emerging field we call "behavioral eco-wellness," with 4 streams of literature converging on a new transdisciplinary science concerned with both personal health and environmental sustainability. The exemplar studies in Tables 1-4 highlight the 4 areas and attest to the rapidly rising importance of this emerging field, with the majority of studies published within the last 5 years.

To our knowledge, no previous reviews have attempted to systematically locate and contextualize published studies of interventions aimed at influencing individual behaviors that impact both personal health and environmental sustainability. While our research team uses the term "eco-wellness" to describe this emerging field, it should be noted that the word "ecowellness" has been used previously by Reese et al, who described it as "a sense of appreciation, respect for, and awe of nature that results in feelings of connectedness with the natural environment and the enhancement of holistic wellness."[64-66] We consider Reese's work to be very much in line with the literature on green space immersion that we identified. We build on Reese's ecowellness work by looking more broadly at scientific studies of behaviors and interventions that influence both human health and environmental sustainability rather than only those aimed at the health benefits of experiencing nature.

The emergent field of eco-wellness research seeks to investi-

gate pathways influencing both sustainability and health. Defining the field of behavioral eco-wellness as the study of how individual behaviors impact personal health and environmental sustainability will allow for a wide variety of research topics to be brought together into a unified yet multidisciplinary field of research, in order to contribute substantively towards both climate change mitigation and the epidemics of obesity, diabetes, and cardiovascular disease. Reaching towards these goals will require new conceptual structures, as well as new assessment tools. Development and validation of new tools for measuring eco-wellness outcomes should be guided by theory and supported by both hypothesis-testing and conceptual restructuring and synthesis.

We would be remiss to not mention the importance of equity embedded within the topic of behavioral eco-wellness. Our search criteria were already so specific in nature by combining health and sustainability that adding a health equity component might have rendered us incapable of producing any useful results. As the field of eco-wellness develops and co-benefit strategies evolve, diversity, equity, and inclusion must remain a top priority. In fact, our colleagues at the University of Wisconsin–Madison recently published a scoping review of active transportation interventions and their effects on health equity, finding that significant gaps exist in our understanding of how health inequities could be mitigated through modifying the active transportation environment because it is understudied and underevaluated.[67]

To expand the field of behavioral eco-wellness, measurement of personal health and environmental sustainability outcomes should become more accessible, standardized, precise, reliable, and easy-to-implement in diverse study designs. For example, improved measurement of physical activities, such as active transportation, will be needed and will likely include global positioning system (GPS)-enabled smartphone applications and other wearable technologies. Our research group has used Moves, Move X, and Arc, which are smartphone apps that map personal movement on streets, walking paths, and bike lanes, yielding estimates of minutes and miles of walking, bicycling, and driving that, in turn, can be used by the researchers to estimate both carbon footprint and personal health benefits.[27,28] These movement-measuring tools were developed to assess personal movement metrics but do not assess other eco-wellness behaviors, such as using stairs rather than elevators or choosing to drive an electric car, a fossil-fueled vehicle, a hybrid car or use public transportation.[68] Currently available tools for estimating the carbon footprint of an individual's transportation behaviors require make, model, and year of vehicle; an assessment of "miles driven;" and application of weighting factors, a process that is effort-intensive. Computer programs and smartphone-based apps to reduce the effort should be developed and tested. Better methods for assessing the health and environmental impacts of public transport also are needed. The creation of a comprehensive smartphone application or wearable technology that accurately tracks active and fossil-fueled transportation with the ability to internally calculate the carbon footprint of an individual's movement could improve the accuracy and accessibility of eco-wellness research.

There are currently no properly validated systems to assess dietary intake for both health and sustainability outcome assessment. Various diet measurement tools, such as food frequency questionnaires, 24-hour recalls, and prospective logs, can estimate dietary intake but are known to be inaccurate as well as time-consuming.[69] A goal of dietary eco-wellness assessment is to identify the quantity of specific foods ingested, then link that information to data from studies looking at health outcomes and sustainability impacts of those foods in terms of carbon footprint.[30] Future directions may include mobile technologies and computerized analysis of photos of meals taken by research participants on their smartphones, such as the Technology Assisted Dietary Assessment (TADA) system developed by researchers at Purdue University.[70-72] Researchers in Australia are adapting the TADA system with the aim of measuring both the health and sustainability impacts of individual diets.[73] As another example, smartphone applications have been used in Denmark grocery outlets in an attempt to provide nutritional and environmental information to supermarket shoppers.[74] While some nutritional information is typically available for many foods, assessment and labeling of different foods' carbon footprints and other environmental impacts will need to be improved for the advancement of eco-wellness research related to food production and consumption.

Although several indoor air quality studies were found in this scoping review, there is an inherent difficulty in measuring sustainability outcomes of improved cook stoves and other air quality technologies. We also know this has links to nutrition as cooking and cooking methods may also affect the nutritional content and nutrient availability of food. Understanding the interplay between the energy we use for cooking and its impact on sustainability metrics is a complicated process. Creating a standardized formula to determine the environmental impacts of cook stoves could propel this area of research forward in the field of eco-wellness. Modeling of clean cook stove interventions does show promise of widespread health and environmental benefits, specifically in low- and middle-income countries.[75] But many indoor air pollution projects fail to address how individuals would realistically utilize these interventions.[76] To advance in this field, improving the design of the interventions and their implementation will be necessary to utilize funding effectively and to improve stakeholder livelihood.[77,78] Assessment of the interactions between new stove use, food choice, and nutritional intake also will be needed. If indoor air quality research does not address realistic practicality in study design and sustainability measurement tools, the adaptation within the eco-wellness framework will continue to be limited.

In addition to improving the toolkits available for measuring the co-benefits of active transportation and dietary intake, better methods are needed to assess potential health and sustainability

outcomes attributable to experiencing the natural environment. During the past few years, a growing body of literature has begun to describe health benefits from spending time in nature.[79-81] Nevertheless, studies to date are almost entirely observational rather than experimental, with interventions and outcomes either poorly described or not yet validated. A few studies in this emergent scientific area have attempted to assess health outcomes, but little attention has been paid to the potential feedback loop toward improvement of environmental preservation and sustainability behaviors. Quite plausibly, nature immersion could lead to improved personal sustainability behaviors and improved health, or even perhaps environmental advocacy or sustainability-directed political activism. Undoubtedly, there is also potential overlap with the domains of active transportation and nature immersion as well as mindful eating and nature immersion, as experiencing nature may change how one is motivated to move and eat more in accordance with sustainability principles. However, without proper testing, such potential co-benefits remain hypothetical rather than empirically tested.

Improvements in study design will be essential in furthering the field of eco-wellness. Many studies found in this field utilize observational methods without any sort of intervention or pre-/post-assessment. This likely is due to multiple reasons, notably the financial feasibility of conducting an intervention, assessing control conditions, and completing baseline and follow-up assessments. Modeling studies are quite popular, especially in the active transportation area of research. These methods allow researchers to illuminate the potential impact of large-scale interventions but do not empirically assess intervention effects. This review found several studies employing observational data and modelling methods but almost no experimental studies assessing the results of interventions. Considering the rapid progression of climate instability and the increasing obesity epidemic worldwide, we conclude that there is an urgent need to develop and test promising behavioral interventions. Moving toward experimental study design methods will be essential for eco-wellness research to take the next steps towards rigorous and generalizable information that can be used to improve human health and environmental sustainability.

We were impressed by the fact that the 4 identified domains not only overlapped but were characterized by potential interactions and perhaps synergy. For example, while we selected Bharucha et al as a dietary study exemplar, that paper also discussed the psychological benefits of interacting with local green spaces and initiatives and so could have instead been categorized under green space immersion.[40] Similarly, many of the indoor air quality studies were based on the development and testing of cook stoves, which has obvious yet largely unexplored implications for healthy and sustainable dietary intake. Less obvious but nonetheless important may be the impacts on active transportation; procurement of fuel and foodstuffs requires movement and transportation, which is likely to be influenced by type of stove, fuel, and cookware used. Another example would be the interactions between transport, green space, and types of food consumed. In both urban and rural communities, choice of foodstuff and considerations such as packaging and shelf life may affect whether walking or bicycling are possible or whether fossil-fueled transportation is needed. Food delivery systems might affect people's physical activity patterns. Developing and protecting greenspace might influence personal transportation choices, both related and unrelated to dietary intake. While fully comprehensive studies may not be possible, the incipient field of behavioral eco-wellness should strive to be holistic and comprehensive enough to take into account as many relevant outcome domains as possible, so as to maximize useful knowledge and perhaps avoid undesirable unintended consequences.

These considerations further highlight the importance of defining search terms, keywords, sub-fields, and domains of study for the field of behavioral eco-wellness to move forward. We used the term co-benefit as part of our search criteria, which may have limited the extent of our findings since it may not be an umbrella term used worldwide. While we did include expert inquiries to help identify potential blind spots in our scoping review's methodology, it is likely that individual studies or even whole fields of relevant research may have slipped past our review. As with all systematic or scoping reviews, papers published in journals not encompassed by the search strategy (nonindexed journals, gray literature) likely will have been missed. With the understanding that the study of eco-wellness is only now emerging (the majority of our exemplars were conducted in the last 5 years), this scoping review does not claim to have exhaustively found all studies in the 4 research domains identified and does not assert that the study of eco-wellness is limited to these 4 areas. It is possible that we missed a study that would have met our strict inclusion criteria. However, even if that were the case, we do not believe that would substantively change our findings, conclusions, or interpretation. In the future, it will be important for research within the field of eco-wellness to be published using consistent terms and for scientists to communicate and work together to consolidate and develop this field.

Given the enormous challenges posed by climate change and the epidemics of obesity, diabetes, and cardiovascular disease, it is incumbent upon us to grow and strengthen these areas of research as swiftly and comprehensively as possible.

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Join the Conversation: Talking About the Health Consequences of Global Heating/Climate Destabilization

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ABSTRACT

Global heating/climate destabilization is likely to be the most serious public health problem in this century. This article encourages health care workers to discuss climate change and provides a short summary of climate change/health information. There are talking points with references that may be of practical use. Although climate change is a global crisis that requires global solutions, by conversing with others, an individual may be able to take effective climate action.

BACKGROUND

Climate change may become the greatest health problem of this century.[1] Children today and future generations face an uncertain and unsafe future caused, in part, by global heating/climate destabilization, often called climate change.[2,3] Discussing its health effects with patients, colleagues, family, and friends may be an effective and practical action for concerned health professionals who have demanding professional duties[4,5] and may result in greater public pressure to reduce greenhouse gas emissions.

This article provides a summary of climate change, air pollution, and health information intended to facilitate discussions for health professionals in their daily conversations. It is organized as a collection of talking points linking health and climate. A broad array of climate and health information is presented to emphasize the importance of climate change and permit the reader to choose from many topics. Table 1 includes a list of talking points about the direct health effects of climate change. Table 2 consists of information about tipping point warnings called "boundaries." These boundaries anticipate major changes beyond which Earth's capacity to sustain life diminishes. The Box lists key messages. Because climate change affects the entire Earth ecosystem, diverse information from different scientific fields has been included. Dissimilar information is included because every topic mentioned is a health topic.

METHODS

The Intergovernmental Panel on Climate Change (IPCC), World Health Organization (WHO), *New England Journal of Medicine*, and *Lancet* commission reports and reviews provided most of the information on the health effects of global heating/climate destabilization and air pollution for this article.[1-3,6-9] For boundary and tipping point information, a PubMed search was conducted for English language articles published from January 1, 2014 through March 31, 2022 using the terms "boundary" and "rockstrom." "Rockstrom" was chosen because Professor Johan Rockstrom is a pioneering researcher in the study of earth system boundaries.[10] Review articles were selected from the PubMed list.

For information about the deposition of particulates in human tissues, a PubMed search for English language articles published from January 1, 2014 through March 31, 2022 was performed using "particulates" and "human placenta," "particulates" and "human heart," and "particulates" and "human brain." A single article that demonstrated the presence of air pollution deposits in heart, brain, or placental tissue was chosen from each search result.

For mortality from heat, a PubMed search for English language articles published from January 1, 2015 through March 31, 2022 was performed using the search terms "heat" and "global mortality." A single modeling study about global heat mortality was selected as an example because the authors were able to provide an

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estimate of annual heat mortality over time compared to the rise in the Earth's mean surface temperature.

The collection of talking points derives from my experience giving presentations and trying to answer questions on climate and health. The US Army War College[11] report is helpful when speaking to someone who discounts climate science. Heating, anoxia, and acidification of water may be appropriate for a person with an interest in Wisconsin lakes or fishing; and discussing the novel *Never Let Me Go*[12] may encourage people to consider an adolescent's perspective on climate change.

RESULTS

The average atmospheric temperature just above the Earth's surface (global mean surface temperature) increased by 1 °C to 1.1 °C (1.8 °F to 2 °F) between the years 1900 and 2017.[6] By 2040, this increase may become 1.5 °C (2.7 °F).[6] An increase in concentration of greenhouse gasses in the atmosphere causes global heating by reducing heat flow to outer space and accumulating heat energy within the atmosphere.[6] Heat accumulation on Earth causes global heating and also destabilizes the climate by causing a greater number of severe weather events. As a result of global heating, a child born today will experience more wildfires, floods, weather-induced crop failures, droughts, and heat waves than a child living in a stable preindustrial climate like Earth had in the year 1750.[13] Between 2000 and 2018, an average of 490,000 persons died each year worldwide from excessive heat.[14] During the years of this modeling study, average global temperature increased by 0.26 °C, and heat deaths increased by 0.21%. As global heating progresses, it is likely that mortality from heat exposure will rise steeply.

There is a close relationship between global heating/climate destabilization and air pollution. Fossil fuel combustion is the dominant cause of global heating and the principal cause of air pollution.[2] Each year, about 4 million people worldwide die prematurely from this outdoor (not household) air pollution.[15,16] Nanoparticles from fossil fuel combustion accumulate not only in human lung tissue, but also brain, heart, and placental tissues.[16-19] These deposits may explain, in part, why fossil fuel pollution causes lung cancer, increased susceptibility to pulmonary infections, myocardial infarction, stroke, preterm birth, low birth weight, and exacerbations of asthma and chronic obstructive pulmonary disease.[20] Reducing climate change helps everyone, regardless of age, by reducing air pollution.

Table 1 lists health effects of global heating/climate destabilization. Because of the complex relationships between health and changes in Earth's ecosystem, it may not be possible to anticipate all of the health problems caused by global heating. For example, the relationship between heat exposure and kidney disease has been recognized only recently. Table 2 describes some boundaries of Earth's ecosystem. A boundary is a warning that the Earth system is approaching a tipping point. The IPCC defines a tipping point as a critical threshold in the Earth system that, when exceeded, can lead to a significant and possibly irreversible change in the state of the system.[7] Crossing a boundary reduces the Earth's ability to sustain life. The climate boundary—thought to be 350 parts per million (PPM) of carbon dioxide (CO_2) in the atmosphere—already has been exceeded. Not only is it important to stop increasing the atmospheric concentration of CO_2, but it may be necessary to reduce it from the current value of 420 PPM to 350 PPM to preserve a healthy planet. The documentary film entitled *Breaking Boundaries* with David Attenborough and Johan Rockstrom explains all of the known Earth ecosystem boundaries, including climate change.[10]

Human influence is the dominant cause of global heating.[9] Human actions cause climate change by releasing greenhouse gases into the atmosphere as a result of fossil fuel extraction and combustion and industrial forms of agriculture. The major greenhouse gases responsible for global heating today are CO_2, methane (CH_4), and nitrous oxide (N_2O). To limit global heating to 1.5 °C, greenhouse gas emissions would probably have to be reduced to zero by 2050.[9,10]

HOW GREENHOUSE GASES HEAT EARTH

The amount of energy at Earth's surface determines its climate;[9] increase the energy and the climate becomes hotter and storms become more powerful. The energy balance of the Earth as a whole is determined by the difference between incoming and outgoing energies at the top of the atmosphere. The greenhouse effect increases a planet's surface temperature by reducing the rate at which the planet loses energy to outer space. This is similar to adding insulation to your home to increase inside temperature without requiring more energy from the furnace.

The atmosphere contains a continuous stream of heat (infrared energy) moving from the Earth's surface to outer space because outer space is colder. Greenhouse gas molecules absorb and emit some of this infrared energy, sequestering heat in the atmosphere and causing Earth to warm.[21,22] Some molecules with 3 or more atoms like CO_2 and CH_4 can absorb and emit infrared energy. Molecules that have the ability to absorb infrared energy usually have an uneven distribution of electrical charge called a dipole within the molecule. Absorption of infrared energy changes the position of the dipole within the molecule. Later, when the infrared energy is emitted, the dipole returns to its former position. This dipole shift is called a vibration. Infrared energy causes vibrations of greenhouse gases in the atmosphere. A greenhouse gas molecule absorbs and later emits a unit (photon or quantum) of energy. The fundamental problem is that the direction of the emitted photon is random. The movement of the photon towards outer space is likely to be lost. This greenhouse gas effect becomes harmful to organisms—as it is now—when greenhouse gas concentrations increase and cause rapid global heating. This is because the more greenhouse gases in the atmosphere, the greater the amount of sequestered infrared energy.[21] Human activities, particularly fos-

Table 1. How Climate Destabilization Affects Human Health

Health Problem	Explanation	Ref
Mental health problems	Observing and hearing about the decline of the natural world; loss of home or occupation from weather disasters; may lead to stress, fear, despair, and other mental health problems.	25
Heat-related illness and death	Hyperthermia is a loss of internal body temperature regulation caused by heat exposure. Heat stroke is hyperthermia plus central nervous system dysfunction, such as fainting, seizure, or coma. Heat stroke may be fatal.	7
Heat-related chronic kidney disease	Uncertain etiology; related to manual labor, dehydration, and extreme heat; particularly affecting outdoor workers in tropical climates.	24
More vector-borne disease	Ticks and mosquitoes migrate towards the poles and to higher altitudes as temperatures warm and summer is longer: eg, malaria, dengue, Lyme disease, West Nile encephalitis, zikavirus, Powassan virus.	8
Threats to sources of fresh water	Drought, mountain glacier loss, toxic blooms, floods, exhaustion of underground aquifers, salt water contamination of coastal aquifers.	25
Reduced agricultural harvests caused by heat, drought, floods, ground-level ozone	Declines in production of maize, wheat, rice, soybeans resulting in food scarcity as global heating continues.	25
Declining air quality	Higher temperatures cause more ground-level ozone. There is more particle pollution from wildfires causing respiratory and cardiovascular disease.	7
Displacement of human populations (forced migration)	Sea level rise, extreme heat, drought, and reduced food harvests force people to leave their traditional homes, increasing geopolitical instability.	11
Possible conflicts over fresh water and other essential resources	Rivers, lakes, and glaciers at national boundaries may be disputed as fresh water resources diminish.	11
Declining seafood harvests due to ocean heating and declining ocean pH	Ocean and lake heatwaves and acidification of water by carbonic acid killing marine life. Since 1899, ocean pH has eclined by 0.2 while ocean temperature has increased by 0.9 °C.	6
Toxic blooms of microorganisms in lakes and oceans	Warming lake and ocean waters contaminated by nitrogen and phosphorous from fertilizer, manure, or sewage cause rapid growth of microorganisms, reduce fresh water availability, and kill marine life.	7
Floods in some areas	Higher water vapor concentrations in the atmosphere cause heavier rainfall in some places, contamination of drinking water by infected or poisoned flood waters, and infrastructure damage.	7
More powerful tropical storms, more precipitation per storm	Warmer ocean waters provide more energy to storms, causing destructive coastal hurricanes and damage infrastructure.	25
Sea level rise	Caused by thermal expansion of water and melting of glaciers on land (loss of Greenland and Antarctic ice sheets and glaciers everywhere).	7
Drought, expansion of desert terrain	In some areas, rainfall does not increase with temperature, causing hot drought (US West megadrought) and reduced crop harvests due to heat and insufficient water.	7
Increase in poverty	Repeated and extensive weather catastrophes and forced population migrations exhaust resources.	8
More water-borne infectious diseases due to floods, warmer ocean and lake water	As waters warm, bacterial populations increase; eg, *Vibrio* bacteria in salt water causing cholera, gastroenteritis, necrotizing fasciitis.	8

Table 2. Examples of Planetary Boundaries[26,27]

Boundary[a]	Description	How Boundary Relates to Health
Climate change	Caused by greenhouse gas emissions into atmosphere, resulting in a hotter Earth with more extreme weather events.	Boundary exceeded – rapid global heating and climate destabilization. Return [CO_2] in atmosphere to 350 PPM.
Biogeochemical flows	Excessive use of synthetic fertilizer causing release of nitrogen and phosphorous into bodies of water.	Toxic blooms when water is warm enough – dead zones in oceans and lakes – boundary exceeded in some locations, such as mouth of Mississippi River.
Freshwater use	Using more fresh water than natural systems can produce, water pollution by human activities and floods	Insufficient water for drinking and agriculture.
Land-system change	Loss of tropical, temperate, and boreal forests caused by clearing for farming, logging, and wildfires	More rapid global heating; less CO_2 removed from atmosphere by trees.
Loss of biosphere integrity	Biodiversity loss due to deaths of plants and animals	Reduced plant and animal populations; mass extinctions.
Ocean acidification and heating	CO_2 in atmosphere dissolves into ocean water forming carbonic acid, reducing pH of water. As oceans warm, O_2 concentrations decline.	Mass extinctions of marine life, loss of coral reefs, reduced seafood harvests.

Abbreviations: CO_2, carbon dioxide; PPM, parts per million; O_2, oxygen.

[a]Not all boundaries are listed. A boundary is a warning of a massive global shift that may be difficult to undo. These global catastrophes are often called "tipping points." Crossing planetary boundaries reduces the ability of Earth to sustain life.

sil fuel extraction (CH_4), combustion (CO_2), and application of synthetic fertilizers (N_2O), increase greenhouse gas concentrations in the atmosphere and ocean. Each year about 35 billion tons of CO_2 and 120 million tons of CH_4 are released by human actions. Water vapor is also a greenhouse gas, as it can absorb infrared energy, but human activities do not directly add water vapor to the atmosphere. However, local increases in water vapor concentrations in the atmosphere are an indirect result of human greenhouse gas emissions and amplify global heating (see below).

CLIMATE DESTABILIZATION TOPICS THAT MAY BE HELPFUL IN CONVERSATIONS

Solvable

Possibly the single most important point about climate change is that we can solve the problem by reducing atmospheric greenhouse gas concentrations. We can stop burning fossil fuels for energy, and we can actively remove CO_2 from the atmosphere using natural means (trees, soil restoration, ocean, and land preservation) and sophisticated machines that capture CO_2. Efforts to reduce greenhouse gas emissions usually also reduce air pollution from toxic chemicals.

Military

The US Army War College issued a report on climate change.[11] Although not intended as a medical report, health considerations occupy an important place in the report. Military strategists worry that global heating worsens existing national security threats by causing geopolitical instability and forced migrations of human populations. There may be displacement of tens of millions of people from the Middle East and Africa due to extreme heat and agricultural collapse. In the future, regions of the planet may become unfit for human habitation, leading to mass migrations on a scale not yet seen. The populations of Pakistan, India, and China depend on Himalayan glaciers for fresh water, creating a potential for dispute. Access to potable water could become a political threat or a weapon of war. Climate change can diminish access to resources, such as food or water, which, in turn, can increase the possibility of conflict.

US Army War College report summary:[11]

- The US military is "precariously unprepared" for climate change.
- Climate change is likely to worsen in coming years.
- Sea level rise, food and water insecurity, and extreme weather events may displace tens of millions of people worldwide.
- Military personnel must provide more humanitarian assistance as weather disasters increase.
- As temperatures increase, military personnel require more water when deployed.
- There are more cases of heat stroke and tropical diseases.
- There are more summer power grid failures as increased demand confronts aging infrastructure.
- Sea level rise affects US coastal and island military bases.
- There is a need for military environmental stewardship and greater energy efficiency.

Methane and Natural Gas

Methane emissions are a special problem caused in part by extraction and combustion of natural gas. Sometimes called "methane gas," natural gas consists of a mixture of organic gases with methane as a major component. During gas extraction, transportation, and use, methane enters the atmosphere. CH_4 is more effective at retaining heat than CO_2 and is responsible for about 15% to 20% of global heating today.[28] It is just as necessary to reduce CH_4 emissions to mitigate climate change as it is to reduce CO_2 emissions. Natural gas use causes less toxic air pollution than coal or oil combustion but emits too much greenhouse gas to be compatible with a healthy future.

Amplifiers of Global Heating

Particular events tend to amplify global heating.

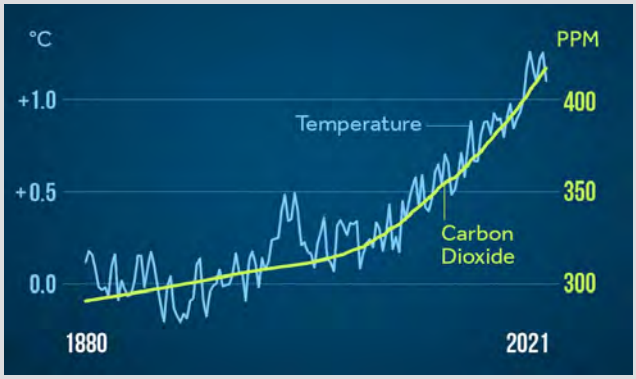
- When ice melts and exposes water or land, less sunlight reflects back to space and more heat is retained on Earth, because ice reflects sunlight while water and ground absorb it. Melting of the Arctic Ocean during summer increases heat accumulation in the Arctic by exposing more water to sunlight. This may explain why the Arctic is heating up faster than tropical and temperate regions.
- Melting of permafrost in the Arctic releases frozen CO_2 stored in the ground, adding extra CO_2 to the atmosphere.
- Increased Earth temperatures permit higher average water vapor concentrations. Since water vapor is a greenhouse gas, this leads to more heating.
- Global heating causes more wildfires, which, in turn, cause deforestation, which, in turn, accelerate global heating by impeding CO_2 removal by trees. In recent years, wildfires have been a destabilizing force in the United States, Russia, and Australia.

Because of these amplifiers, climate destabilization may progress more rapidly than predicted in some climate models.

Oceans and Lakes

Oceans and lakes face two different threats from CO_2 emissions: heating and acidification. Presently, about 30% of CO_2 emissions dissolve into water. Some of the absorbed CO_2 reacts with water to form carbonic acid ($H_2O + CO_2 \rightarrow H_2CO_3 \rightarrow H+ + HCO_3$), causing pH to decline. This extra acid makes it more difficult for marine organisms to form calcium carbonate skeletons and is directly harmful to organisms with shells. In addition, oceans and lakes become hotter as Earth becomes hotter. As ocean and lake waters warm, oxygen becomes less soluble and oxygen concentrations in water decline. The combination of lower oxygen concentrations, acidification, and heating is more harmful to marine life than any one factor alone. The Great Barrier Reef north of

Figure. Annual Carbon Dioxide Peak and Temperature



Global temperature anomalies averaged and adjusted to early industrial baseline (1881-1910).

Source: National Aeronautics and Space Administration Goddard Institute for Space Studies, National Oceanic and Atmospheric Administration National Center for Environmental Education, Earth System Research Laboratories.

Figure reprinted with permission from Climate Central. Accessed July 12, 2022. https://www.climatecentral.org/climate-matters/peak-co2-heat-trapping-emissions

Box. Suggested Talking Points About Health and Climate Change[a]

- Global heating-climate destabilization directly affects human health. *(See Table 1)*
- Crossing boundaries diminishes Earth's ability to sustain life. *(See Table 2)*
- Greenhouse gases heat Earth by absorbing and emitting photons of infrared energy trapping them in the atmosphere.
- Climate change causes geopolitical instability and population migration
- Individual choices can lessen global heating.
- National and international cooperation can curtail global heating.
- Particulate air pollution accumulates in the human body.
- The climate crisis can be solved by drastically lowering fossil fuel combustion.
- Some factors such as reduced ice cover speed up global heating.
- Acidification and lower oxygen concentrations in oceans and lakes reduce seafood harvests.
- Extreme heat, droughts, and floods reduce agricultural harvests.
- Literature may address global heating-climate destabilization in ways that are more powerful than science.

[a]Although disparate, these messages are all about human health.

Australia – the largest shallow water reef system in the world and home to approximately a million marine species – already has lost half its corals.[7]

Hunger

Global hunger and undernutrition are expected to increase because of climate destabilization. Tropical and subtropical farmers will experience greater difficulty growing crops due to heat and drought. While farmers in northern latitudes may experience a longer growing season and higher yields, the net effect is expected to be an agricultural decline. The IPCC has predicted an 8% to 14% reduction in corn production at 2 °C (3.6 °F) of warming.[7] If this warming occurs, central Europe, the Mediterranean and Amazon regions, and most of Africa are expected to experience more hunger and undernutrition, while drought may reduce farm yields in the western US.[7]

Literature

The novel *Never Let Me Go* by Kazuo Ishiguro is a science fiction story about adolescents becoming aware of terrible information that their adult caregivers are trying to conceal. [12] This tale may offer insight into how a 10- or 12-year-old child may perceive climate change as they hear information fragments from different sources.This is a powerful story read from a climate change perspective and may be easy to bring into a conversation.

QUICK ACCESS TO CLIMATE DATA

During a conversation, finding weather data quickly and easily may be helpful, but these data are vast and may require specialized knowledge to locate. One site that permits easier and faster searches is www.climatecentral.org. The climate scientists and meteorologists who maintain this website have tried to create a user-friendly site for nonspecialists.

To search for a temperature change in a particular city, click on "resources," then "graphics," then type in the name of the city. The website provides the state. When you click on the state, the website repeats the city name. Click on the city name and graphs of data from that city appear below. Graphs are labeled and easy to understand.

To search for information on weather disasters or climate science, go to "resources," then "graphics," then "search for topics." Click on a topic and related graphs appear below.

To search by keyword, go to "resources," then "graphics," then "keyword" and enter your word. Related graphs will appear. The figure is an example of a climate central graph of Earth temperatures and atmospheric CO_2 concentration over time.

ACTIONS TO MITIGATE CLIMATE CHANGE

Acting as an individual[28]

- Use your vote to protect children.
- Reduce personal carbon emissions (see below).
- Study climate change, talk about the weather.
- Create an emergency plan and kit (planning varies by location, prepare for floods in Wisconsin).
- Participate in or donate to an organization that advocates for climate stability.
- Plant a garden or trees

Reducing personal carbon footprint[30,31]

- Avoid flying.
- Reduce driving and/or drive a high gas mileage or electric vehicle.
- Use and support investment in public transportation.
- Bike or walk when possible.

- Choose renewable energy whenever possible.
- Eat less beef or, if possible, eat grass-fed beef.
- Use light emitting diode (LED) light bulbs.
- Replace old appliances at the end of their lifecycle with Energy Star appliances.
- Weatherize your home.

Global and national goals to mitigate climate destabilization[32-34]

- Produce electric trucks, buses, cars, and ships.
- Build electrically powered buildings.
- Restore topsoil with cover crops and reduced tillage; use less synthetic fertilizers.
- Raise grass-fed, rather than crop-fed, animals.
- Protect half of the oceans and land as nature sanctuaries.
- Produce all plastic to be recycled/no single-use plastic.
- Reduce CO_2 emissions from steel and cement production.
- Remove greenhouse gases from the atmosphere by both natural means (forest, land, and soil restoration) and engineering methods (carbon capture and storage).
- Maintain a stable (not increasing) human population.

CONCLUSIONS

The key message about health and climate change is that a drastic reduction in the burning and mining of fossil fuels solves the problem. Otherwise, the health of people will suffer from agricultural and seafood declines, geopolitical instability, lack of potable fresh water, and heat and weather extremes. Droughts and floods are expected to be a frequent manifestation of climate breakdown, more powerful cyclones will probably destroy infrastructure and create enormous expense, and heat waves will likely cause many human deaths. On the other hand, everyone would live a healthier life in a world that has a clean energy economy.

Sadly, the cumulative emissions of greenhouse gases are a key factor in determining the health and quality of life today and for future generations. Preserving as much climate stability as possible reduces the health effects of global heating, air pollution, and ocean acidification. This can be accomplished with drastic reductions in atmospheric greenhouse gas concentrations. It may not seem like one person can make a difference; however, discussing climate change may be one way an individual can address the climate crisis. Although lives are busy, climate and health conversations are possible. It is also possible that taking action to reduce the climate crisis will reduce one's personal fear about climate destabilization. Action has been called the antidote to despair.

Health care providers are among the trusted voices in our society and can be an effective voice for children and future generations. Consider talking about the scientific consensus on climate change and why scientists and physicians have recommended drastic reductions in greenhouse gas emissions. Swedish environmental activist Greta Thunberg, who started school strikes for climate, says that no one is too small to make a difference.[35]

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Joseph E. Kerschner, MD

Continuing to Address the Shortage of Family Medicine Physicians

Joseph E. Kerschner, MD

The United States is facing an ever-worsening shortage of primary care physicians – about 40% of whom are family medicine practitioners, according to the American Academy of Family Physicians (AAFP). This shortfall of primary care physicians is expected to top 52,000 by 2025. To address this shortage, the AAFP and seven other national and international family medicine organizations have worked together to increase the number of family medicine physicians in the US and to enhance the likelihood that US medical students pursue family medicine as their specialty.[1]

In Wisconsin in particular, the shortage of primary care physicians is acute. A report published in 2018 by the Wisconsin Council on Medical Education and Workforce found that there would be a shortfall of 745 primary care doctors in the state by 2035, at which time about 40% of family doctors are expected to retire.[1]

More recently, a 2021 baseline scorecard that tracks support for high-quality primary care (funded in part by the Milbank Memorial Fund and The Physicians Foundation) noted that in 2020, there were only 39 primary care physicians in medically underserved areas in the state per every 100,000 population, and 78 primary care physicians per 100,000 population in areas not medically underserved. Also in 2020, there were only 36 primary care residents per 100,000 population and only 20% of new physicians entering the workforce in Wisconsin were primary care physicians.[3] The scorecard further found that the US is systematically underinvesting in primary care; the primary care physician workforce is shrinking and gaps in access to care appear to be growing; and too few physicians are being trained in community settings.

...the US is systematically underinvesting in primary care; the primary care physician workforce is shrinking and gaps in access to care appear to be growing; and too few physicians are being trained in community settings.

The Medical College of Wisconsin (MCW) has long held that primary care improves population health and decreases health disparities, and that a robust family medicine workforce is critical to ensure that patients throughout the country have appropriate, effective and accessible care for generations to come.

In my "Dean's Corner" in the July 2019 issue of the *Wisconsin Medical Journal* on "Helping to Alleviate the Projected Physician Shortage" (clearly a continuing problem!), I noted that among the most impactful ways to address this issue is through the creation of additional graduate medical education (GME) residencies.[4] I shared a number of MCW's successes in this area, including the creation of two new 4-year residency programs attached to our regional medical school campuses in central and northeastern Wisconsin, as well as new family residency programs in the Milwaukee area and Green Bay. I concluded the column with the promising words, "We look forward to providing additional data on these successes in the years to come."

Fast forward to 2021, when, under the leadership of Joseph Gravel, MD, chair of MCW's Department of Family and Community Medicine, the new Froedtert & MCW South Side Family Medicine Residency Program was accredited – offering bilingual and culturally competent care to Milwaukee's Hispanic and Latinx patients and their families.[5] In June 2023, the Froedtert & the Medical College of Wisconsin Forest Home Health Center

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opened; it serves as the home for this new 3-year family medicine residency program training six residents per year – with 18 total residents by the third year. The goal of the program, led by MCW Associate Professor Sabrina Hofmeister, DO, is to train family physicians with the expertise and skills to provide individualized, evidence-based, culturally competent care to patients and families to address the growing need for compassionate and skilled family physicians who can provide care to underserved communities.

In October 2022, the Froedtert & MCW North Side Family Residency Program achieved full accreditation through a partnership of Milwaukee's North Side community health centers – led by Milwaukee Health Services, Inc. (MHSI), MCW's Department of Family and Community Medicine, and Froedtert Hospital.[6,7] The new residency program will address the growing need for compassionate and skilled family physicians who can provide outstanding care to underserved communities, directly addressing existing health inequities, especially among the Black/African American community. Funding for this new 3-year residency in family and community medicine is being provided by the US Department of Health Resources and Services Administration (HRSA) to MHSI, which will pass it along to MCW through the Medical College of Wisconsin Affiliated Hospitals, Inc. (MCWAH).[8,9]

Training of the first 14 residents in the initial cohort began in July 2023 under the leadership of residency program director, MCW Associate Professor Camille Garrison, MD. By July 2025, the program will be training the full complement of 42 residents. Outpatient rotations will occur at MHSI and other affiliated northside Milwaukee affiliated community health centers, Froedtert & MCW specialty office practices and northside community organizations. Inpatient adult medicine rotations and specialty rotations will occur at Froedtert Hospital and inpatient pediatric rotations at Children's Wisconsin. The program will promote physicians to become health advocates within their respective communities as well as the medical community at large – incorporating a deep understanding of social determinants of health and a commitment to actively reducing health inequities. Through competency-based education and interaction with innovative health care systems and leaders, this new residency program will equip graduates with the foundation needed to practice successfully in the most challenging of clinical settings and align with the needs of the community. The program also seeks to help build a pathway for underrepresented in medicine (URM) students for primary care practice while increasing healthcare access for people living on the north side of Milwaukee.

The diligence and exceptional planning of the people of MCW and its health system and community partners enabled this new residency program to be created and funded by HRSA within a period of less than 6 months instead of the usual 2-year process!

MCW's Department of Family and Community Medicine has a rich 50-year history of training family physicians in the Milwaukee area and beyond to serve diverse individuals through full-service clinics with proactive clinical and social service offerings. Today's MCW family medicine residents can expect a broad and rich experience with learning opportunities across the spectrum of care, specifically dedicated toward learning the aspects of care most important to underserved and underresourced patients and communities.

The new health center and residency programs will increase MCW's reach and improve access to quality health care in the communities we serve – building on the foundation of providing the right care, in the right place and at the right time to the region's diverse populations.

We hope that MCW's recent efforts to expand residency programs in family medicine will be duplicated throughout the state so that our communities (and our patients) will not face as dire a shortfall of primary care physicians as is expected at present. Additionally, we hope that MCW's model of partnering with community health centers will become the gold standard in family medicine residency training.

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