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Gender-Affirming
Practice

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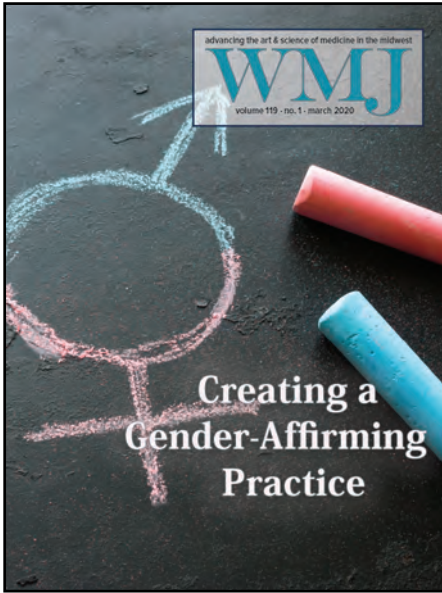
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COVER THEME
Creating a Gender-Affirming Practice

Transgender, nonbinary, and gender-nonconforming patients experience many health disparities compared to the cisgender population. An article in this issue of *WMJ* reviews existing research and explores recommendations for making primary care practices more affirming for this patient population.

Cover design by Kendi Neff-Parvin

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The *WMJ* would like to thank everyone who served as a manuscript reviewer in 2019. Manuscript review is an important collegial act and is essential to the integrity of *WMJ*. We are grateful for the assistance of these individuals in ensuring authors receive objective and insightful feedback on their work.

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117 Years and Going Strong

Sarina Schragger, MD, MS, *WMJ* Interim Editor-in-Chief

Published continuously since 1903, the *Wisconsin Medical Journal* is one of the longest-standing generalist journals in the world. And while it has been undergoing some changes in management, content remains the same.

The transition from being published by the Wisconsin Medical Society to The Medical College of Wisconsin and the University of Wisconsin School of Medicine and Public Health continues to provide new opportunities for the journal. At the same time, the editors remain committed to providing high quality papers from researchers, educators, and clinicians in the Midwest. We encourage junior faculty to submit to the *WMJ* and spend a great deal of time working with young authors to improve their papers. Last year, we used nearly 100 peer reviewers, and each and every one contributed to the final outcome of an article. We thank all of them for their dedication and effort to help maintain the quality of this journal, and we encourage all readers to volunteer as a reviewer. (Sign up at www.wmjonline.org.)

Because the *WMJ* is a generalist journal, we publish a wide range of papers about very disparate topics. Thus, we need both generalist and specialty reviewers. It is often helpful to the editorial team to get a sense of what our “general readers” think about a paper. If it is understandable and engaging even to someone with a different specialty, then it can be a valuable addition to the journal.

For example, in this issue alone, there are papers about clinical, educational, and health care utilization topics. Lodhi et al write about a patient who was hospitalized after taking an overdose of verapamil.¹ The case report outlines how this calcium channel blocker caused acute respiratory distress syndrome.

Hueston and Treat² describe characteristics of applicants to the Medical College of Wisconsin’s regional 3-year campus and compare these applicants to people who apply to the Milwaukee campus’s traditional 4-year pro-

gram. They found that applicants to the 3-year campuses were significantly older and had higher Medical College Admission Test scores. Bryan et al describe resource utilization of patients who access the patient portal through their electronic medical record.³ Perhaps surprisingly, they found that patients who use the patient portal actually had increased utilization of traditional formats of care as well.

This issue also includes review articles and a commentary on timely topics. Bizub and Allen review guidelines for creating a gender-affirming primary care practice;⁴ Wolf et al provide an overview of the array of pathogenic microorganisms carried by *Ixodes scapularis* ticks in the Upper Midwest;⁵ and Kalet et al share their views on allowing medical students to respond to the COVID-19 pandemic.⁶

For faculty members at Wisconsin’s medical schools and for practicing physicians around the state, being a peer reviewer can have many benefits. Reviewers have the opportunity to learn about new topics or read updates on old topics. Serving as a reviewer is an opportunity to start thinking about your own writing as well. What worked well in this article? What didn’t work well?

Reviewing papers is an essential compo-

nent of an academic job and is integral to the academic community as a whole. The editors also welcome senior faculty to mentor their junior partners or fellows in the reviewing process, thereby continuing the academic cycle.

We thank all of our peer reviewers
for their dedication and effort to help maintain
the quality of *WMJ*.

The *WMJ* is an excellent resource for faculty, students, practicing physicians, and other clinicians. In order for it to remain relevant in the current medical environment, it’s essential that contributors, reviewers, and readers all engage in the process of reading, writing, and peer reviewing. Here’s to another 117 years.

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Hearing the Call of Duty: What We Must Do to Allow Medical Students to Respond to the COVID-19 Pandemic

Adina L. Kalet, MD, MPH; Fabrice Jotterand, PhD, MA; Martin Muntz, MD; Bipin Thapa, MD, MS; Bruce Campbell, MD

In the coming weeks, the needs of critically ill patients will likely stretch Wisconsin's hospitals beyond their resource and personnel capacities as the COVID-19 pandemic rolls across the nation. New York City and other regions have been – or will soon be – forced to adopt crisis standards of care (CSC),¹ where health care systems are so overwhelmed that they find it impossible to provide the “standard” level of care to patients, thus confronting health care workers with choices never-before seen in their lifetimes. *In this context of emergency and scarcity, should students be “deployed” to care for patients?* These issues must be

• • •

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addressed now, before this rapidly evolving crisis – and the next one – reaches us.

A week ago, when the discussions were mostly theoretical, our conversations turned on pragmatic concerns around the ethics of least harm: removing students from all patient-contact clinical settings was necessary because (1) they deplete precious personal protective equipment (PPE) that other health care workers desperately need, and (2) as students, medical students are neither adequately prepared nor obligated – as they will be after graduation – to accept personal risk or contribute meaningfully to patient care under extraordinary circumstances.

Medical Education Disrupted

Over the past few days, most US medical students, sidelined in response to bans on group gatherings and the American Association of Medical Colleges (AAMC) recommendations to dial back all clinical education,² have predictably displayed a surge of volunteerism. Although welcome, this phenomenon exposes a third reason to consider prohibiting students from clinical care: if given the option to volunteer, some students might feel coerced to serve, worrying that their absence would trigger reprisal, such as lower grades or being excluded from future opportunities for training or research.

What Others Are Doing

In New York, and other states, senior students are being given the choice to graduate early

and begin their residencies in mid-April instead of in early July.³ Medical educators everywhere are scrambling to connect medical students with meaningful opportunities to serve patients, communities, and health care workers, while linking these activities with course and clerkship objectives. Patient and community education, virtual COVID-19 journal clubs, and telehealth for acute and chronic health issues are a few examples of activities implemented to match community needs, medical student skills, and learning objectives, while still limiting spread of the virus.

Adult Learners Capable of Making Their Own Judgements

Society views adults as being capable of making their own judgements and acknowledges that adults possess and can exercise freedom of choice without undue coercion. Several professions require participants to work in high-risk settings dedicated to the preservation of the lives of other individuals and the protection of society. Much as other young adults right out of high school or college seek out risk-inherent careers as fire fighters, police officers, nurses, first responders, and members of the military, medical students enter their chosen field with a social contract that includes possible hazardous duty.

Adult Learners Ready to Participate

Of course, under usual circumstances, society offers thorough training and requires certification prior to working in risk-exposed profes-

sions. Society also makes contingencies, under extraordinary circumstances, to allow individuals who are incompletely trained to serve.⁴ Although all medical students have gaps in their clinical preparedness, they should, at this stage of education, be adept at “learning how to learn.” Preclinical medical students should be capable of adopting skill sets allowing them to provide supervised medical care. Clinically experienced senior medical students, having already worked in interprofessional teams with practicing clinicians, should be proficient at learning how to screen, monitor, triage, and provide basic, urgent care for patients with symptoms of COVID-19 and other patients with a host of acute or chronic concerns. Moreover, their skills can readily be augmented with focused, succinct training; our duty is to develop and deliver this training.

Professionalism, Moral Agency, and Professional Identity Formation

Medical students participate in ceremonies during orientation to medical school where they receive their first white coats and usually recite a professional oath that they will reiterate at the time of graduation. As medical students, they enter as novices into a profession that has a clear and unambiguous commitment to moral fidelity, justice, and service.

We believe that enabling the safe and effective deployment of our students back into the clinical arena is the responsibility of medical educators; it is our civic, moral, and educational duty to quickly and creatively enable our students to act on their altruism, courage, and sense of duty.

Fundamentally, a particular student’s response to a “call to duty” is a combination of their sense of professional obligation, moral agency, ability to tolerate moral ambiguity, level of emotional resilience, and maturity of their professional identity. Professional Identity Formation (PIF), a critical goal of medical education, is defined as “the process of internalizing the medical profession’s core values and beliefs,” so that one begins to “think, act, and feel like a physician.”⁵ Medical students develop their medical PIF at different points in their education.⁶ On entry to medical school, some have already internalized this identity.

Others – even as they near graduation – have yet to do so; but most are already thinking, acting, and feeling ready to act as physicians.

We believe that frustrating the altruism of our novices is paternalistic, disingenuous, and detrimental to their future careers in medicine. Even while preserving PPE, most medical students can be deployed to procure, produce (with a sewing machine!), and distribute this equipment. And although there are risks to students re-entering the clinical arenas, medical education leaders must collaborate with health systems to develop meaningful roles for students to fill identified needs, effectively and efficiently train them and other health care workers to collaboratively care for patients in our transforming work and learning environment, and study the impact of student re-entry. We need to understand and tolerate the reality that some students, as is the case with other health care workers, will not be able to safely participate in all activities due to underlying health conditions, personal exigencies, and other risk factors. As the situation evolves, the needs to care for our community will change and, in response, students will nimbly adapt.

Avoiding Coercion

Clerkships will be transformed and students will have multiple options. Those that choose to volunteer to participate under supervision should undergo interviews that screen for students enlisting for the wrong reasons (eg, a sense of coercion, a “hero-type” approach, worrisome psychological conditions, etc) and make certain that they understand the implications and unknowable risks of their service.

As an institution dedicated to training the next generation of physicians according to the triple aim of medical education – character, caring, and competence – we have an obligation to create the conditions for these students to demonstrate their altruism, courage, vulnerability, and dedication to be present to ease suffering. Ultimately, however, this effort will require a commitment of the whole education community and the world beyond to support, nurture and help those rising to the call.

In Summary...

A few times each generation, there are crises. This is ours to seize.

Because we are health care professionals, we seek opportunities to help patients and colleagues, even though it is safer to stay home. The instinct to run toward terrifying, uncertain situations rather than away is a result of our character, education, and training. We watched our role models do the same. Our students are already showing that they, too, have this instinct, and it is up to us to develop safe, meaningful, and life-affirming opportunities for them to serve.

Our goal is to work together, finding ways to—as safely as possible—integrate students into the fold. As medical educators we will use the pandemic as a teaching moment while everyone strives to provide compassionate, character-driven, competent care and healing for as many of our fellow human beings as we possibly can.

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A Review of Clinical Guidelines for Creating a Gender-Affirming Primary Care Practice

Brian Bizub; Brittany Allen, MD

ABSTRACT

Introduction: Transgender, nonbinary, and gender-nonconforming (TNG) patients experience many health disparities compared to the cisgender population. Despite numerous recommendations for working with TNG populations in health care, many TNG patients report having negative health care experiences in and are unable to access competent and affirming primary care.

Objective: To review the literature and current recommendations for primary care clinicians to make the clinic setting more affirming for TNG patients.

Methods: We conducted a literature review of existing recommendations and research surrounding creating affirming primary care environments for TNG patients.

Results: Clinicians can make clinic environments more affirming by making the physical space TNG friendly, documenting gender identity properly, addressing patients according to how they identify, ensuring confidentiality, understanding insurance issues, using affirming language and clinical approaches, and accessing training about working with TNG patients.

Conclusions: In cooperation with clinic administration, clinicians should utilize guidelines available to advocate within their own clinic to make recommended desired changes to the clinic environment. While current literature and recommendations exist, they often lack specific guidance on how to accomplish many of these changes. Future guidelines should include specific examples and implementation methods. Many changes to the clinic environment necessitate cooperation from clinic administration.

INTRODUCTION

There are numerous health disparities among transgender, nonbinary, and gender-nonconforming (TNG) people compared to the cisgender population.¹ (See Table 1 for definitions.^{2,3}) Depression

• • •

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is much more common in TNG populations, with estimated rates as high as 4 times that of the general population.⁴ A recent study of TNG adolescents found that 14% of all respondents had attempted suicide, with half of transmasculine adolescents reporting suicide attempts.⁵ In TNG adults, 41% report at least 1 suicide attempt in their lifetime.⁶ Risk behaviors, such as smoking and substance use, are also more common in the TNG population,⁷ and TNG people are more likely to have multiple chronic conditions and higher rates of disability.⁷ The burden of HIV is higher in the TNG population, with rates of HIV infection as high as 16% to 25%.⁸ Gender-based rejection, victimization, discrimination, and lack of identity affirmation contribute greatly to health disparities among the TNG population,^{9,10} and this minority stress is thought to be the etiology for poor mental and physical health outcomes in TNG populations.¹

TNG patients also have difficulty accessing quality health care. In a 2015 survey of TNG individuals, only 6% of respondents indicated that their routine care clinician knew almost everything or most things about TNG care.¹¹ Nearly one quarter of respondents that sought health care reported having to teach their provider about TNG health care, and more than one third of TNG adults have experienced more than 1 negative experience in health care in the last year.¹¹ One in 5 (21%) of TNG adults experienced verbal harassment in the health care setting,¹² while others have been outright denied care by clinicians.¹³ Based on this data, it is no surprise that nearly one third of TNG adults reported that they had not revealed their gender to any of their health care providers, and 23% of TNG respondents

did not see a doctor when they needed to because of fear of being mistreated.¹¹ In a study among Canadian TNG youth, 68% of respondents reported forgoing needed mental health care and 33% reported forgoing needed physical health care in the last 12 months.¹³ More than half of those who chose to forgo care cited being afraid of what the doctor would say or do as a reason for not getting care.¹³

To address these barriers to care, numerous recommendations now exist as a reference for clinicians to make their practice more affirming to TNG patients. Despite this, physicians still perceive numerous barriers to providing care to TNG patients, among them the lack of educational and training resources.¹⁴ We aimed to review the recommendations available for clinicians to improve their ability to provide affirming care for their TNG patients.

OBJECTIVE

To synthesize existing literature and recommendations for how clinicians can make their clinic environments more affirming to facilitate positive health care experiences and improve accessibility to health care for TNG patients.

METHODS

An initial literature search of existing recommendations for improving primary care environments for TNG patients was done using Google, Google Scholar, Pubmed, and Web of Science searches. Search terms included “affirming environments for LGBTQ (lesbian, gay, bisexual, transgender, queer/questioning) patients,” “affirming environments for transgender patients,” “affirming environments for LGBTQ youth,” “affirming environments for transgender youth,” “transgender youth primary care,” “transgender primary care,” “transgender health care,” and “LGBTQ youth primary care.” Selected articles from the literature search included recommendations, review articles, and primary research on creating affirming environments for LGBTQ and TNG populations. These came from advocacy organizations, professional organizations, nonprofit organizations, and academic research from any country. Excluded articles included articles published before 2000, recommendations on medical management of TNG patients, and recommendations that were not intended for primary care or health care environments. After the initial literature search, references from 3 prominent guidelines^{2,15,16} were used to supplement the articles found in the first search.

The authors excluded articles from the study if they failed to provide unique, novel, or useful information compared to other

Table 1. Terms Providers May Use or Hear When Talking With Patients About Gender Identity^{2,3}

Cisgender	A person whose gender identity aligns with their sex as signed at birth.
Gender-affirming surgery (GAS)	Surgery that changes a person’s body to more closely align with the gender they identify with.
Gender binary	The idea that there are two genders: male and female. This concept is often challenged as there are people with gender identities that do not fall within the gender binary.
Gender dysphoria	Distress experienced by some individuals from conflict between assigned sex or gender and their gender identity.
Gender fluid	A person who does not identify with a single, fixed gender. This may mean that their gender identity changes from day to day.
Gender identity	A person’s internal sense of being male, female, both, neither, or another gender.
Gender nonconforming	When gender expression differs from societal norms of boy/girl or man/woman.
Nonbinary	A person whose gender identity is something other than strictly man or woman.
Transgender	An umbrella term to describe when a person’s gender identity differs from the sex assigned at birth.
Trans man/transgender man/female-to-male (FTM)	A person whose gender identity is male or masculine; generally their assigned sex at birth was female.
Trans woman/transgender woman/male to female (MTF)	A person whose gender identity is female or feminine; generally, their assigned sex at birth was male.
Transition	The process of coming to recognize, accept, and express one’s gender identity.
Transphobia	The fear of, discrimination against, or aggression toward TNG people.

articles. The authors accepted recommendations based on expert opinion, observational studies, or randomized clinical trials. During the literature review, the authors noted common themes that the reviewed articles focused on and used these distinct domains to organize results.

RESULTS

Following the literature search, one of the authors identified a total of 44 articles; 24 met inclusion criteria for full review. Themes identified as areas for intervention included the physical clinic environment, clinic policies, documenting sex and gender, confidentiality, insurance coverage, clinical interactions with TNG patients, and training for staff and clinicians.

The Physical Environment

A primary theme identified was recommendations for creating an affirming clinical space for TNG patients, with recognition that these visual cues can send a message that increases TNG patients’ comfort¹⁷ and signals to TNG patients that it is safe to disclose their gender identity. Considerations in creating an affirming physical space include reviewing visible cues in clinical and waiting spaces, language used on forms or intake paperwork, and patient facilities, such as bathrooms and changing rooms.

Media available in public and waiting spaces can send a powerful message. Signage and artwork prominently displayed in the clinic should represent diverse experiences,¹⁷ including artwork that depicts LGB couples, TNG individuals, or LGBTQ-friendly symbols such as rainbows or safe space terminology.¹⁸ Informational handouts and posters should avoid assuming the reader is cisgender or heterosexual.¹⁹ Clinics should have informational materials specifically for TNG patients, such as information

on talking about gender identity with clinicians and family, social transition, safe practices for tucking genitals so that they are less visible, safe uses of binders to conceal breast tissue, and information on gender-affirming hormones.¹⁶ LGBTQ-themed magazines and handouts should also be included in waiting areas literature.²⁰ Clinicians and staff can indicate that they are LGBTQ friendly by wearing LGBTQ-friendly pins or lanyards.¹⁹ They can also indicate their preferred pronouns on their nametags or identification badges, promoting the discussion of gender identity with patients.²¹

Forms or other paperwork are often one of the first interactions that patients have in a clinical setting, and the questions asked can lay the framework for patients' expectations about whether a clinic is a safe place for TNG people. Language in forms or intake paperwork should be designed to be open and affirming. Examples of affirming language include using "partner" instead of "boyfriend" or "girlfriend" and "parents" instead of "mother" and "father."^{16,20,22,23}

Bathroom access is a particularly important opportunity to provide an affirming physical environment for TNG patients. Single stall unisex restrooms provide optimal privacy for patients.¹⁶ If restrooms must be separated by gender, clinics should implement a policy that allows patients to use whichever restroom they are most comfortable using. Restrooms should be prominently display this policy so that patients are aware of it. Installing stalls with walls that reach all the way down to the floor can also provide more privacy in shared bathrooms.^{19,21}

These steps to ensure affirming space should not just be limited to waiting rooms and common areas. Exam rooms should also contain affirming physical elements such as artwork, safe space stickers, or informational materials.^{16,17,24} Spaces outside the clinic that patients commonly use while entering or exiting the clinic should also be affirming. This includes parking lots or shared spaces with other offices in the same building. Interactions with staff of nearby establishments, signage inside and outside of shared physical space, and interactions with other users of nearby spaces should all be considered as potential impacts on patient experience.¹⁷

Clinic Policies

In order to communicate to patients and staff that serving patients of all gender identities is a priority, all clinics should have a non-discrimination policy that explicitly states that it welcomes all patients regardless of gender identity or sexual orientation.^{19,20} Additionally, clinics should establish a patient Bill of Rights that ensures patient privacy and confidentiality for all patients.²⁵ This should outline a patient's right to refuse care from any medical personnel that are not essential, such as medical students or residents. While all patients should be encouraged to welcome learner participation, it is important to recognize that it may be important to have protected avenues to minimize any unwanted contact

with staff, particularly for populations with a history of negative experiences in health care.²⁵ Clinics should establish a policy for addressing inappropriate behavior or comments in the clinic by staff, learners, or other patients.²⁶ Outside of specific posted policies, clinics can actively show their support for the LGBTQ community by observing, supporting, and participating in days such as LGBTQ Pride Day or Pride Month, National Transgender Day of Remembrance, and Day of Silence.²⁰

Documenting Gender Identity

Collecting gender identity information can contribute to establishing an affirming environment for TNG patients in a number of ways: (1) identifying for clinic staff how each patient would like to be addressed; (2) providing clinicians information about gender identity that is necessary to provide the highest quality care; and (3) enabling the collection of population health data to further research on LGBTQ health and health disparities.²⁷ Collecting gender identity on intake forms is a convenient way to gather information in a way that allows patients to self-identify their own chosen name and pronouns, gender identity, sex assigned at birth, and, if appropriate, sexual orientation.²² While there is sometimes the concern that patients will be offended by adding gender identity as a item on intake forms, a distinct minority (only 3%-11%) of all LGBTQ and non-LGBTQ patients reported being offended by such questions.²⁸

Forms should allow for patients to record their legal name in addition to a name that they choose to be called (chosen name).²⁶ The chosen name should be used in any communication with or about the patient if the patient notes that as their preference.² The patient's legal name should be used only when necessary, such as billing the patient's insurance or labeling lab orders and prescriptions, or if requested by the patient due to safety or other concerns.^{15,27,29} In addition to listed options, forms also should have spaces for patients to write in responses to questions about gender identity or sexual orientation so that they can self-identify with a term or label that best describes them.²⁹ Some patients may not be comfortable with disclosing sexual orientation or gender identity, so questions about these preferences should include an option to decline to answer.¹⁷ Patients may be more comfortable with disclosing this information if provided with information on how the clinic plans to use and store their responses; this can be described in a patient education handout or a description on the intake form.¹⁷

While collecting gender identity and other patient information is useful for clinic staff, staff still must use patients' chosen names and pronouns correctly for this practice to be affirming. To encourage these practices, it is critical to incorporate gender identity information properly in the electronic health record (EHR).^{29,30} The chosen name and pronouns of each patient should, if possible, be displayed on the EHR banner at the top of each patient chart so that staff utilize the correct patient identifiers,²⁹ and all

staff should be trained on using these tools for this purpose. EHR systems can also support clinicians in the preventive medical care of TNG patients, as decision support tools in some EHRs can remind clinicians to do routine health screenings on patients based on their anatomy.²⁹

A common barrier identified in collecting and using gender identity information is the inflexibility of EHR systems.³¹ A workaround to EHR limitations is to use communication tools in the EHR to remind staff members to address a patient properly. For example, EHR tools such as FYI flags, sticky notes, banners, comment fields, and the patient problem list are all places where a patient's chosen name or pronouns could be stored, as long as staff are oriented to that workflow.

Clinics can achieve change by organizing a team of staff members to serve as “champions” to implement collection of gender identity. Such a team might consist of an administrator, representatives from health information technology, and clinical and non-clinical staff, and also would be responsible for ongoing quality improvement of the implementation process.²⁸ Clinics may want to initially test and evaluate gender identity collection on the EHR in a single clinician's patient panel and then expand this to multiple clinicians after identifying and addressing barriers to implementation and finding appropriate workarounds where needed.

Legal Issues and Confidentiality

Clinicians should be prepared to provide support in processes around legal documentation of gender when caring for TNG patients. To change legal gender on federal documents such as passports, clinicians are required to certify that the patient has undergone “necessary” medical or psychological treatment for transition. Since there is no definition of what these treatments are, clinicians are free to interpret what “necessary treatment” is.³² For state documents such as driver's licenses and birth certificates, requirements vary depending on the state.³²

Ensuring confidentiality is critical for building trusting relationships with all patients and is essential when asking patients to disclose their gender identity.^{19,33} If a clinician divulges confidential information such as gender identity to an employer, parent, school, or others, it may result in significant harm or distress to the patient.³⁴ Gender identity should be treated as confidential information; it should not be shared with anyone else beyond health care personnel who need to know this information for patient care, including parents if the patient is an adolescent.³² It is not the duty of clinicians to inform parents of their child's gender identity,³⁴ however, clinicians should be ready to assist families with accepting their child's gender identity, if the patient would like the clinician to be involved in this discussion.^{30,35}

Clinicians also must be aware of how patients would like sensitive information to be shared with them outside the clinic. Patients may request that their gender identity not be shared with certain entities, such as their family, school, or work. If this is the

case, it may be helpful to make a specific plan with the patient about how to best honor their confidentiality when trying to reach them.¹⁹ In cases where clinicians must divulge confidential information, such as in the cases of abuse or significant risk of harm to self, the minimal amount of information necessary should be shared. The patient's gender identity need not be included in a report if it is not relevant to the reason for having to report patient information.¹⁹ It is important to be aware that there are conflicting opinions regarding the confidentiality of gender identity outside of the medical community. House Bill 658 is a proposed policy in Ohio that would require clinicians working with TNG minors to report the child's gender identity to their parents,³⁶ despite the direct conflict that this offers to widely recognized tenets of medical professionalism and ethics.³²

Insurance Coverage

Coverage for gender-affirming care such as hormone therapy and gender-affirming services varies among insurance providers. While Medicare does cover hormone therapy and gender-affirming surgery deemed medically necessary by clinicians, Medicaid coverage of these services varies from state to state, and private insurance coverage varies between insurance providers.³⁷ Private insurance providers may deny coverage of preventive services based on patient anatomy if it does not correlate with the patient's listed gender. Clinicians should be aware of this issue and be ready to appeal coverage denials.¹⁴ They should be able to access information about what gender-affirming interventions a patient's insurance will likely cover, how patients can meet the criteria for coverage of an intervention, and changes to the patient's policy that may affect their coverage for gender-affirming care.³¹

In 2016, the Department of Health and Human Services extended a provision in the Affordable Care Act so that private insurers could not change covered services based on gender identity.³⁸ This means if an insurance provider covers a service for cis-gender patients, such as hormone therapy or breast implants, they must also cover the same services for TNG patients. However, this policy has been targeted recently by both local and federal entities.³⁸ In response, many states have passed their own health insurance gender discrimination laws. Because of the ever-changing landscape of health care policy and gender-affirming services, it is important that clinicians pay attention to federal and state policies that affect insurance coverage for TNG patients. As navigating insurance issues for TNG patients places an increased administrative burden on the clinician, clinics may consider designating a staff member to do this.³¹

Interacting with TNG Patients in the Clinic

To best treat TNG patients, clinicians need to be aware of their own misconceptions, bias, and stereotypes, as well as other communication barriers that may influence the care of these patients.^{16,17} Displaying discomfort when treating TNG patients may result in

Table 2. Examples of Terms and Phrases Providers Can Use to Talk to Patients in a Gender-Affirming Way^{2,43}

Asking for a patient's preferred name and pronouns	What do you prefer to be called? What name would you like us to use? Pronouns are the words that others use to describe us when we're not there. What pronouns do you use?
Asking about names if they do not match health records	Could your chart be under another name? What is the name on your insurance?
Apologizing for using a name or pronoun that are not the patient's preferred name or pronoun	I apologize for using the wrong pronoun: I work hard to make sure I address all my patients appropriately and did not mean to disrespect you. How would you like to me to refer to you?
Asking patients what their gender identity is	What is your current gender identity?
Asking younger patients what their gender identity is	Some of my patients feel as though they're more of a boy, or a girl, or even something else. How would you identify yourself?
Asking patients for their assigned sex at birth	What sex were you assigned at birth as shown on your original birth certificate?

lower quality care and cause patients to feel uncomfortable with seeking medical care.³³ Clinicians that have bias against TNG patients have less knowledge of TNG care independent of amount of education they receive on the subject.³⁹ Trainings and activities around the TNG population and addressing unconscious bias are essential for clinicians. When speaking with patients, the use of hetero- or cisnormative statements or questions—those that assume that the patient is cisgender and heterosexual—should be avoided. For example, a person that identifies as female may be asked if she has a partner rather than a heteronormative question around whether she has a husband or boyfriend. Clinicians should also refrain from referring to cisgender patients as “normal” when comparing them to TNG patients, knowing that TNG patients have normal, healthy gender identities.^{15,16,26} While some TNG patients may be eager to provide information, some patients may prefer to build a relationship with their clinician before sharing personal information about their gender identity.^{19,40} Clinicians should honor and respect a patient's decision to provide information about their gender identity and be mindful that TNG patients may have had prior negative experiences in health care.¹⁶

Primary care clinicians should ask about gender identity on a regular basis.⁴¹ While clinics may ask about gender identity on intake forms, some patients may be more comfortable disclosing this information to only the clinician.⁴² When asking about a patient's gender identity, clinicians should not assume the patient's gender identity based on appearance and, if unsure about the patient's gender identity, should ask open-ended questions for clarification.¹⁶ Because this is often a sensitive topic for patients, clinicians must be intentional about asking about gender identity in an appropriate manner that includes affirming language.^{16,41} Terms that assume gender identity such as “sir” or “ma'am” should also be avoided and replaced with words such as “the patient” (in 3rd person) or “you” (when talking to the patient).² (See Table 2 for examples.)

TNG patients may use varying terminology to describe their

gender identity. For example, TNG patients in Native American communities may refer to themselves as “Two-Spirit,” a term for people who are both masculine and feminine.⁴⁴ When clinicians know common terminology used by TNG populations, this can help signal knowledge and experience to TNG patients.^{15,18} When discussing a patient's gender identity with the patient or with other staff, clinicians should use the terminology that a patient uses to identify themselves.^{16,19} For example, if a patient refers to themselves as “gender non-conforming,” this is the term that should be used when discussing their gender identity; in this case, terms such as “transgender” or “non-

binary” may not be appropriate to describe this patient's gender identity. Clinicians also should do the same with the patient's chosen name and pronouns. To obtain a patient's chosen name, clinicians should ask patients what they prefer to be called.¹⁶ Clinic staff that do not use a patient's chosen name or pronouns should be corrected even if the patient is not present.^{2,19}

As with any patient, a thorough history is necessary to provide quality primary care for TNG patients. Clinicians also must decide what is appropriate to ask TNG patients depending on the context of the visit. For example, an anatomical inventory is not appropriate to obtain if the patient is presenting with an upper respiratory infection.¹⁵ In providing primary care, a thorough social and sexual history should be taken as it should be for all patients to screen for risk factors for depression, suicidality, trauma, exposure to violence, HIV, sexually transmitted infections, and substance use. Primary care providers should take an inventory of a patient's anatomy and be ready to provide screenings and treatment based on anatomy rather than assumptions about gender identity or sex assigned at birth.³¹ A patient's history or plans for gender-affirming surgery should be elicited as well. While many TNG patients benefit from gender-affirming surgery, clinicians should not assume that all patients will want or pursue gender-affirming surgery.⁴⁵ Clinicians should also ask about a patient's plans for hormone therapy. If a patient reports that they are receiving hormone therapy, the clinician should inquire the source of the hormones they are taking. Patients may obtain hormones from a source other than their clinician and inject these hormones on their own,⁴⁶ which increases risks related to injection and impure medications. Clinicians also should ask about practices such as tucking genitals so they are less visible, using binders to conceal breast/chest tissue, and injecting silicone into breast tissue to make the breasts appear larger.³¹ Clinicians should become aware of the potential sequelae of these practices, and be ready to treat and counsel patients experiencing these.¹⁵

If they have avoided health care settings, TNG patients may have not had a complete physical exam in years. As for all patients, a physical exam may be uncomfortable, traumatic, or embarrassing for some TNG patients, and they may have intense emotional reactions to parts of an exam.⁴⁵ To relieve anxiety, clinicians should discuss the aspects of the physical exam with the patient and explain why sensitive parts of the exam are necessary. A chaperone should be offered when sensitive exams are to be performed.³² Physicians should give all patients extra autonomy during the exam. For example, clinicians may allow a patient to insert the speculum themselves when performing a cervical exam.³¹ During an exam, the use of anatomical terms associated with a gender such as breasts or testicles should be avoided and replaced with gender neutral terms such as chest and genitalia or the words that the patients uses to describe their anatomy.⁴⁵ Physicians should be able to recommend resources to patients, such as gender-affirming surgeons, behavioral health providers, hair removal providers, and social support resources that are competent in working with TNG patients.³¹

Training

By training staff on providing affirming care for LGBTQ patients, clinics can prevent future mistreatment of TNG patients.^{2,16} All clinicians and clinic staff should receive training so that TNG patients receive appropriate care when with any clinic staff.^{18,40} While some TNG patients may be willing to teach their clinician about TNG care, they do want their clinician to have basic knowledge of care and resources for patients.⁴⁷ As discussed in this review, training topics may include TNG health issues and cultural competency, gender-affirming care, collection and use of gender identity, and confidentiality. Inviting local TNG community members to discuss their experiences and treatment in health care settings may be a powerful training method that connects real-life experience with recommendations,²⁴ though care should be taken to compensate people appropriately for their time and expertise. The Human Rights Campaign recommends that staff receive, at minimum, 1 hour of training on working with LGBTQ populations annually.⁴⁸

Training for working with LGBTQ patients should become standard practice for all new employee hires.^{15,27,29,49} Because health care for TNG patients is a rapidly developing field, regular trainings on health topics for TNG patients are recommended. Clinicians should familiarize themselves with both local and electronic resources for TNG patients so that they are able to refer patients appropriately.^{16,18} See Appendix 1 for trainings and resources that can be used in health care settings.

CONCLUSIONS

Current literature and recommendations on creating affirming clinic environments for TNG patients have a very clear consensus with consistent themes that involve addressing the physical

environment of the clinic; collection and use of patients' gender identity information, chosen names, and pronouns; clinic policies around nondiscrimination and confidentiality; health insurance issues related to gender-affirming care; affirming language and clinical interactions; and training for all staff.

Many recommendations and policies that are suggested in this review are beyond the control of a single staff person or provider. Creating an affirming environment for TNG patients necessitates not only the cooperation of clinicians, but also staff and clinic and organizational leadership. Despite this challenge, providers and staff can act as advocates to promote affirming practices at the clinic level while advocating for system-wide change. To evaluate areas for improvement, a needs assessment of clinic practices with regard to standards of care for TNG patients should be conducted,³¹ and clinic teams may also reach out to TNG community members to understand their primary care needs and involve them in advocating for clinic changes.³¹ There are many checklists available for use to evaluate the primary care environment (see Appendix 1). To encourage involvement of clinic leadership, clinicians can meet to describe the rationale of change toward gender-affirming care, goals for clinical interventions, and potential costs. If greater support is needed, clinicians can build support by inviting TNG individuals to come speak about their experiences, showing videos or films about TNG experiences, and encouraging other clinicians to do educational activities on TNG health for continuing education credits.³¹

For more information on how to start a TNG health care program at your clinic, refer to "Creating a Transgender Health Program" by the LGBT Health Education Center included in Appendix 1. Current literature and clinical guidelines on TNG health care often lack concrete examples for implementation. For this reason, we have included resources that clinicians and clinic staff can utilize to access specific instructions and trainings on working with TNG patients (see Appendix 1). Future research on creating affirming environments for TNG should address how to implement changes for a more affirming clinic environment and measure impact on the experiences of TNG patients. Further development of interactive trainings and educational opportunities for clinicians, clinic leadership, and clinic staff help ensure that these are universal and accessible.

Despite these shortcomings, there are many accessible resources available for clinicians to provide affirming primary care for TNG patients. If clinicians commit to turning their practice into an affirming space, they can provide access to quality, gender-affirming primary care that TNG communities need and deserve.

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Appendix: The Appendix is available online at www.wmjonline.org.

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Ixodes scapularis: Vector to an Increasing Diversity of Human Pathogens in the Upper Midwest

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ABSTRACT

Introduction: The black-legged tick, *Ixodes scapularis* (*I scapularis*), is now recognized as the deadliest tick vector in the United States. The Upper Midwest, particularly Wisconsin and Minnesota, are endemic to a diversity of tick-transmitted infectious diseases. Although *Borrelia burgdorferi*, the agent of Lyme disease, still accounts for the majority of diagnosed infections, *I scapularis* is known to transmit other bacterial, viral, and parasitic agents.

Objective: To provide an overview of the array of pathogenic microorganisms carried by *I scapularis* ticks in the Upper Midwest.

Methods: A literature review was conducted to collect and analyze current information about *I scapularis* lifestyle, transmission, microorganisms carried by the arthropod vector, and the diseases that occur as a result of infections with these microorganisms in the Upper Midwest.

Results: Diagnosis of co-infection from tick-borne zoonosis in humans has increased over the last 2 decades. Since *I scapularis* can transmit multiple pathogens, it is clinically important because different diagnostic testing and treatment strategies may need to be implemented for a patient with *I scapularis*-borne infection(s).

Conclusions: This review has concentrated on *I scapularis*-transmitted diseases affecting the Upper Midwest and has explored the ecology of the *I scapularis* vector and its role in pathogen transmission.

INTRODUCTION

In 1982, the black-legged tick, *Ixodes scapularis* (*I scapularis*) was recognized as the vector for transmission of *Borrelia burgdorferi* (*B burgdorferi*), the causative agent of Lyme disease.¹ Lyme disease is the most frequently reported vector-borne infection in the United States, with more than 300,000 estimated cases occurring

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in the United States.² Besides *B burgdorferi*, *I scapularis* also can transmit *Anaplasma phagocytophilum* (human granulocytic anaplasmosis), *Borrelia miyamotoi* (*B miyamotoi* disease), *Borrelia mayonii* (Lyme disease), *Babesia microti* (babesiosis), *Ehrlichia muris* subsp *eauclairensis* (ehrlichiosis), and Powassan virus/deer tick virus (viral encephalitis).³⁻⁵

Human disease caused by *I scapularis*-transmitted pathogens correlates with vector abundance and pathogen endemicity. Vector transmission is spreading beyond known endemic areas due to climate change and the dispersion from source populations by hosts.^{6,7} Pathogen hosts acquire, maintain, and transmit pathogens, spreading them to naïve and already infected tick populations.⁸ The growing prevalence of host co-infection in endemic areas allows for black-legged tick-based transmission of

multiple pathogens to susceptible populations. The risk of human infection with *I scapularis*-borne pathogens depends on complex factors, including the tick distribution in an ecosystem, reforestation, the attachment time of ticks on humans, and the prevalence of pathogens in ticks and reservoir hosts.^{6,8,9}

DISTRIBUTION OF *I SCAPULARIS*

I scapularis is endemic to parts of the Midwest, Northeast, West, Southeast, and Southern United States, and its distribution is correlated with complex ecological factors. The availability of mammalian hosts, landscape, vegetation, and climate indices are all linked to where the vector can survive and thrive. The most important host for black-legged tick survival and reproduction is the white-tailed deer (*Odocoileus virginianus*). Approximately 50%

to 95% of the adult female ticks feed on white-tailed deer.^{9,10} Deer are the primary host of mating ticks, supporting high populations of black-legged ticks.¹⁰

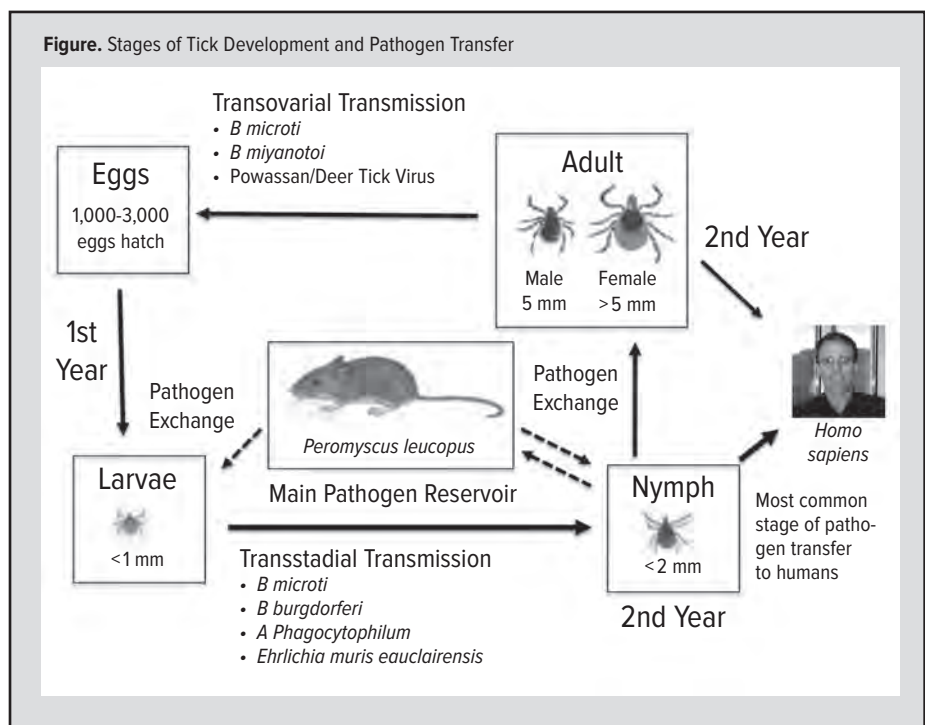
Although white-tailed deer can be hosts, the majority of larvae and nymphs feed on small vertebrate mammals. The most abundant and important host for all *I. scapularis*-acquired pathogens is the white-footed mouse, *Peromyscus leucopus* (*P. leucopus*).¹¹ While *P. leucopus* eradication efforts have led to decreased vector abundance, mouse populations are not linked to *I. scapularis* survival in all habitats.^{12,13}

An abundance of size-appropriate vertebrate mammals is a critical factor in establishing a tick population, but an appropriate landscape and vegetation also are needed for survival. Since the late 19th century, repurposing of landscapes from farmland to forest led to more land suitable for black-legged tick establishment.¹³ These second-growth forests (forests re-grown after a timber harvest) have created appropriate “edge” habitats for black-legged ticks and hosts, resulting in increased tick populations.¹⁰ The type of forest associated with *I. scapularis* can vary; however, second-growth forests are the most suitable for black-legged ticks. Leaf litter maintains moisture while providing cover that is important for *I. scapularis* survival. Black-legged tick populations can be reduced 72% to 100% by removal of leaf litter.¹⁰ During active life stages, *I. scapularis* is most abundant in woods but also can be found in shaded areas of lawn. Black-legged ticks do not survive in strictly agricultural cropland, and the repurposing of even small tracts of farmland to deciduous forest can foster *I. scapularis* proliferation and maintain a transmission cycle of pathogens.¹⁴

Besides the landscape, climate factors—particularly high relative humidity—can increase *I. scapularis* survival. Moisture availability, specifically >82% relative humidity in leaf litter, increases *I. scapularis* activity and abundance and is a limiting factor to survival if the leaf litter cannot retain enough moisture.¹⁵ Temperature is also important in areas with *I. scapularis*. As climate change trends warmer, higher temperatures would allow immature black-legged tick larvae more opportunities for feeding and increase the probability of becoming a mating adult in regions once inhospitable for black-legged ticks.¹⁶

LIFE CYCLE OF *I. SCAPULARIS*

I. scapularis has a 2-year life cycle and is a 3-host tick, taking a blood meal from different size-appropriate hosts to transition from larva to nymph and nymph to adult life stages (Figure). This feeding allows ticks to acquire and transmit pathogens between a variety of



hosts, increasing the opportunities for transmission and pathogen maintenance.¹⁷ Larvae feed in the summer after hatching, nymphs feed in the late spring or summer of the second year, and adults feed in the fall. Larvae and nymph-stage ticks are known to feed on small animals and become infected by larvae and nymphs.^{12,17}

P. leucopus is the main reservoir host of all *I. scapularis* pathogens in the environment.^{11,12} Mice can become infected from larvae or nymphs, depending on the pathogen transmitted (Figure). For example, *B. burgdorferi* passes only transstadially and not transovarially in tick vectors. Transstadially transmitted pathogens can pass from the larval to the adult stage, while transovarially transmitted pathogens can pass from the adult female to the eggs. *P. leucopus* has bacteremia without symptomatic infection, allowing for efficient and sustainable transmission of pathogens to Ixodes vectors.¹¹

Nymphs are the most infectious vector stage to humans as they are more likely to carry pathogens and less likely to be observed than adults. Adult ticks feed on white-tailed deer or other large mammalian hosts, including humans. Deer and humans are dead-end hosts because the microbes are not further transmitted. While deer are dead-end hosts, they allow increased distribution and survival of black-legged ticks.^{10,18}

Nymphs molt into adults during the fall of the second year after which their sex can be first differentiated. *I. scapularis* are hard-bodied and adults are dark brown to black in color. At the adult stage, the female body becomes orange-red as opposed to the larger grey to black color of the male. Once they become adults, males may attach to deer seeking female mates. Only female ticks take significant blood meals—mainly from white-tailed

Table. Symptoms, Diagnosis, and Treatment of *Ixodes scapularis* Tick-borne Diseases

Organism	Symptoms	Treatment
<i>Borrelia burgdorferi</i>	Myalgia, arthralgia, fever	100 mg doxycycline 2 times/day for 10-21 days or aoxicillin 3 times/day for 10-21 days if doxycycline is contraindicated
<i>Borrelia miyamotoi</i>	Myalgia, arthralgia, chills, headache, high fever (potentially relapsing)	100 mg doxycycline 2 times/day for 10-21 days
<i>Borrelia mayonii</i>	Myalgia, arthralgia, high fever, headache	100 mg doxycycline 2 times/day for 10-21 days
<i>Anaplasma phagocytophilum</i>	Myalgia, fever, arthralgia, headache	100 mg doxycycline 2 times/day for 10-21 days
<i>Ehrlichia muris</i> subsp <i>eaucalarensis</i>	Fever, fatigue, headache, malaise, nausea, vomiting	100 mg doxycycline 2 times/day for 10-21 days
<i>Babesia microti</i>	Malaise, myalgia, fatigue, fever	Combination of atovaquone plus azithromycin or clindamycin plus quinine for 7-10 days
Powassan virus/Deer Tick virus	Fever, lethargy, rash, myalgia, stiff neck, headache	Supportive care including hydration therapy and pain management

Abbreviation: subsp, subspecies.

deer—acquiring and transmitting disease. Reproduction between adult male and female ticks occurs on white-tailed deer or in vegetation.^{10,19} Male black-legged ticks die after copulation. Females release 1000 to 3000 eggs in the leaf litter, typically in late May, and die soon afterwards.¹⁰

ACQUISITION AND TRANSMISSION OF PATHOGENS BY *I SCAPULARIS*

The small size of black-legged tick nymphs, the potential to carry pathogens, and the ability to feed on larger hosts, make nymphs the most probable tick life cycle stage for pathogen transmission to humans.^{17,19} Nymphs and adults use their front legs to attach to a host. After attachment, the tick finds a feeding spot and takes a blood meal. Pathogen acquisition and transmission is due to saliva transfer and gut regurgitation. Ticks can acquire and transmit pathogens consecutively or simultaneously over the course of their lives.²⁰

Adult *I scapularis* ticks have the highest level of multiple pathogen infections, in part because they feed on 2 hosts.²¹ Copevalence of 2 or more pathogens was observed in 26% of black-legged ticks from Westchester, New York.²² Pathogen carriage by ticks in the Upper Midwest includes *B burgdorferi* as the most common (26%), followed by *A phagocytophilum* (8.9%), *B miyamotoi* (7.1%), *B microti* (5%), and Powassan/deer tick virus (POWV/DTV) 2.9%.²³⁻²⁶

Pathogen transmission from tick to host depends on the microbe, the tick attachment time, and the tick's infectious status. Infection risk after a single tick bite is low (1.3%-3.0%), even in endemic areas.²⁷ In animal models, *B burgdorferi* transmission exponentially increased after 72 hours, correlating with an 18% to 25% incidence of Lyme disease.²⁷ Transmission of *A phagocytophilum* and *B microti* take 12 to 24 hours and 36 to 48 hours,²⁸

respectively. *B miyamotoi* is transmitted in approximately 24 hours,²⁹ whereas POWV/DTV can transfer in as little as 15 minutes.³⁰ *B mayonii* transmission times are similar to *B burgdorferi*. Little research has been done on transmission times for *E muris* ssp *eaucalarensis* (EME) bacteria. Acquisition and transmission of pathogens does not seem to be affected by the prevalence of multiple pathogens.²⁰ Co-infection of *I scapularis*-transmitted pathogens in humans is becoming a prominent clinical concern, making the symptoms, diagnostics, and treatment of each pathogen infection critical.

B burgdorferi (Lyme Disease)

Lyme disease was first recognized in 1975 in Lyme, Connecticut. William Burgdorfer isolated and linked the etiological agent, named *B burgdorferi*, to *I scapularis* ticks.¹ Lyme disease is the most common black-legged tick-associated illness.² Around 70% to 80% of patients will exhibit a “bull’s-eye” pattern rash—known as erythema chronicum migrans—about 7 days post-exposure (Table).³¹ Fever, headaches, myalgia, stiff neck, arthralgia, and lymphadenopathy are often seen during early infection.^{28,31} The bacteria may also spread to regional lymph nodes, the brain, and the heart.³² In the last stage of Lyme disease, the spirochetes can penetrate tight joint spaces, causing arthritis in about 10% of patients.³²

B miyamotoi Disease

Another tickborne *Borrelia* pathogen is *B miyamotoi*. The first US patient infected was identified in 2013. The organism has been isolated from numerous *Ixodes* tick species in North America.³³ Infection rates vary greatly in the United States by region and locality, with a ~12% prevalence of *B miyamotoi* from ticks in Indiana and a 0% to 6.8% prevalence on the East Coast.³⁴ Unlike *B burgdorferi*, this pathogen is able to pass transovarially in the tick (Figure).

Patients with *B miyamotoi* disease have muscle aches, fever, and headache similar to tick-borne relapsing fever symptoms, but Lyme disease symptoms including erythema migrans, facial palsy, and arthritis are uncommon.³⁵ *B miyamotoi* is part of the relapsing fever group of *Borrelia* (unlike *B burgdorferi*), with multiple cycles of high fever, chills, marked headache, and myalgia or arthralgia. Blood tests will show elevated liver enzyme levels, neutropenia, and thrombocytopenia indicative of a shock-like condition.

Borrelia mayonii Disease

Borrelia mayonii is the most recent tick-borne pathogen identified in the Upper Midwest regions of the United States, remaining centered in Wisconsin and Minnesota.^{5,36} Eventual identifi-

cation occurred in 2016 after irregular polymerase chain reaction results were seen from blood and synovial fluid samples at the Mayo Clinic in Rochester, Minnesota.³⁷ Of 100,545 clinical samples tested during 2003-2014, six specimens received after 2012 yielded melting temperature results outside normal limits for other *Borrelia* species. Furthermore, the species was not detected in specimens tested from states in the Northeast. *B. mayonii* was found to have 93.83% sequence homology to *B. burgdorferi*.³⁸

The newly identified species is transmitted by *I. scapularis* ticks, eliciting a Lyme-like borreliosis in humans.³⁸ Some studies have confirmed that white-footed mice and the American red squirrel serve as *B. mayonii* hosts.^{39,40} Given the absence of *B. mayonii* disease in the Northeast, where equally suitable tick vectors and potential reservoirs are abundant,^{36,40} other factors besides tick vectors and animal reservoirs may be in play.

B. mayonii infected patients have unique manifestations of disease compared to traditional Lyme disease.^{5,37} *B. mayonii* causes 1 to 3 cases of Lyme-like disease within Minnesota per year.^{30,41} Clinical presentation in infected patients is largely congruent with Lyme disease: myalgia, headache, arthralgia, neck pain, and fatigue (Table).³⁸ The familiar “bull’s-eye” erythema migrans rash is sometimes associated with *B. mayonii* disease, but more frequently there is a diffuse unconventional rash over a wider area.^{5,37} *B. mayonii* infections may be differentiated based on acute onset unusually high fever, as well as nausea and vomiting not seen in other *Borrelia*-induced illness.⁴¹ Markers such as thrombocytopenia, lymphopenia, and increased levels of hepatic enzymes also have been seen.³⁰

***A. phagocytophilum* (Human Granulocytic Anaplasmosis)**

A. phagocytophilum causes human granulocytic anaplasmosis, first identified in Minnesota and Wisconsin. In Wisconsin, seroepidemiological data suggest that 15% of the population was infected.⁴² Human granulocytic anaplasmosis (HGA) causes disease mainly in older patients (median age 50-60 years).⁴³ The case-fatality rate of HGA is <1% in the United States. Human granulocytic anaplasmosis cases have increased every year. According to the Centers for Disease Control and Prevention, there were 1,761 cases of HGA in the United States in 2010.⁴³ Originally, *A. phagocytophilum* was named the human granulocytic ehrlichiosis (HGE) agent. The formerly named HGE agent, along with the ruminant and equine pathogens, *E. phagocytophila* and *E. equi*, are now called *A. phagocytophilum*.⁴² *A. phagocytophilum* invades granulocytes, mainly neutrophils, creating vacuoles of replicating bacteria called morulae.⁴⁴

Humans infected with *A. phagocytophilum* display fever (89%), headache (82%), and fatigue (84%). (See Table.) Myalgia, chills, and shaking are also common symptoms. Nausea, arthralgia, vomiting, abdominal pain, and cough are less common symptoms of HGA. Severe symptoms may include hemorrhage, renal failure, or neurologic problems.⁴⁵

***Ehrlichia muris euclairensis* (Ehrlichiosis)**

Until recently, only *E. chaffeensis* and *E. ewingii* were thought to cause ehrlichiosis in humans in the United States. In 2009, a novel pathogen was recognized in patients from Wisconsin and Minnesota. Genetic analyses revealed that this new *Ehrlichia* species is closely related to *E. muris*. Formerly called *Ehrlichia muris*-like, EME infection produces symptoms closely resembling those observed in *A. phagocytophilum* and *E. chaffeensis* infections. Males are infected more often than females (1.7 to 1), and the average patient age is 61 years. In 2014, there were 12 confirmed cases of EME in Wisconsin, bringing the total to 39 confirmed cases in Wisconsin since 2009.⁴⁶ *I. scapularis* ticks found in Minnesota and Wisconsin appear to be the only vector, since ticks from other states were negative.

The most common symptoms of EME infection include fever, malaise, fatigue, headache, nausea, and vomiting (Table). A rash is not commonly reported with EME infections compared to *E. chaffeensis* infections. Clinical laboratory findings in patients include increased liver enzyme levels, thrombocytopenia, and reduced numbers of lymphocytes.⁴⁷

***Babesia microti* (Babesiosis)**

The apicomplexan parasite *B. microti* is an emerging zoonotic intraerythrocytic organism of humans. The majority of cases (97%) come from 5 Northeastern states, Minnesota, and Wisconsin. Of 1,762 reported cases in 2013, 57% of patients were 60 years or older.⁴³ Human disease is usually self-limiting, and most patients recover without treatment. Immunosuppressed (especially asplenic) patients, as well as patients with co-infection, are at risk for symptomatic disease. The mortality rate for clinically apparent infections is 5% in the United States.⁴ *Babesia* species may be transmitted transovarially, as well as transstadially in the tick (Figure).

Human babesiosis has a broad spectrum of symptoms dependent on the level of parasitemia. Low level parasitemia is more typical and often self-limiting. However, a high level of parasitemia may lead to a fulminating malaria-like infection characterized by malaise, chills, myalgia, anemia, fatigue, and fever that is more often observed in asplenic patients (Table).⁴

Powassan/Deer Tick Virus (Viral Encephalitis)

Deer tick virus, a variant of Powassan virus, is a positive-sense RNA Flavivirus. The name deer tick virus (DTV) has been established recently to differentiate this distinct Powassan virus lineage found only in *I. scapularis* from the prototypical Powassan virus lineage found in *I. cookei*, also known as the ground hog tick.⁴⁸ Genetic sequencing can separate the 2 lineages. Disease caused by this arbovirus is very rare but is often fatal in those who are symptomatic. Currently, there has been only 1 case of sequence-confirmed DTV in Minnesota. Wisconsin has had 3 cases of confirmed POWV/DTV, in 2003, 2006, and 2007, respectively.⁴⁹

A POWV/DTV infection may include a fever with headache, myalgia, arthralgia, and possible accompaniment of skin rash, lymphadenopathy, or central nervous system disease (meningitis or encephalitis) (Table). Severe symptoms that begin 8 to 34 days after POWV/DTV infection include respiratory distress, tremors, seizures, paralysis, and coma.⁴⁸ Most symptomatic patients with POWV/DTV infection develop meningoencephalitis.⁵⁰

TREATMENT OF BLACK-LEGGED TICKBORNE DISEASES

Patients with Lyme disease, *B mayonii* disease, anaplasmosis or ehrlichiosis are typically treated with 100 mg of doxycycline twice a day for 10 to 21 days (Table).⁴³ Babesiosis is treated with a combination of atovaquone plus azithromycin or clindamycin plus quinine for 7 to 10 days, and supportive care with hydration is used for POWV/DTV infections.

CONCLUSION

Multiple tick-borne infections from the tick vector *I scapularis* are endemic in the Upper Midwest and can present as undifferentiated febrile illness. Age, immunocompetence, and co-infection play important roles in disease severity. Patients with underlying medical conditions that require immunosuppressive medication have an increased likelihood of opportunistic and novel infection that can be lethal. The diversity of pathogens carried by *I scapularis* found in the Upper Midwest makes it imperative that a proper diagnosis followed by treatment is carried out.

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Medical Education with 3-Year Regional Campuses: Do They Attract a Different Type of Applicant?

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ABSTRACT

Background: In response to calls to increase class sizes, the Medical College of Wisconsin (MCW) opened two new 3-year community-based regional campuses in 2016 and 2017. The goal of this study was to analyze whether the applicants and accepted student pools differed for the school's 3-year and 4-year campuses.

Methods: Deidentified data from Wisconsin applicants to MCW for the class enrolling in 2017 were categorized based on their preference for the Milwaukee or a regional campus. Applicants and admitted student data were compared on Medical College Admissions Test (MCAT) score, undergraduate school grade point average (GPA), sex, age, research intensity of their undergraduate school (Carnegie 1 classification vs all others) and Wisconsin county of residency.

Results: Regional campus applicants were significantly older (24.6 vs 23.7, $P=0.023$), more likely to reside in nonurban counties (33% vs 13%, $P<0.001$), attend nonresearch-intensive undergraduate schools (65% vs 44%, $P<0.001$) and had lower mean MCAT scores ($d=0.77$, $P<0.001$) than applicants to the Milwaukee campus. Regression models indicated 4 applicant qualities were associated with a preference for 4-year (values >1.0) or 3-year (values <1.0) campus: graduation from a Carnegie 1 undergraduate school (OR=1.626; 95% CI, 1.01-2.62), a higher age at the time of application (OR=1.092; 95% CI, 1.01-1.18), total MCAT score (OR=0.916; 95% CI, 0.89-0.95), and permanent residence in a rural Wisconsin county (OR=0.349; 95% CI, 0.21-0.59). When we examined students who were accepted and matriculated as opposed to just applicants, regression models showed that students with higher ages were more likely to attend the 4-year campus (OR=1.42; 95% CI, 1.15-1.76), while a higher total MCAT score (OR= 0.83; 95% CI, 0.76-0.91) and rural county residency (OR=0.27; 95% CI, .1-0.73) were associated with matriculation to the 3-year regional campuses.

Conclusions: These results indicate that the regional 3-year campus model is attracting and selecting students with some differences from those at MCW's 4-year campus. After adjusting for other characteristics, students matriculating to the regional 3-year campuses are nearly 4 times more likely to come from a rural county and have slightly higher MCAT scores.

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INTRODUCTION

In 2015 and 2016 the Medical College of Wisconsin (MCW) opened 2 new regional campuses in Green Bay and Wausau, Wisconsin. The expanded size of the medical school class at MCW was consistent with calls from the Association of American Medical Colleges to increase class sizes by 30% in order to address anticipated shortages in physicians in the coming decades.¹ More importantly, the Wisconsin Hospital Association published a study in 2011 forecasting that Wisconsin would suffer a significant shortfall in future physician supplies and that this deficiency would be most acute in the northern half of the state.² These findings were confirmed in additional analyses 5 years later by the Wisconsin Council on Medical Education and Workforce.³ MCW chose a strategy of opening new regional campuses in areas with the greatest projected shortages, with an aim to recruit different types of students who would be more likely to choose residency programs in these areas for the next phase of their training and then remain in the state's less-populated regions and choose specialties needed in these areas.

In addition to locating these campuses in regions of the state where an increased need for physicians in future years is anticipated, the campus curriculum was modified so that by starting 6 weeks earlier than the Milwaukee campus and doing clinical rotations over summer months, motivated students could complete their medical training in 3 years rather than the customary 4 years. This adaptation was implemented to allow students

interested in careers in primary care and psychiatry—two areas of high needs in the central and northern portions of Wisconsin—to graduate with less debt and accelerate their entry into residency and the workforce.

Development of these new campuses required a sufficient number of prospective medical students from Wisconsin who would be interested in attending medical school in an environment not intimately linked to a tertiary-quaternary care academic medical center. Even more important was to recruit students who were from smaller cities and rural areas, since previous research has reported that students with rural backgrounds are more likely to choose specialties and practice sites in smaller towns.⁴⁻⁶ When MCW chose to establish these new campuses, the University of Wisconsin School of Medicine and Public Health already had established a program—the Wisconsin Academy for Rural Medicine (WARM)—that offered students the opportunity to perform their clinical years in smaller communities in central and northeastern Wisconsin. The WARM program enrolls 25 students a year who spend their final 2 clinical years of training either in Green Bay, Marshfield, or smaller communities. Given that this program was already recruiting students from rural areas of the state, it was unclear if there was a sufficient number of additional qualified students to justify the construction of two new regional medical school campuses. Based on application data from previous MCW classes in Milwaukee, there were several well-qualified Wisconsin residents who were denied admission to MCW simply because there were not enough spaces available in the class, but that alone did not assure that these students would be the right individuals for the 3-year regional campus model.

This report reviews MCW's experience in the admissions process for students to the regional campuses in Green Bay and Wausau in 2017. Based on applicants from Wisconsin who wished to be considered for either of the regional campuses, Milwaukee campus, or both campuses, the report examines differences in the applicant pool to determine whether the regional campuses are attracting a different type of student who may be more likely to locate their future practice in nonurban areas of the state or if applicants to the regional campuses are no different than those who currently apply and attend medical school in Milwaukee but are simply motivated to finish a year earlier.

METHODS

Subjects

Data from the application pool of candidates to MCW for the class enrolling in 2017 were deidentified and aggregated. During the application phase for medical school, applicants to MCW could indicate whether they were interested in applying only to the Milwaukee campus, only to Green Bay, or to both campuses. Applicants who submitted an application to both campuses also were asked to indicate which campus they preferred. To help students with this choice, links on the application website were

provided so that students could learn more about the mission of each campus and the curriculum. Aspiring students were required to complete a secondary application that included a 1-question (for Milwaukee) or 3-question (for regional campuses) essay on why they were interested in each campus. The application fee was the same regardless of the campus or number of campuses on the application.

Applicants were categorized by whether prospective students indicated on their application that they were only interested in the Milwaukee campus or preferred that campus (Milwaukee campus preferred) or if they were only interested in or preferred a regional campus (regional campus preferred). Because the regional campuses indicated to applicants that preference would be given to Wisconsin residents, only applicants from Wisconsin were considered for this study.

Measures

Characteristics of the applicants were included in data extracted from the student's American Medical College Application Service (AMCAS), which serves as a single application vehicle for all allopathic medical schools in the United States. Applicant age was defined as the age of the prospective student on January 1 in the year they applied. Undergraduate school attended was categorized based on the research intensity of the college the student graduated from based on the Carnegie categories; undergraduate schools were defined as either Carnegie 1 institutions (the highest level of research intensity) or non-Carnegie 1. The student's county of residence was defined as urban or nonurban based on the 2013 Rural-Urban Continuum Codes developed by the United States Department of Agriculture.⁷ The student's cumulative grade point average (GPA) and Medical College Admission Test (MCAT) score were taken from the self-reported figures provided on the AMCAS application.

The total number of applicants refers to applicants who forwarded their AMCAS application to MCW before the deadline for application and completed the secondary application, which includes submitting their application fee. Matriculated students refers to applicants who accepted an admission offer to MCW and were present on the first day of classes.

Analyses

Bivariate analyses were conducted using Student *t*-test with Cohen's *d* effect size, Pearson chi-square, and logistic regression modeling with IBM® SPSS® 24.0.

Human Subject Approval

This research was approved by MCW's Institutional Review Board.

RESULTS

The desired class sizes for Milwaukee and regional campuses were set at 204 and 25 at each regional campus, respectively, for the

Table 1. Applicant Characteristics With Preference for 3-Year Regional vs 4-Year Milwaukee Campus

	Milwaukee Preferred (N=647)	Regional Preferred (N= 108)	P-value
Male sex	340 (53%)	47 (44%)	0.082
Residence of urban county	549 (87%)	70 (67%)	<0.001
Carnegie 1 college graduate	364 (56%)	38 (35%)	<0.001
Total MCAT (Mean, SD)	507.52 (7.41)	501.55 (7.12)	<0.001
Cumulative GPA (Mean, SD)	3.65 (0.27)	3.60 (0.29)	0.080
Age (Mean, SD)	23.7 (2.7)	24.6 (3.9)	0.023

Abbreviations: MCAT, Medical College Admissions Test; GPA, grade point average.

Table 2. Accepted Student Characteristics of Those Admitted at 3-Year Regional vs 4-Year Milwaukee Campus

	Milwaukee Preferred (N=102)	Regional Preferred (N= 41)	P-value
Male sex	55 (53%)	18 (41%)	0.165
Residence of urban county	86 (84%)	29 (71%)	0.064
Carnegie 1 college graduate	53 (52%)	19 (43%)	0.358
Total MCAT (Mean, SD)	510.14 (5.42)	506.00 (4.45)	< 0.001
Cumulative GPA (Mean, SD)	3.76 (0.20)	3.67 (0.23)	0.020
Age (Mean, SD)	23.0 (1.9)	24.3 (2.8)	0.011

Abbreviations: MCAT, Medical College Admissions Test; GPA, grade point average.

Table 3. Multivariate Results Assessing Contributions to Student Factors Among Applicants and Matriculating Students for MCW-Milwaukee vs Regional Campuses

Variables	OR	95% CI	P-value
Applicant Multivariate Model^a			
Carnegie 1 college graduate			
Regional campus (comparison)	1	—	0.047
Milwaukee campus	1.626	1.006-2.626	
Age			
Regional campus (comparison)	1	—	0.022
Milwaukee campus	1.092	1.013-1.178	
Total MCAT			
Regional campus (comparison)	1	—	<0.001
Milwaukee campus	0.916	0.888-0.945	
Rural county residence			
Regional campus (comparison)	1	—	<0.001
Milwaukee campus	0.349	0.207-0.589	
Matriculating student multivariate model^a			
Age			
Regional campus (comparison)	1	—	0.001
Milwaukee campus	1.422	1.146-1.764	
Total MCAT			
Regional campus (comparison)	1	—	<0.001
Milwaukee campus	0.830	0.755-0.914	
Rural county residence			
Regional campus (comparison)	1	—	0.010
Milwaukee campus	0.271	0.100-0.732	

Abbreviations: MCAT, Medical College Admission Test; GPA, grade point average.
^aModels adjusted for age, sex, urban/rural residence, college GPA, MCAT score, and Carnegie 1 college designation.

application cycles under consideration. Six hundred forty-seven applicants indicated they preferred the Milwaukee campus, while 108 indicated a preference for the regional campuses. As shown in Table 1, applicants to the Milwaukee campus were more likely to be male, reside in an urban Wisconsin county, have graduated from a research-intensive college, and had a higher MCAT score and college GPA. Students who preferred a regional campus were, on average, about a year older than those who indicated a preference for Milwaukee.

In 2017, the Milwaukee campus enrolled 204 students with 25 students each in Green Bay and Wausau. One hundred two (50%) of the students in Milwaukee were Wisconsin residents, while 41 (82%) of accepted students in the regional campuses were from Wisconsin. Table 2 shows that similar trends were noted among students who were accepted, although only MCAT, GPA, and student age were statistically significant ($P \leq .050$).

Multivariate modeling was used to evaluate the independent effect of prospective student characteristics. Table 3 provides the results of these models for both applicants and accepted students. The regression model shows that for applicants graduating from a Carnegie 1 college, attendance was a strong independent predictor for preferring Milwaukee (adjusted OR 1.626; 95% CI, 1.006-2.626), while being from a rural county in Wisconsin was independently associated with being significantly less likely to prefer the Milwaukee campus (adjusted OR=0.349; 95% CI, 0.27-0.589). When we examined students matriculating to the campuses, Carnegie classification was no longer significantly different between the campus, whereas residing in a rural county was even more strongly independently associated with attending the regional 3-year campuses

DISCUSSION

These results demonstrate that the regional campuses of MCW in Green Bay and Wausau are attracting and accepting students with similar academic aptitude and prior experience but who are more likely to have grown up in a nonurban or rural community than those who attend MCW in Milwaukee. The strongest predictor of whether students are interested in and attend the regional campuses is that they are from Wisconsin rural counties. Students who apply to Milwaukee are more likely to come from Carnegie 1 research intense colleges, but once students are accepted, this no longer differentiates students at the regional campuses compared to Milwaukee. This implies that students who graduated from research-intensive institutions fare better than when considered in the application review process at the regional campuses.

These results indicate that accepting more students to the regional campuses did not require a significant accommodation in academic preparation as defined by student GPA or MCAT scores. Adjusting for the student's age, sex, research intensity of their college, and whether they came from a rural background, GPA was not significantly different for students who applied to

or were accepted at the regional campuses. The regression model also showed that higher MCAT scores were weakly associated with acceptance and attendance at a regional campus. These findings are similar to those from other schools that have examined whether recruiting and accepting more students from rural backgrounds has a negative effect on the academic credentials of their medical students.⁸

While the 2 regional campuses appear to be attracting and accepting different students than the Milwaukee campus, this does not assure that these students will enter the specialties that are needed in the target areas of the state or whether they will practice in those areas. One study showed that the student's own perception of "growing up rural" was more important than permanent address in predicting future rural practice.⁹ This study used the rurality of the student's home county, but this might not reflect a student's own perception of her or his home town. Additionally, other factors, which include the learning environment, curriculum, and mentoring, may influence a student's ultimate career choice and practice environment.¹⁰ To achieve the goal of producing more doctors for Wisconsin's smaller towns, simply enrolling students from small towns might not be enough.

CONCLUSION

This study shows that compared to MCW's Milwaukee campus, the 2 new regional campuses are attracting students from smaller and rural communities in both the application and acceptance processes. Other than students at the regional campuses being slightly older, other student characteristics, including previous academic performance, appear to be similar.

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Resource Utilization Among Portal Users Who Send Messages: A Retrospective Cohort Study

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ABSTRACT

Purpose: To examine the association between patients' use of online health portal-based secure messaging and the likelihood of traditional encounters (office visits and telephone calls) and to identify patient characteristics associated with use of the messaging feature of health portals.

Methods: This retrospective cohort study used EHR data from 80,801 patients aged 18 and older to determine traditional encounter rates among portal users who sent at least 1 message compared to those who sent none. Association between the number of messages sent and number of traditional encounters, while accounting for other covariates (including number of traditional encounters the year before account activation and other patient characteristics) was examined using a hurdle negative-binomial (NB) model.

Results: In the year after their portal account activation, 22,789 (28%) patients sent at least 1 message (median=3, mean=5.38). Patients who sent messages were more likely to be female (63.9% vs 58.0%, $P<0.001$), white (92.2% vs 90.0%, $P<0.001$), and have depression (27.0% vs 24.2%, $P<0.001$) than those who sent none. We observed a positive association between sending messages and number of traditional encounters. Patients who sent messages were more likely to have a traditional encounter and have more traditional encounters in the year after account activation than those who sent none (mean 17.6 vs 11.4, $P<0.001$); they also had more in-person office visits (7.6 vs 5.0, $P<0.001$) and telephone calls (9.9 vs 6.4, $P<0.001$) when examined separately.

Conclusions: Our study adds to the growing literature that EHR messaging is associated with increased traditional resource utilization. This has the potential to add to workload while diminishing productivity and increasing the risk of staff and physician burnout. Health systems should prepare for the increased visits and calls expected as more patients use secure messaging.

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INTRODUCTION

The nature of the traditional office visit in primary care was dramatically changed by the Health Information Technology for Economic and Clinical Health (HITECH) Act, enacted by Congress in 2009 “to establish programs to improve health care quality, safety, and efficiency through the promotion of health IT, including electronic health records and private and secure electronic health information exchange.”¹ Administered primarily by the Office of the National Coordinator for Health Information Technology (ONC) and the Centers for Medicare & Medicaid Services (CMS), this act defined the concept of the “Meaningful Use” of electronic health records (EHR) and contributed to their rapid adoption.

While initially EHRs were developed to serve as billing and documentation tools for physicians, many now are also linked to an online patient portal, a service that enables patients to view laboratory results, schedule appointments, or send messages through a secure interface similar to email.

As of 2017, 52% of patients nationwide were offered online access to their medical record via a portal, an increase of 24% over 3 years.² In 2012, CMS encouraged the use of online portal-based secure messaging by requiring that 5% of an Accountable Care Organization's (ACO) patients send electronic messages to their physician before incentive payments can be collected,³ and secure messaging systems linked to the patient portal are now a standard feature of most EHRs. Almost half (48%) of portal users have used their EHR portal to communicate with their health care

team via a secure message.² As a result, the volume of electronic messages received by physicians is increasing at a rapid pace, with 1 health system reporting a near tripling of messages received per provider over a 10-year period.⁴

Most frequently, patients message their provider to discuss a new health condition, a change in a previously existing condition, for clarification regarding lab results or drug dosages, or starting a new drug.⁵ While almost half of patients have utilized the messaging feature of the portal, there has been less uptake among physicians; in 2016, only 26% of practicing physicians who used EHRs reported communicating with patients directly using the patient portal.

Most patients desire access to physicians via electronic messaging⁶ and the use of secure patient-physician messaging has been associated with improved performance on HEDIS measures,⁵ including A1c and LDL control in patients with diabetes.⁷ Despite these advantages, physicians have expressed concern that patient-initiated messages may increase their workload⁸ while decreasing productivity and compensation.⁹ Furthermore, over half of physicians currently using patient portals did not feel that patient messaging improved efficiency.¹⁰ A recent study showed primary care clinicians at the University of Wisconsin health system (UW Health) are currently spending almost 6 hours per day on the EHR and 20 minutes per day on the messaging feature of the portal alone.¹¹

Though it has frequently been suggested that patient messages have the potential to improve physician productivity by replacing telephone calls and office visits,¹² the literature conflicts on the extent to which electronic messaging can substitute for other clinical services.¹³⁻¹⁸ Most studies to date have compared traditional clinical encounters (office visits and telephone calls) among patients who use EHR portals (including, but not limited to, the messaging feature) with patients who do not use EHR portals and do not truly isolate the use of the messaging feature from other features of the portal. Previous research suggests that there are significant differences between portal users and nonusers,^{19,20} as well as between portal users who use the messaging function and those who do not.^{21,22}

Given the trend toward increasing portal messaging, the aim of this study is to further examine rates of traditional clinical encounters among patients who use EHR portals to send messages to physicians and those who have access to EHR portals but send none.

METHODS

The study was conducted at UW Health, a large Midwestern academic medical center with 349,142 members. UW Health uses Epic Systems Corporation's²³ EHR software, customized for our institution and called HealthLink. HealthLink is a fully integrated application that includes features for documentation, scheduling, order entry, and billing. The patient portal interface, MyChart, features access to online records, including laboratory and radiol-

ogy reports, appointment scheduling, health maintenance reminders, and the ability to send and receive secure messages. Use of the messaging system is provided at no cost to patients, and there is no direct compensation for providers to send or respond to a message.

We conducted a retrospective cohort study to examine the relationship between sending a MyChart message and the number of traditional encounters (office visits and telephone calls) in the 12-month period after MyChart account activation. Data used for this study were extracted using the UW Health database (Clarity). The cohort comprised all adult patients 18 years of age and older who activated a MyChart account during the time period January 1, 2012 through June 1, 2016. To ensure continuous enrollment during the study period, subjects for analysis were required to have had at least 1 traditional encounter in the 1- to 3-year period both before and after the first account activation. This criterion was chosen to increase confidence in the encounter and messaging totals recorded by ensuring people were not lost to follow-up due to death or transferring to another health system. Because no patient identifiers were included in the analysis, this study was determined exempt by the University of Wisconsin Health Sciences Institutional Review Board.

We examined additional covariates, including the total number of traditional encounters in the year before activation (prior utilization). We also examined patient characteristics at time of first activation: age, sex, race/ethnicity (white, black, Hispanic, and non-Hispanic other), insurance type (private/health maintenance organization [HMO], Medicaid, Medicare, fee-for-service, contracted, paid-to-hospice, and none), and presence of chronic disease, including diabetes, hypertension, congestive heart failure (CHF), and depression, as indicated in the Clarity database at the time of first activation.

Differences in number of traditional encounters and the covariates were compared between patients who sent at least 1 message the year after activation and those who sent none. Mann-Whitney tests were used to compare continuous items, Fisher exact test was used for binary items, and chi-square test was used for categorical items.

Analyses were performed using a hurdle negative-binomial (NB) model, with logistic-link generalized linear model (GLM) modeling zeros, and a log-link truncated NB GLM modeling positive counts. Hurdle models are a class of models developed to count data with excess zeros (which are commonly encountered in health research and were present in our data due to the large number of patients who activated an account but did not send a message).

The hurdle model structure splits the interpretation of results into 2 parts. The first part (zero part) examines the association between the covariables and presence or absence of the outcome variable (whether or not a traditional encounter occurred in the year after account activation). The results are interpreted like a logistic regression in which the covariates estimate the odds of the

Table 1. Subject Characteristics for Whole Sample and by Any Messages Sent vs No Messages Sent

	Whole Sample	No Messages Sent	≥ 1 Message Sent	P-value	Test
N	80801	58015	22786		
Messenger status (%)	22786 (28.2)				
Messages sent [mean (SD)]	1.52 (5.16)	0.00 (0.00)	5.38 (8.58)		
Type of encounter [mean (SD)]					Mann-Whitney
Traditional	13.16 (15.47)	11.44 (13.90)	17.55 (18.16)	<0.001	
Office	5.76 (6.49)	5.03 (5.83)	7.61 (7.63)	<0.001	
Telephone	7.41 (10.83)	6.41 (9.73)	9.94 (12.88)	<0.001	
Prior use [mean (SD)]					Mann-Whitney
Traditional	10.25 (12.64)	9.82 (12.21)	11.34 (13.61)	<0.001	
Office	4.39 (5.30)	4.26 (5.13)	4.74 (5.69)	<0.001	
Telephone	5.86 (8.75)	5.56 (8.47)	6.60 (9.40)	<0.001	
Age [mean (SD)]	47.44 (16.55)	47.70 (16.63)	46.79 (16.31)	<0.001	Mann-Whitney
Male (%)	32579 (40.3)	24356 (42.0)	8223 (36.1)	<0.001	Fisher exact
Race/ethnicity (%)					Chi-square
White non-Hispanic	73192 (90.6)	52185 (90.0)	21007 (92.2)	<0.001	
Black non-Hispanic	2498 (3.1)	1942 (3.3)	556 (2.4)	<0.001	
Hispanic	1882 (2.3)	1431 (2.5)	451 (2.0)	<0.001	
Other non-Hispanic	3229 (4.0)	2457 (4.2)	772 (3.4)	<0.001	
Insurance (%)					Chi-square
Medicare	7751 (9.6)	5883 (10.1)	1868 (8.2)	<0.001	
Contracted	19239 (23.8)	13526 (23.3)	5713 (25.1)	<0.001	
Fee-for-Service	4095 (5.1)	2956 (5.1)	1139 (5.0)	<0.001	
HMO	41888 (51.8)	29931 (51.6)	11957 (52.5)	<0.001	
Hospice	176 (0.2)	110 (0.2)	66 (0.3)	<0.001	
Medicaid	4790 (5.9)	3508 (6.0)	1282 (5.6)	<0.001	
None	2862 (3.5)	2101 (3.6)	761 (3.3)	<0.001	
Diabetes history (%)	5075 (6.3)	3589 (6.2)	1486 (6.5)	0.079	Fisher exact
Depression history (%)	20192 (25.0)	14038 (24.2)	6154 (27.0)	<0.001	Fisher exact
Hypertension history (%)	15433 (19.1)	11215 (19.3)	4218 (18.5)	0.008	Fisher exact
CHF history (%)	719 (0.9)	535 (0.9)	184 (0.8)	0.124	Fisher exact

Abbreviations: HMO, health maintenance organization; CHF, congestive heart failure.

outcome. The second part (positive part) examines the association of the covariates with the quantity of the outcome variable (how many more or fewer traditional encounters occurred in the year after activation) and is interpreted like a Poisson regression.

Secondary analyses examined telephone calls and in-person office visits as 2 separate outcome variables. Two additional hurdle models were used to analyze each secondary outcome, with prior use of in-person office visits or telephone calls used as covariates in their respective models.

All analyses were performed using R version 3.4.4.²⁴ Regression analysis was performed using the “pscl” package.²⁵

RESULTS

Nearly 81,000 (n=80,801) patients met the criteria for inclusion in the study. Table 1 shows the characteristics of the overall sample and details the characteristics of those who did and did not send messages. Of the total patients included in our analyses, 22,789 (28%) sent at least 1 message during the year after activation, with the median and mean number of messages sent of 3 and 5.38, respectively.

Patients who sent messages were more likely to be female

(63.9% vs 58.0%, $P<0.001$), white (92.2% vs 90.0%, $P<0.001$), and more likely to have depression (27.0% vs 24.2%, $P<0.001$) than those who sent none.

Compared to those who sent none, patients who sent messages had greater odds of having a traditional encounter in the year after activation (Figure 1). As the number of messages sent increased, so did the odds of having an encounter. Patients who sent 1 message had 2.4 times greater odds of having a traditional encounter; patients sending the mean (5.4) number of messages had 10.1 times greater odds of having an encounter (Figure 2).

In addition to messaging, several other covariates were found to be significantly associated with increased odds of having at least 1 traditional encounter in the year following activation: number of encounters in the year prior to activation (prior use), black race/ethnicity compared to white (OR 1.34; 95% CI, 1.03-1.77), and presence of depression (OR 1.54; 95% CI 1.38-1.72), diabetes (OR 1.70; 95% CI, 1.27-2.28), and hypertension (OR 1.98; 95% CI, 1.72-2.29).

The strongest predictor of having a traditional encounter in the year after account activation was number of prior encounters in the year before activation, followed by messaging.

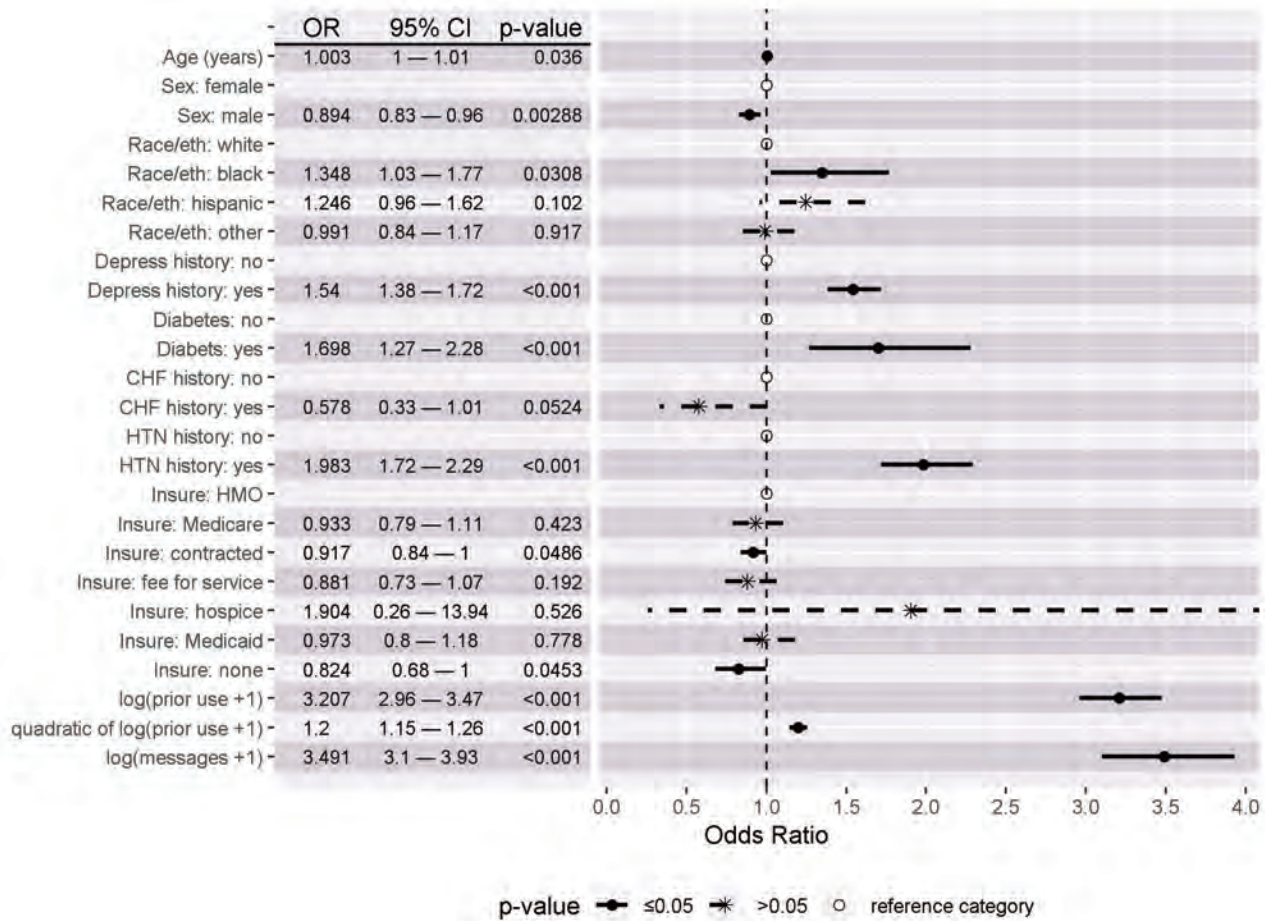
The second part of the hurdle model showed that patients who sent messages also had a greater number of traditional encounters the year after activation than those who sent none (mean 17.6 vs 11.4, $P<0.001$); they had both more in-person office visits (7.6 vs 5.0, $P<0.001$) and telephone calls (9.9 vs 6.4, $P<0.001$) when examined separately. As the number of messages sent increased, so did the number of encounters.

Figure 3 displays the expected increase in number of traditional encounters for these same increases in messaging. Compared to those who sent none, a patient sending 1 message is expected to have 21% more traditional encounters in the year after activation; a patient sending the mean (5.4) number of messages would have 65% more encounters. Findings were also consistent across secondary analyses for both office visits and telephone calls when analyzed separately.

DISCUSSION

We found that adult patients who activated a MyChart account and used it to send at least 1 message were more likely to have an office visit or a telephone call to the office in the year after

Figure 1. Odds of Having a Traditional Encounter in the Year After Account Activation by Variable



activation than those who activated an account but did not send a message. Patients who sent a message are also expected to have more traditional encounters within that year than similar patients who sent fewer or no messages, including a higher number of both office visits and telephone calls when examined separately. The effect is not subtle: patients sending just the average number of messages are expected to have around 50% more traditional encounters than patients who send none.

While number of encounters in the year prior to activation (prior use) was a strong predictor of number of traditional encounters, given 2 patients with the same level of prior use, the patient who sent a message will have a greater likelihood of an encounter, and a greater expected number of encounters, than the patient who did not send a message.

Contrary to initial expectations, we found patients who sent messages are expected to have more telephone calls in the year after account activation. We believed that patients would have a decreased likelihood of telephone calls as they show a willingness to communicate via messaging. However, we found that patients who sent messages had a higher number of traditional encounters (prior use) in the year before account activation compared

to patients who did not send messages (11.34 vs 9.82), which was primarily due to a difference in prior telephone use (6.60 vs 5.56) as opposed to a difference in prior number of office visits (4.74 vs 4.26). A reasonable explanation for our finding, then, is that the expected increase in telephone calls are patient initiated: patients who were already inclined to communicate with the office will adopt secure messaging as an additional method of communication. This effect has been shown in other settings, such as the banking sector, and is termed the “gateway effect.”²⁶ Furthermore, patients might phone in to ensure a message was received or acted upon in a timely manner. An alternative explanation is that at least some proportion of the increase in telephone calls is physician or staff generated, as the asynchronous nature of electronic communication does not always enable adequate symptom triage.

Our study design improves upon previous research in a number of ways. Because patients typically choose to activate an account at an office visit, there is an association between account activation and short-term increases in traditional encounters (typically for follow-up or management of a newly identified problem). To control for this spike, previous studies have cho-

Figure 2. Odds Ratio of Having an Encounter in the Year After Account Activation, By Encounter Type and Number of Messages Sent

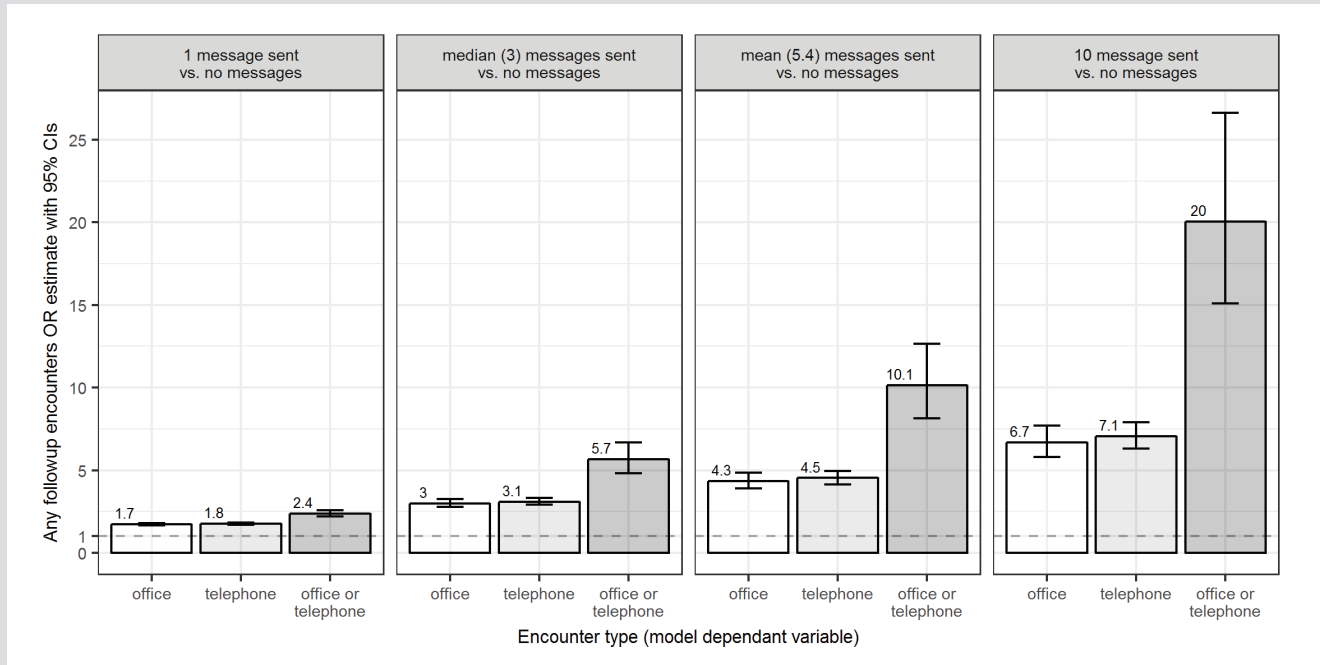
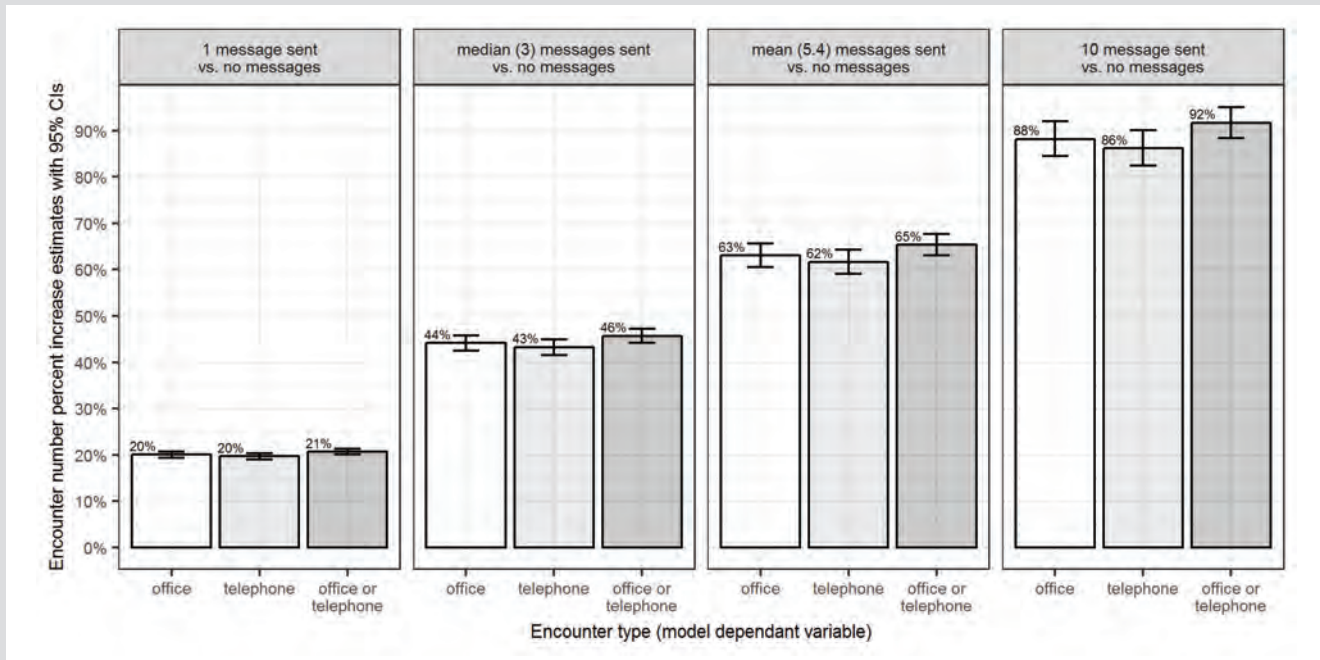


Figure 3. Expected Increase in Number of Encounters in the Year After Activation, by Encounter Type and Number of Messages Sent



sen to exclude from analysis data for a varying length of time (ranging from 30 days to 6 months) after activation. We did not believe we needed to exclude any data because enrollment in our study was predicated upon account activation and so any visit spike should theoretically be the same between groups. We believe this provides a more robust analysis in terms of actual work that the health care system will need to prepare for after

an account is activated. We also developed a regression model that accounted for many factors, including demographic characteristics, insurance status, presence of chronic disease, and prior use of the health care system, and found a strong and important association between number of messages sent and number of traditional office visits. Accounting for prior use of the health care system before account activation had the added benefit of adjust-

ing for utilization effects of patient health conditions that were not directly estimated by parameters in the model.

Although it may seem more intuitive to combine telephone calls and electronic messages together as “nontraditional encounters” as neither typically generate revenue or require a visit to the office, we believed it made more sense to combine office visits and telephone calls together as traditional encounters. Office visits always occur synchronously and require the staff, patient, and provider to be present in the same place at the same time. Telephone calls, though allowing for distance, are for the most part answered in real-time and require staff availability at the time of patient demand. Electronic messages (typically sent directly to a physician or advanced practice provider) require less real-time staff input and are less likely to directly affect decisions around staffing and clinic workflow.

Our study has several important limitations. First, we did not examine the temporal association between sending messages and having a traditional encounter, so we cannot say that the observed association is causal. Second, to ensure that we had a large enough sample size for the study, we included for analysis all patients in the UW Health system, including those in both specialty and primary care. This may have introduced confounding variables as we could not determine which services the messages were sent to and which services the office visits were in. A follow-up study in a single department may help clarify these factors.

Also of note, we did not differentiate between who initiated the exchange of MyChart messages (message threads). Patients who start message threads could have different rates of traditional encounters compared to those who respond to threads started by the health care team. For example, messages sent by the office to remind patients to present for age-appropriate health screenings would logically be expected to increase encounter totals. Similarly, patient-initiated messages could be expected to have contradictory effects on resource utilization based on whether the context of the message substituted for or triggered further follow-up.

We also likely have not included all potentially relevant explanatory covariables in our models. Physician factors have been shown to affect the number of messages sent by patients,²² and severity of acute illness may be a better predictor of use of traditional encounters than the chronic illnesses we accounted for. Unfortunately, we could not easily access this information through our EHR database. However, we believe prior utilization was an effective alternative method of adjusting for all other acute and chronic illnesses at the individual patient level.

Finally, our study sample may not be representative of a broader population. Most patients were insured during the study period, which limits generalizability to this subset of the entire patient population. Since they voluntarily chose to activate a portal account, we also assume they all had access to a computer or smart phone. The compensation system at UW Health is partially

capitated, which may limit a physician’s incentive to convert a MyChart message to an in-person visit. Despite this factor, which could be expected to decrease the number of expected traditional encounters, we still found a positive association between messaging and encounters.

CONCLUSION

While electronic messaging is often portrayed as having the potential to increase clinician efficiency, our study adds to the growing literature that messaging is associated with increased resource utilization (office visits and telephone calls) by patients. Messaging does not appear to serve as a simple substitution for other forms of clinical services. Instead, it may act as a gateway to increase the number of traditional clinical encounters, all of which require staff and clinician time and attention. In an era of ever-increasing burnout,^{27,28} it is increasingly important to recognize additional sources of work for both providers and staff.²⁹ Furthermore, health systems need to be prepared for the increase in visits and calls (in addition to the obvious increases in messages) that are expected as more patients enroll in patient portals and participate in the messaging feature.

Future research should focus on which features of messages or characteristics of patients who send them are most likely to be associated with the expected increase in traditional encounters: does the content of the message itself or a gateway phenomenon explain our findings? We remain optimistic that there are certain subsets of messages that have the potential to increase clinician efficiency without a cost-prohibitive increase in staff resources compared to other categories of messages. Additionally, research should continue to focus on how messaging affects other important aspects of care, including quality of care and patient satisfaction. Further qualitative studies utilizing record reviews should be done to help elucidate the reasons that patients use portal-based messaging systems.

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Effect of a Statewide Controlled-Substance Monitoring Requirement on the Opioid Prescribing Practice for Treatment of Acute Pain

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ABSTRACT

Background: The US government affirmed the opioid epidemic as a public health emergency in late 2017. Prior to that, as part of the Heroin, Opiate, Prevention, and Education (HOPE) Agenda, the state of Wisconsin enacted 2015 Wisconsin Act 266. This law, which went into effect April 1, 2017, requires prescribers to review data from the state's enhanced Prescription Drug Monitoring Program (ePDMP) before issuing an opioid prescription, in order to reduce inappropriate prescriptions and, ultimately, decrease opioid overuse.

Objective: To evaluate the effect of 2015 Wisconsin Act 266 on opioid prescriptions for acute pain in Mayo Clinic Health System sites in northwest Wisconsin.

Patients and Methods: This retrospective review included all eligible patients who were discharged from emergency or urgent care departments in the Mayo Clinic Health System at northwest Wisconsin sites during the study period. The quantity of opioids prescribed (measured in morphine milligram equivalents per patient encounter) and the total number of opioid prescriptions were compared for the periods May and June 2016 (prior to implementation of Act 266) versus May and June 2017 (post-implementation of Act 266).

Results: A 33% reduction occurred in the median opioid quantity prescribed per patient encounter in the post-implementation period vs the pre-implementation period ($P < .001$). In addition, a 13% relative reduction occurred in the percentage of patient encounters that involved an opioid prescription ($P < .001$). No difference was observed in opioid prescription agents between time periods, except for an increase in morphine prescriptions ($P < .001$).

Conclusion: The HOPE Agenda, specifically 2015 Wisconsin Act 266, appears to have had a positive effect on decreased opioid prescriptions for acute pain at Mayo Clinic Health System sites in northwest Wisconsin.

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INTRODUCTION

In late 2017, the US government affirmed the opioid epidemic as a public health emergency.¹ Opioid medications have been prescribed for the treatment of acute pain in various medical settings.² The Centers for Disease Control and Prevention (CDC) reported the number of overdose deaths related to opioid use was 5 times higher in 2016 than 1999.³ In the United States, approximately 115 people die daily because of opioid overdose. Despite a decrease in nonmedical opioid users, adults ages 45 to 54 years had the most overdose deaths, and adults ages 55 to 64 years had the greatest increase in overdose deaths between 2005 and 2015.² The latter group reported the highest medical use of opioids and had little change in heroin morbidity during the same period. This observation highlights that dependence, rather than abuse, appears to be an important factor in the opioid crisis.

Several agencies and expert panels have developed guidelines that describe the appropriate use of opioids for treatment of

chronic pain, but expert guidance on opioid treatment of acute pain is lacking. Thus, standardization of opioid prescription for treatment of acute pain is a goal for many institutions seeking to reduce the risk of addiction, diversion, and overdose-related deaths.

A 22.2% decrease in opioid prescriptions occurred in the United States from 2013 through 2017, and 19 million fewer opioid prescriptions were dispensed nationally from 2016 through 2017.⁴ More judicious prescribing practices may be due, in part, to increased utilization of state prescription drug monitoring pro-

Table 1. Comparison of Encounter Type Between Implementation Periods

Encounter Type	Patients Per Period, No. (%) ^a		
	Pre-implementation ^b (n=17,557)	Post-implementation ^c (n=17,004)	Total (N=34,561)
Clinic outpatient	5,994 (34.1)	5,624 (33.1)	11,618 (33.6)
Emergency department	8,644 (49.2)	8,512 (50.1)	17,156 (49.6)
Hospital outpatient	2,919 (16.6)	2,868 (16.9)	5,787 (16.7)

^a The difference between the encounter types was not significant ($P=.11$).
^b Pre-implementation of 2015 Wisconsin Act 266, May and June 2016.
^c Post-implementation of 2015 Wisconsin Act 266, May and June 2017.

grams (PDMPs). More than 1.5 million providers nationwide were registered in state PDMPs in 2017—a substantial increase from 471,896 providers registered in 2014. In addition, providers nationwide queried PDMPs 300.4 million times before prescribing an opioid in 2017, an increase of 121% from 2016.⁴

In Wisconsin, the prescription rate for opioid medications in 2015 was 69.1 prescriptions per 100 persons—slightly below the national average of 70 prescriptions per 100 persons.⁵ The drugs most commonly associated with death due to prescription drug overdose were hydrocodone, oxycodone, and methadone.⁶

In 2016, as part of the Heroin, Opiate, Prevention, and Education (HOPE) Agenda, the state of Wisconsin enacted 2015 Wisconsin Act 266. This law, which went into effect April 1, 2017, requires prescribers to review data from the state’s enhanced Prescription Drug Monitoring Program (ePDMP) before issuing an opioid prescription, to reduce inappropriate prescriptions and, ultimately, decrease opioid overuse.⁷ The law does not require prescribers to review the ePDMP when the number of doses being prescribed is intended to last the patient 3 days or less. In January 2017, there were approximately 100,000 queries to the Wisconsin ePDMP by health care professionals; this number rose to approximately 600,000 per month from April through December 2017. From April 1 to June 30, 2017, the number of opioid doses dispensed in Wisconsin was 17.5 million less than for the same period in 2016—a decrease of approximately 12%.⁸ In addition, the number of dispensed opioid prescriptions in 2017 was 20% less than in 2015.⁹

The primary objective of this study was to evaluate the effect of Wisconsin Act 266 on opioid prescriptions for acute pain within Mayo Clinic Health System sites in northwest Wisconsin to ensure that the organization is following similar trends. A secondary objective was to identify any change in opioid agents prescribed, for example, a shift from prescriptions for oxycodone to tramadol.

METHODS

Study Design and Patient Selection

A multicenter retrospective review was conducted in urgent care and emergency departments at Mayo Clinic Health System sites in northwest Wisconsin. Patients were included in the study if they

presented to and were discharged from these departments (each classified as a patient encounter) during May and June 2016, or May and June 2017, (pre- and post-implementation of Wisconsin Act 266, respectively). Study criteria excluded patients admitted to the hospital from these departments and patients who had the medication or medications administered exclusively during their encounter. All data were obtained from the health system’s electronic health record and included patient name, health record number, name of the prescribed opioid, quantity of the opioid, and the site and department where the prescription originated. Medications analyzed included codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, and tramadol. The Mayo Clinic Institutional Review Board approved the study protocol.

End Points

The primary end point of the study was comparison of the quantity of opioids prescribed in morphine milligram equivalents (MME) per patient encounter in the urgent care and emergency departments during the pre-implementation period vs post-implementation. Secondary end points were whether an opioid was prescribed in the encounter and the number of prescriptions issued for each opioid agent.

Statistical Analyses

Encounter characteristics were compared for the 2 periods with use of the Pearson χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables. Among patients with an opioid prescription, the MMEs per encounter were compared for the pre- and post-implementation groups using the Kruskal-Wallis test. Pearson χ^2 test was used to compare the proportion of all encounters in which an opioid was prescribed pre- vs post-implementation. Differences in the agents prescribed between groups were assessed with Pearson χ^2 test or Fisher exact test, depending on data sparsity. Statistical software (SAS version 9.4; SAS Institute Inc) was used for all analyses.

RESULTS

Patient Characteristics

Data on all patient encounters in the urgent care and emergency departments were reviewed for the study periods. In total, 34,561 patients were included in the study. Distribution of encounter type was similar for both periods (Table 1), and a total of 2,680 patients received an opioid prescription during one of the periods. Among those patients who received an opioid prescription, no statistical difference was found in age and sex (Table 2), and the median age was 44 years.

Outcomes

For the primary end point among patients with an opioid prescription, the median (interquartile range) MMEs prescribed per

patient encounter were 90 (60-120) in the pre-implementation period and 60 (60-120) in the post-implementation period. This represents a 33.3% reduction between the two periods ($P<.001$) (Figure).

The number of urgent care or emergency department encounters in which an opioid was prescribed was 1,464 (8.3%) in the pre-implementation period vs 1,216 (7.2%) post-implementation. This absolute reduction of 1.1% is a relative reduction of 13% ($P<.001$).

Among specific opioid agents prescribed during the time periods, the only statistically significant difference was for morphine, which had an absolute increase of 1.4% in the post-implementation period ($P<.001$) (Table 3). Hydrocodone was the most-prescribed opioid for both periods; no statistical difference existed for tramadol prescription rates. Far fewer prescriptions were written for the other agents, and no statistically significant difference was observed for codeine, hydromorphone, fentanyl, and methadone rates between the two periods.

DISCUSSION

This study demonstrates significant decreases in both total MMEs per encounter and in urgent care and emergency department encounters in which an opioid was prescribed. The requirement for clinicians to check the Wisconsin ePDMP before prescribing an opioid appears to have helped reduce opioid prescriptions for treatment of acute pain at Mayo Clinic Health System sites in northwest Wisconsin. Prior to data analysis, postulation was that a shift to more prescriptions for a less potent agent (eg, tramadol) may have occurred, but this shift was not seen. There was, however, an increase in morphine prescriptions from the pre-implementation to the post-implementation period. The reason is not clear, although it may have been due to a prescribing preference for morphine by providers working more during the post-implementation period vs pre-implementation. Another potential reason may be that during the second timeframe, more patients had allergies to opioids other than morphine, leading providers to prescribe morphine on discharge.

A limitation of this study is the assumption that patients in the urgent care and emergency departments received opioid prescriptions for the indication of acute pain. When developing the study protocol, we were challenged to define acute pain in an all-encompassing way. We initially trialed the idea of pulling data from the *International Statistical Classification of Diseases, Tenth Revision* (ICD-10) related to acute pain to specifically include the patients who received opioid prescriptions for such pain. However, in many scenarios, acute pain is secondary to another diagnosis, thus determination of the appropriate inclusion criteria was difficult for ICD-10 codes. In addition, not all ICD-10 codes may be included in an encounter or potentially are coded incorrectly,

Table 2. Demographic Comparison Between Periods Among Patients With an Opioid Prescription

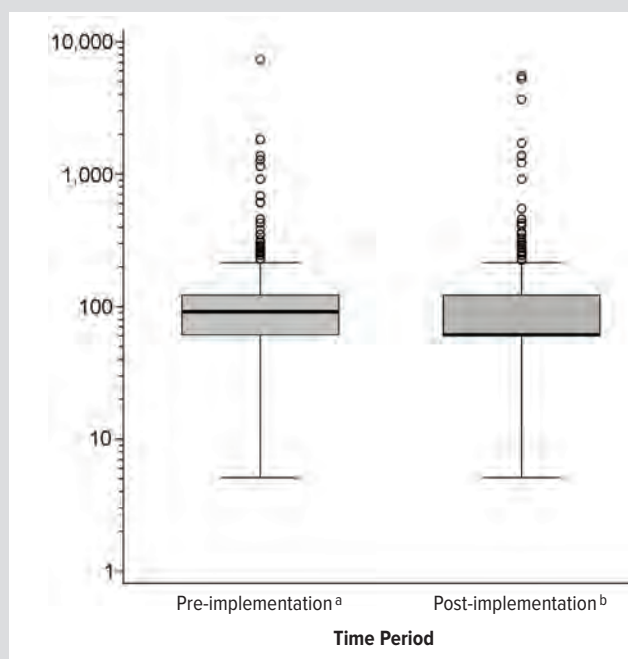
Variable	Period With Opioid Prescription			P-value
	Pre-implementation ^a (n=1,464)	Post-implementation ^b (n=1,216)	Total (N=2,680)	
Age, median (IQR), y	43 (32-60)	45 (31-60)	44 (31-60)	.60
Female sex, no. (%)	812 (55.5)	651 (53.5)	1,463 (54.6)	.32

^aPre-implementation of 2015 Wisconsin Act 266, May and June 2016.

^bPost-implementation of 2015 Wisconsin Act 266, May and June 2017.

Abbreviation: IQR, interquartile range.

Figure. Opioid MME per Patient Encounter per Period



Abbreviation: MME, morphine milligram equivalent.

^aPre-implementation of the 2015 Wisconsin Act 266, May and June 2016.

^bPost-implementation of 2015 Wisconsin Act 266, May and June 2017.

The median MME per encounter was 90 for the pre-implementation timeline and 60 for the post-implementation timeline ($P<.001$). The band within the interquartile range boxes represents the median. Bars extend to the minimum and maximum values within 1.5 times the interquartile range beyond the lower and upper quartiles.

Table 3. Comparison of Specific Opioid Prescription Rates After Implementation of 2015 Wisconsin Act 266

Prescribed Opioid	Rate of Opioid Prescriptions, No. (%)			P-value
	Pre-implementation ^a	Post-implementation ^b		
Codeine	29 (2.0)	16 (1.3)		.23
Fentanyl	1 (0.1)	3 (0.2)		.34
Hydrocodone	900 (61.5)	750 (61.6)		.95
Hydromorphone	4 (0.3)	7 (0.6)		.24
Methadone	1 (0.1)	0 (0)		>.90
Morphine	3 (0.2)	20 (1.6)		<.001
Oxycodone	285 (19.5)	218 (17.9)		.31
Tramadol	268 (18.3)	218 (17.9)		.79

^aPre-implementation, May and June 2016.

^bPost-implementation, May and June 2017.

which could lead to missing or extraneous data. By focusing our analyses specifically on urgent care and emergency departments, it was thought that chronic pain would not be treated in most encounters within these settings. It is possible, however, that some opioid prescriptions for chronic pain and acute exacerbations of chronic pain may have been included in the data.

Another study limitation is that the later timeframe for data analysis occurred almost immediately after implementation of Wisconsin Act 266 in April 2017, requiring providers to query the ePDMP before prescribing an opioid. Thus, opioid prescriptions in May and June 2017 may have been affected particularly. After learning about the new requirement, providers could have been more vigilant in checking the ePDMP, potentially leading to a reduction in the quantity of opioids prescribed. In contrast, some providers may not have been aware of the requirement or the details surrounding it, so it may not have altered their prescribing pattern. However, Wisconsin ePDMP data show that prescriber queries stayed high for the remainder of 2017, after implementation of Wisconsin Act 266.⁸

One barrier encountered was the inability to obtain organization-specific data on the number of provider queries in the ePDMP, which initially were intended to be an end point of the study. The Wisconsin ePDMP provides data at the statewide level for research purposes, including the number of provider queries per month, but the functionality currently does not allow researcher acquisition of institutional data. A medical coordinator account is required to obtain access to institution-specific data, and to study this data, each provider must show written consent to the established medical coordinator. This is possibly a future option for sites to better use ePDMP data and functionality.

The results of this study will contribute to the Wisconsin ePDMP efforts to reduce inappropriate prescription of opioids for acute pain and to develop more standardized practices for opioid prescription in the urgent care and emergency department settings. Quantities of opioids prescribed at a statewide level have decreased over the past several years, and it is important to sustain these efforts by continuing to analyze prescribing data and how the data correlate to opioid overdose deaths in Wisconsin.

CONCLUSION

The HOPE Agenda, specifically 2015 Wisconsin Act 266, appears to be associated with a decrease in opioid prescriptions for patients with acute pain presenting to urgent care and emergency department settings.

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A Survey of Eating Attitudes and Behaviors in Adolescents and Adults With Phenylalanine Hydroxylase Deficiency

Sharon Luu, MGCS, LCGC; Therese Breunig, RD; Nicoletta Drilias, RD; Ashley Kuhl, MS, CGC; Jessica Scott Schwoerer, MD; Paula Cody, MD, MPH

ABSTRACT

Introduction: Phenylalanine hydroxylase deficiency, commonly known as phenylketonuria (PKU), is an inborn error of metabolism that manifests in severe neurological damage when left untreated. Routine newborn screening has made early identification and treatment of affected individuals possible, changing the prognosis of PKU from devastating to excellent. The most effective treatment for PKU involves lifelong dietary restriction of protein, nutrition supplementation via medical foods, and frequent monitoring of amino acid levels in the blood. However, it has been observed that imposing strict medical control over daily dietary habits can lead to destructive attitudes towards eating and body image. This study investigated whether people with PKU are at increased risk of disordered eating behaviors and attitudes.

Methods: Fifteen patients with PKU between the ages of 12 and 35 from the University of Wisconsin (UW) Biochemical Genetics Clinic were surveyed about their metabolic management and eating attitudes and behaviors.

Results: While this study was too small to make conclusions of clinical significance, our findings did suggest that patients with poor metabolic control exhibited symptoms of disordered eating at a higher frequency than those with good metabolic control.

Conclusions: There is currently no validated screening tool to evaluate for disordered eating behaviors in individuals with PKU, which makes identifying and treating disordered eating and related conditions difficult. The development of this project emphasized the importance of tailored screening and provider awareness for disordered eating for populations with chronic illnesses.

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BACKGROUND

Phenylalanine hydroxylase deficiency, often known as phenylketonuria (PKU), is an inborn error of metabolism caused by a deficiency of phenylalanine hydroxylase (PAH), a hepatic enzyme that metabolizes phenylalanine (Phe) into tyrosine (Tyr).¹ Left untreated, PKU leads to systemically high levels of Phe and low levels of Tyr, leading to neurotoxicity and impaired brain development.² The typical presentation of untreated PKU includes irreversible severe to profound cognitive impairment, seizures, autistic behavior, psychiatric disturbances, eczema, decreased pigmentation, and a musty body odor. Advent of the newborn screening program in the 1960s made it possible to detect and initiate treatment for PKU from the neonatal period, thereby preventing the devastating neurotoxic sequelae of the condition.^{3,4}

PKU is typically treated through a diet that is low in Phe.⁵ Patients are limited to natural foods that are very low in protein, such as vegetables, fruits, and low-protein variants of pantry staples like bread and pasta.² This diet alone is nutritionally deficient, so patients also must ingest artificial low-Phe medical foods often referred to as “formula” in the forms of powders, tablets, pills, and shakes. Formula contains micronutrients to promote normal growth and development.⁵ and sometimes carbohydrates and fats to help satiety.² Over time, PKU medical foods have become more diverse, convenient, and palatable,⁶ but most patients are still unable to eat a “standard American diet.”

Metabolic clinics also request regular blood samples from their

patients with PKU to monitor Phe levels at least once a month. The American College of Medical Genetics and Genomics (ACMG) recommends that all patients maintain Phe levels in a “goal” range between 2 mg/dL (120 μ mol/L) and 6 mg/dL (360 μ mol/L), though these recommendations vary slightly from clinic to clinic.⁷

Pharmaceuticals can also help with PKU treatment, the most accessible of which is sapropterin dihydrochloride salt, a synthetic version of tetrahydrobiopterin (BH₄) that acts as an essential cofactor for PAH.² Phenylalanine ammonia lyase⁸ is a new drug that is also being used to treat PKU, though it comes with significant side effects. Pharmaceuticals can help some individuals manage their condition better, but diet remains the primary and most effective treatment.

Eating Disorders and Disordered Eating in Individuals With Chronic Illness

Eating disorders are defined as disturbances of eating or eating-related behavior that result in an altered consumption or absorption of food significant enough to impair the individual’s physical health or psychosocial functioning.⁹ Disordered eating refers to abnormal behaviors focused around eating or feeding but that do not fit the pattern of a specific eating disorder. These can manifest in behaviors such as restrictive eating, emotional eating, or uncontrolled eating. Maladaptive thoughts or behaviors surrounding food and body image can be triggered by many external factors including, but not limited to, socioeconomic status, familial influences, and differences between individual personalities and social experiences.¹⁰

Individuals with chronic illnesses requiring lifelong dietary management may be at even higher risk of developing disordered eating. For instance, adolescent girls and adult women with type 1 diabetes have demonstrated increased frequency of disordered dieting behaviors, including fasting, dietary restriction, food preoccupation, laxative use, excessive exercising, body image disturbances, and even omitting insulin for weight control.^{11,12} Disordered eating behavior has also been observed in individuals with cystic fibrosis, celiac disease, Crohn’s disease, ulcerative colitis, inflammatory bowel disease, and irritable bowel syndrome.^{11,13,14} For these individuals, the pressure to remain on a special diet to keep symptoms at bay may be a stressor that can trigger disordered eating behaviors or eating disorders.¹¹ Additionally, some of the drugs used to treat these conditions can dramatically alter body composition, and therefore negatively impact body image.

Exploring Incidence of Disordered Eating in Individuals With PKU

The correlation between disordered eating and PKU has never been established, but like other chronic illnesses, it is likely that individuals with PKU are also at increased risk for disordered eating.^{12,15} Lifelong dietary management is recommended; however, compliance in adolescence and adulthood is notoriously poor. Over 70% of adults with PKU have Phe levels elevated above

treatment range.⁷ This may be due to both social and economic barriers. People with PKU often report feeling isolated due to significant dietary restriction. Formula is expensive and is not always covered by insurance or government-run programs. Patients who cannot bear this financial burden will turn to higher Phe foods to meet their nutritional needs.

While people with PKU who go off-diet in adulthood are not at risk for irreversible neurological damage, they still can develop subtle cognitive deficiencies like anxiety, depression, decreased executive function, and attention deficits,¹⁶ all of which are known risk factors for disordered eating.¹⁰ Additionally, patients with inadequate formula intake can have nutritional deficiencies that can lead to both poor growth² and obesity.¹⁷ As a result, they may struggle with body image, another significant risk factor for developing an eating disorder.¹⁰

Metabolic health care clinicians have expressed concerns that their patients with PKU may be experiencing disordered thinking patterns, but lack of training and resources makes identification of disordered eating in the population difficult and inconsistent (Luu S, Breunig T, Cody P, unpublished data, March 2018). This study aims to investigate the behaviors and attitudes that people with PKU have regarding food and eating. We explored this by reviewing the literature regarding factors that can increase risk for disordered behaviors in populations with chronic illness and by creating a tool that surveyed for disordered eating behaviors specifically in people with PKU.

METHODS

Recruitment

Study participants were recruited from the University of Wisconsin (UW) Biochemical Genetics Clinic in Madison, Wisconsin. Patients were eligible for the study if they were being treated for PKU at the clinic, were born on or between the years of 1983 and 2005, and were brought to clinical attention by newborn screening. The eligible participants were all adolescents or adults at the time of the study and had been prescribed a low-Phe diet and medical formula for life, a protocol that was enacted at the UW Biochemical Genetics Clinic in 1983. Patients were excluded from participation if they had a diagnosis of cognitive impairment, intellectual disability, or a prior eating disorder. Eligibility criteria were determined from UW Health electronic medical records.

Procedure

Recruitment letters were sent to each eligible participant’s home address. The recruitment letter introduced the study team, summarized the purpose of the study, and informed the recipient to expect a follow-up package in a week. A week later, eligible participants were mailed a consent form (accompanied by an assent form for minors), a copy of a paper survey, and a postmarked envelope in which to return the survey. Patients also were given a scannable

code if they opted to take the survey online. All recruited individuals were informed that participation in the study was anonymous, completely voluntary, and would not be shared with the metabolic care team at the UW Biochemical Genetics Clinic.

The first part of the survey asked patients to provide demographic information, including sex, age, ethnicity, and race. Participants also were asked to identify the individual who was answering the questions because the survey was only designed for self-reporting.

The second part of the survey asked patients to answer a series of questions designed to identify potential disordered eating attitudes or behaviors. These questions were loosely adapted from the Eating Attitudes Test (EAT-26).¹⁸ The language in the questions was simplified to accommodate for the age of the adolescent participants and any PKU-related neurocognitive deficits caused by being off-diet. Some questions from the EAT-26 were eliminated because they would be answered abnormally by individuals on the PKU diet. Additional qualifying questions were added to elucidate the cause of a behavior that might otherwise be considered “disordered” in the general population (Appendix A). Participants were asked to answer all the behavioral questions using a Likert scale of “Always,” “Usually,” “Often,” “Sometimes,” “Rarely,” and “Never.” Their responses were assigned scores of 1 through 6 respectively.

The third part of the survey asked patients about their medical compliance. Participants were asked about their height, weight, their recommended treatment, the frequency at which they checked their Phe levels, their last blood Phe concentration, and whether they were pregnant or trying to become pregnant. They also were asked to evaluate how well they thought they managed their PKU. Lastly, participants were asked to disclose any other diagnoses that could possibly require additional dietary management or change their mental status or learning abilities. Disclosure of additional diagnoses was considered in data analysis but did not exclude any participants from the study.

Data Management and Analysis

The study team compiled and deidentified all responses. The data were analyzed by the UW Department of Biostatistics and Medical Informatics and the study team. All descriptive and statistical analyses were performed in Microsoft Excel. Wilcoxon rank sum tests were used to evaluate significance among ranked variables.

This study protocol was reviewed and approved by the UW-Madison Health Sciences Institutional Review Board.

RESULTS

Fifty-eight eligible participants were identified from the UW Biochemical Genetics Clinic medical records. Eight of the recruitment letters were returned to the sender because the documented patient address was no longer current. Fifteen responses were collected, yielding a 30% response rate.

Table 1. Patient Demographics

Demographics	N = 15 (100%)
Sex	
Male	9 (60%)
Female	6 (40%)
Age (years)	
12 - 17	6 (40%)
18 - 35	9 (60%)
Mean: 20.8 ± 7.1	
Median: 20	
Range: 12 - 34	
Ethnicity	
Hispanic or Latino	0 (0%)
Not Hispanic or Latino	15 (100%)
Race	
White	15 (100%)
Body Mass Index	
Underweight (<18.5)	0 (0%)
Normal (18.5 - 24.9)	15 (100%)
Overweight (>24.9)	0 (0%)
Survey Method	
Paper	12 (80%)
Online	3 (20%)

Demographics

Forty percent of participants were adolescents at the time of the study while 60% were adults (18 years and above); 60% of participants were male and 40% were female. All participants identified as white, and all had body mass indexes (BMI) in the average range (Table 1).

Compliance to Treatment

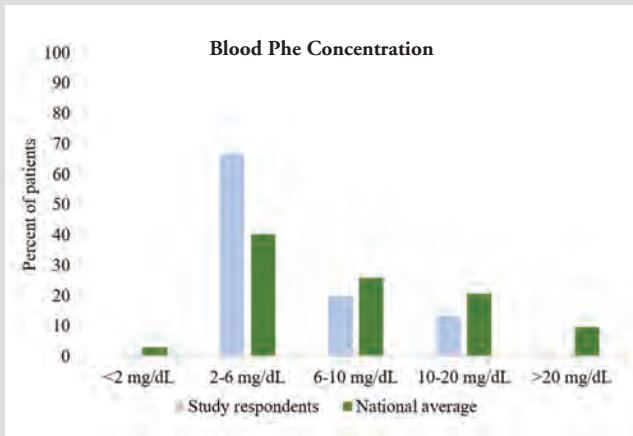
Study participants’ compliance to medical recommendations were compared to a nationally representative survey that asked metabolic clinics about their patients’ medical compliance. The study participants also were asked to self-evaluate how well they thought they controlled their PKU. Sixty-six percent of participants maintained Phe levels between 2 mg/dL and 6 mg/dL, and 60% of participants checked Phe levels monthly in compliance with ACMG guidelines, compared to a national average of 40% and 24%, respectively.⁷ Fifty-three percent of study participants believed that they managed their PKU “very well” (Figure 1). Overall, a participant’s self-reported metabolic control was consistent with their Phe levels and frequency of Phe checks.

Eating Behaviors and Attitudes

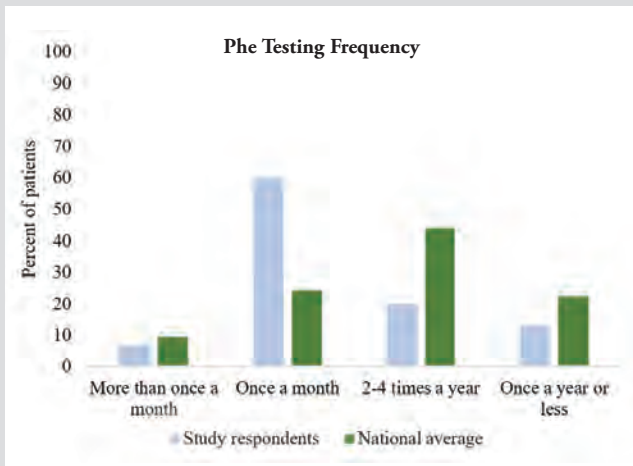
Participants answered 38 behavioral questions on a Likert scale of “Always,” “Usually,” “Often,” “Sometimes,” “Rarely,” and “Never.” Their responses were scored 1 through 6, respectively, except for the question, “Eating is enjoyable for me,” for which the numerical scores were reversed. The mean score for each question was calculated. Lower scores for a question indicated that the surveyed sample was more symptomatic for that behavior.

The behavioral question responses were compared between participants who had been recommended a restricted protein

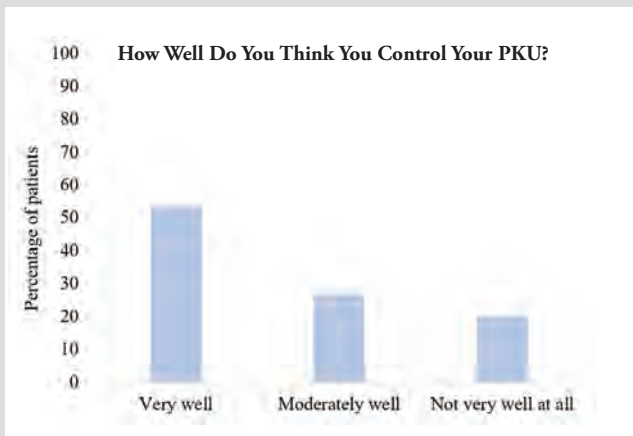
Figure 1. Study Participants' Compliance to Phenylketonuria (PKU) Management vs National Average



A. Blood Phe concentrations of patients with PKU. Study participants self-reported their last Phe concentration (n=15). National average was reported from 44 metabolic clinics, totaling 1,278 actively managed PKU patients between ages 13 and 29 years.



B. Frequency of blood Phe testing. Study participants self-reported their frequency of blood Phe testing (n=15). National average was reported from 44 metabolic clinics, totaling 1,328 actively managed PKU patients between ages 13 and 29 years.



C. Study participants self-evaluated how well they managed their own PKU.

diet with those who had not. Patients who had been prescribed a restricted protein diet reported that they were preoccupied with thoughts of food more often than patients who had not been prescribed a restricted protein diet ($P < 0.05$) (Figure 2).

Finally, the behavioral question responses were compared between participants who responded that their PKU was “well controlled” with participants who responded that their PKU was “not very well controlled.” Patients who self-reported poor metabolic control had disordered eating thoughts more often on 7 of the 38 items when compared to patients who self-reported good metabolic control ($P < 0.05$). Patients who self-reported good metabolic control only had disordered eating thoughts more often than patients who self-reported poor metabolic control on 1 of the 38 items ($P < 0.05$) (Figure 3).

DISCUSSION

Prevalence of Disordered Behavior in People With PKU

This study found that the average participant “Sometimes,” “Rarely,” or “Never,” demonstrated maladaptive eating and dieting behaviors or attitudes. It is reasonable to conclude that this sample of individuals with PKU did not exhibit thinking patterns concerning for disordered eating. All study participants also had average BMIs, further evidence to support that none of them were showing disordered behaviors severe enough to affect physical body composition, though it should be noted that some individuals with eating disorders can have normal BMIs.

One exception was that all participants averaged an unusually low or symptomatic score (3.87) for the item, “I take longer than others to eat my meals.” It is possible that individuals with PKU may need to take more time to determine the protein content of their meals, but there are no anatomical or physiological differences that would cause patients to take more time to eat.

Eating Behaviors Between Patients On and Off Protein-Restricted Diets

Most patients with PKU need to eat a low-protein diet and medical foods for life to maintain Phe levels within goal range; however, some individuals with more mild disease presentation may be able to eat less restrictive or even normal diets. It was anticipated that patients on restricted diets would think about food much more often than those not on a restricted diet, because they must strictly control their oral intake to meet Phe goals.¹⁹ This hypothesis was supported: patients on a restricted protein diet were statistically preoccupied with food more often, not only before checking their Phe levels, but also at all other times as well (Figure 2).

While preoccupation with food may be a symptom of disordered eating behavior in the typical population, it may not be a negative attitude in the well-controlled PKU population. Instead, it may be an indicator that patients are motivated to maintain good long-term metabolic control. Study participants on protein-

restricted diets did not report feeling like their PKU caused them stress with family or friends, caused them problems at work or school, or that “food controlled [their] lives” more often than their counterparts not on diet – all reassuring attitudes for patients’ metabolic control and mental health.

Eating Behaviors Between Patients With Good and Poor Metabolic Control

Patients who self-reported poor metabolic control were preoccupied about food “all of time” much more often than patients who self-reported good metabolic control (Figure 3). However, there was no statistical significance in the frequency at which patients thought about food before Phe checks, regardless of how well they controlled their PKU. In fact, poorly controlled patients were less likely to think about food before checking their Phe than during other points of the day. This suggests that food is a pervasive thought for patients who do not manage their PKU well but, perhaps, they fail to draw the connection between diet and Phe levels.

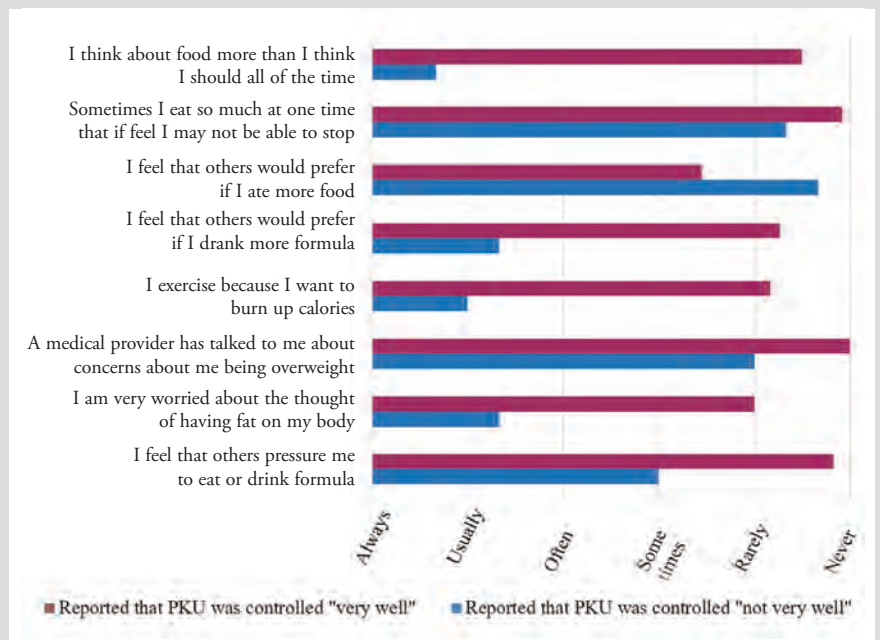
Patients who reported poor metabolic control also reported more disordered behavior in dieting and body image. Patients who felt they did not manage their PKU well were more worried about gaining weight and engaged in activities to lose weight more often. They acknowledged that others seemed concerned about their dietary habits, suggesting that patients with poor metabolic control were more likely to limit their oral intake. In addition to the higher frequency of dieting behavior, these patients also were more likely to report that they had been clinically overweight. There is a strong correlation between dieting and dissatisfaction of body image, often due to frequent and dramatic fluctuations in weight.²⁰ Lastly, patients with poor metabolic control did report bingeing behavior more often than patients who controlled their PKU well; however, the small deviation between the groups and tiny sample sizes leaves the significance of this item in question (Figure 3). These data are worrisome; results suggest that patients with PKU who are not well-controlled are still thinking about food, but in a way that does not improve their overall health and instead infiltrates into

their body image and healthy socialization, when compared to well-controlled patients who seem to think about dieting purely as a way to manage their condition.

Limitations

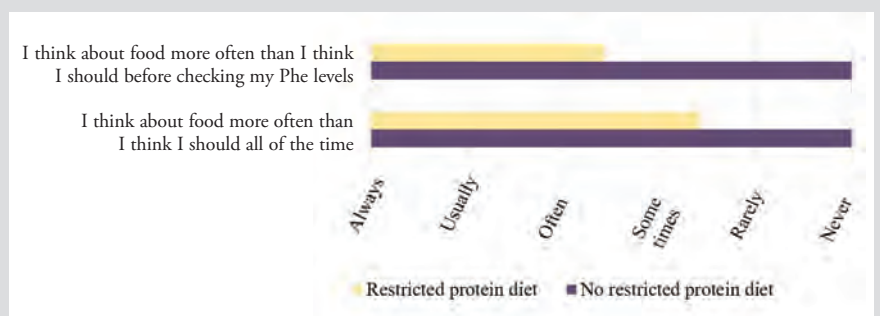
This study did yield statistically significant findings, but the sample size was small (n=15) and had evidence of selection biases. There are over 7,000 people diagnosed with PKU in the United States, and approximately 40% of those patients are between the ages of 12 and 35.⁷ This study only surveyed a very small pro-

Figure 2. Comparison of Eating Behaviors and Attitudes Between Patients Who Had Been Recommended to Follow a Restricted Protein Diet With Those Who Had Not



All behavioral items displayed showed statistical significance between the group that was on a restricted protein diet (n=12) and the group that was not on a restricted protein diet (n=3) on a Wilcoxon rank sum test ($P \leq 0.05$).

Figure 3. Comparison of Eating Behaviors and Attitudes Between Patients Who Self-Reported Good and Poor Metabolic Control



All behavioral items displayed showed statistical significance between the group who reported that their PKU was “very well” controlled (n=8) and the group who reported that their PKU was “not very well” controlled (n=3) on a Wilcoxon rank sum test ($P \leq 0.05$).

portion of patients with PKU and was not representative of the national population. While the study sample included male and female patients, it was racially and ethnically homogeneous (Table 1). PKU is most common in people of European ancestry, but it can affect people of all ethnicities.²⁰ Therefore, this cohort is not demographically representative.

Additionally, it appears that this study only sampled a subset of the population with exceptional metabolic control. In the United States, roughly half of adult patients with PKU are lost to follow-up.⁷ All the participants in this study responded to mail contact and many gave responses to medical management questions that suggested they were seen in their metabolic clinic regularly. On average, participants in this study also reported much better medical compliance (lower Phe concentrations and more frequent Phe checks) than patients with PKU of a nationally representative sample (Figure 1).

It should be noted that PKU care is unique in the state of Wisconsin because every diagnosed individual is eligible to receive medical formula and low-protein foods for life. Most other states have restrictions on the kinds of foods that are covered and the ages of people who can receive them,²¹ therefore creating access barriers that are not present for patients in Wisconsin.

Lastly, statistically significant findings in this study should be regarded with caution. Questions in the study survey were changed significantly from the original EAT-26 (Appendix A), and the survey was scored with a different scale. EAT-26 only assigns scores to responses of “Always,” “Usually,” and “Often;” it considers all other responses nonsymptomatic.²² This study, however, ranked all responses, therefore imparting varying levels of pathogenicity to any answer.

Future Directions

This small study yielded intriguing results, but these results would be of more consequence in a larger sample. Ideally, the scope of this project would be expanded to encompass a nationally representative sample.

Anecdotal evidence suggests that metabolic dietitians are concerned that PKU patients would be at higher risk for disordered eating, but also feel powerless to improve the situation because they were the ones imposing the dietary restrictions.¹⁷ Formally surveying dietitians may speak for a much wider and representative population of PKU patients, as well as offer a different perspective on this issue.

This research study demonstrates the difficulties in identifying disordered eating behaviors in people with PKU. Disordered eating in this population may be missed because they can be mistaken as behaviors used to maintain their medically recommended diet. Existing validated screening tools for eating disorders often do not work on people with PKU or other diet-managed conditions because these individuals often answer questions differently due to their disease or prescribed treatment, leading

to low sensitivity or high false positive rates. The survey used in this study was a screening tool for research purposes. Subsequent iterations could prepare the questionnaire for clinic utilization.

CONCLUSIONS

This nascent study suggested that patients with PKU may be more prone to have certain thoughts regarding eating and body image that could possibly impede social functioning or physical health. Factors such as restricted diet or medical compliance may put certain individuals at greater risk for developing disordered eating.

However, identifying and treating disordered eating in people with PKU is challenging. Protocols to address a suspected eating disorder vary from clinic to clinic; there is no consensus on what should be done if a medical provider suspects an eating disorder in a patient. There is even less certainty when that patient also has a chronic illness such as PKU. Therefore, metabolic health care providers should maintain a low threshold for suspecting disordered eating in their patients with PKU. Developing guidelines to identify and care for this population with eating disorders or maladaptive behaviors and attitudes towards food can lead to more effective and consistent care for patients in all areas of their health.

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Multimodal Care for Knee and Hip Osteoarthritis: A Pilot Feasibility Study of a Novel Approach to a Common Problem

Kathryn A. Miller, MD; Linda M. Baier Manwell, MS; David Rabago, MD

ABSTRACT

Background: Osteoarthritis is common and debilitating. Evidence-based care exists; there is a gap between recommended and received care. Multimodal treatment is recommended, with unknown effectiveness. We report pilot feasibility data for a new university-based clinic providing multimodal care for knee and hip osteoarthritis (KHOA).

Methods: Quality-improvement case series with the first 50 patients. A multidisciplinary team provided care. Feasibility outcomes included treatment duration, patient adherence, provision of guideline-recommended care, and satisfaction. Secondary outcomes included self-reported and objectively assessed patient measures.

Results: Fifty patients (59±10.5 years, 32 female) received guideline-recommended care; 40 adhered to 3.83±2.21 follow-up visits over 12.24±7.79 months; satisfaction was high. Objectively assessed outcomes improved, but self-reported outcomes did not.

Discussion: Early data suggest multimodal care for knee and hip osteoarthritis is feasible and may be associated with improved outcomes.

BACKGROUND

Knee and hip osteoarthritis (KHOA) are the most common forms of arthritis, affecting over one-third of older Americans. Their prevalence is rising with the population's age and weight; 43% of Wisconsin adults report functional limitations due to arthritis.¹ KHOA leads to increased morbidity and mortality, lost productivity, and worsening quality of life.² It is associated with metabolic

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syndrome, diabetes, cardiovascular disease, and falls,² which complicate the management of each.

KHOA treatment is challenging and should be tailored to individual patient needs.³ Care can involve surgery, which is expensive, has risks, and is not available or appropriate for everyone. Many patients require long-term medications, including nonsteroidal anti-inflammatory drugs and opioids, which have limited effectiveness and major side effects; curbing opioid use is a national priority. National agencies including The Institute of Medicine call for new approaches to osteoarthritis care.⁴

Practice guidelines and consensus statements recommend 6 evidence-based core care strategies: (1) education on disease and self-management; (2) assessments of pain, function, and quality of life; (3) nutritional assessment and counseling with weight loss for overweight patients; (4) medication counseling and management; (5) physical activity counseling and management; and (6) psychological health assessments of coping and mood.⁵ Each strategy improves outcomes but is only partially effective. Little is known about patient receipt of core strategies. A European study found only 48% of patients with knee osteoarthritis receive guideline-recommended treatment.⁶ A US study of frail patients over age 75 reported that 57% received some guideline-recommended care for osteoarthritis.⁷ A medical record review of KHOA care at UW Health from 2011 to 2017 revealed that only 33% of patients received all core care components. Interviews by the study team with UW Health primary care physicians and patients revealed patient and care team barriers to provision and uptake of guideline-driven care.

Coordinated delivery of all core care elements across multi-specialty teams, ie, multimodal care, may be synergistic⁸ and is

recommended for ongoing KHOA management by the Osteoarthritis Research Society International (OARSI).⁵ No reports describe multimodal KHOA care in the United States and the evidence for it worldwide is limited.⁹ In 2017, the lead author (KAM) founded the UW Health Knee and Hip Comprehensive Non-Surgical Osteoarthritis Management Clinic (UW KHOA Clinic) to provide individually tailored, multimodal care. We conducted a pilot-level quality improvement (QI) project to explore clinic feasibility and initial patient-oriented effects.

METHODS

Study Design

Data from the UW KHOA Clinic (July 1, 2017 to June 30, 2019) were analyzed. Institutional Review Board review was not required; in accordance with federal regulations, this QI project does not constitute research as defined under 45 CFR 46.102(d). This report follows Squire 2 guidelines for QI reporting.

The clinic was designed by the lead author and medical director (KAM) and stakeholder colleagues, informed by OARSI recommendations⁵ to: (1) decrease gaps between guideline-recommended and received care, (2) improve KHOA-specific outcomes, and (3) reduce the negative impact of common associated conditions including medication-related adverse effects. Clinical operations were developed over 8 months with input from patients, clinicians, and UW Health administrative leadership. The clinic opened in July 2017 at 1 day per week.

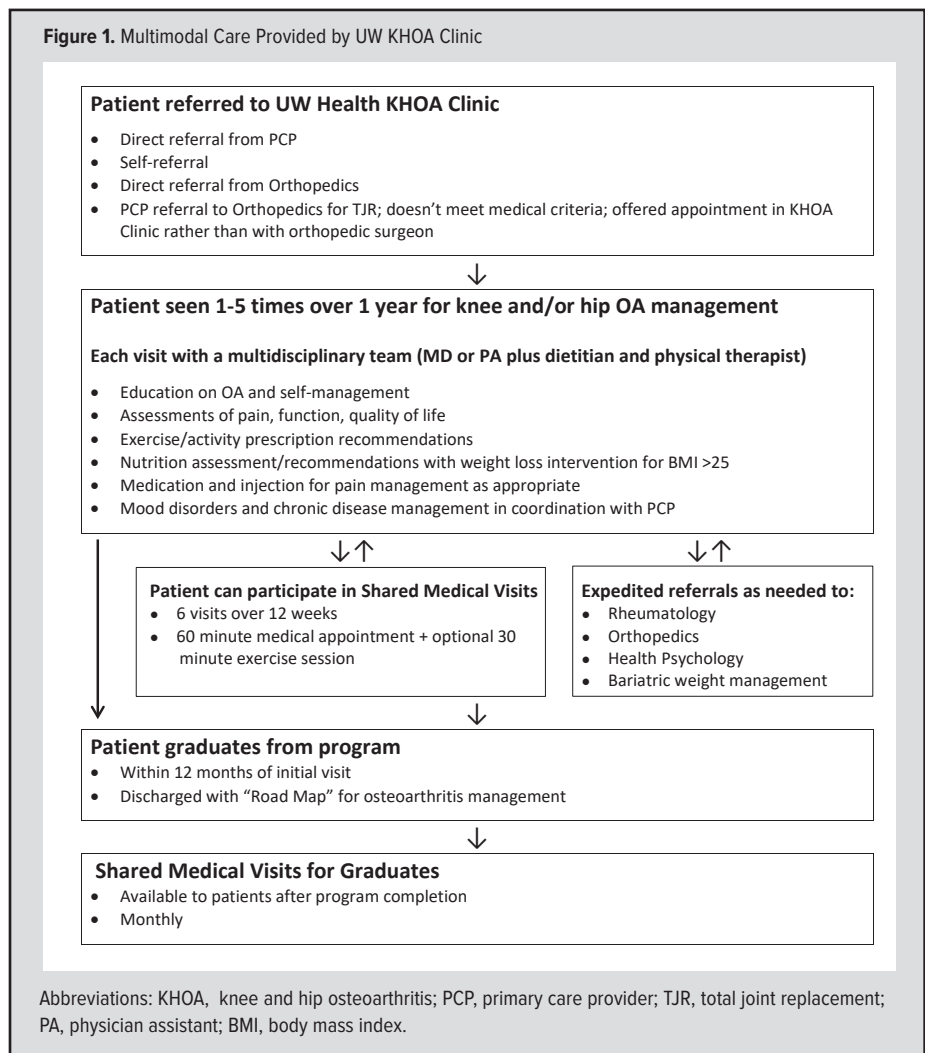
Participants and Settings

Eligibility criteria included adult patients with a diagnosis of knee or hip osteoarthritis who visited the UW KHOA Clinic at least once.

Intervention

A team comprised of a general internist, physical therapist, and dietitian provided multimodal care guided by patient history, symptoms, health, and function (Figure 1). Expedited referrals were made to health psychologists, and for ultrasound-guided injections, nerve blocks, and rheumatologic or orthopedic care as needed. Patients were seen 1 to 5 times over 6 to 12 months and could choose to participate in shared medical visits (six 1-hour visits over 12 weeks) to focus on lifestyle changes, goal setting, recipe

Figure 1. Multimodal Care Provided by UW KHOA Clinic

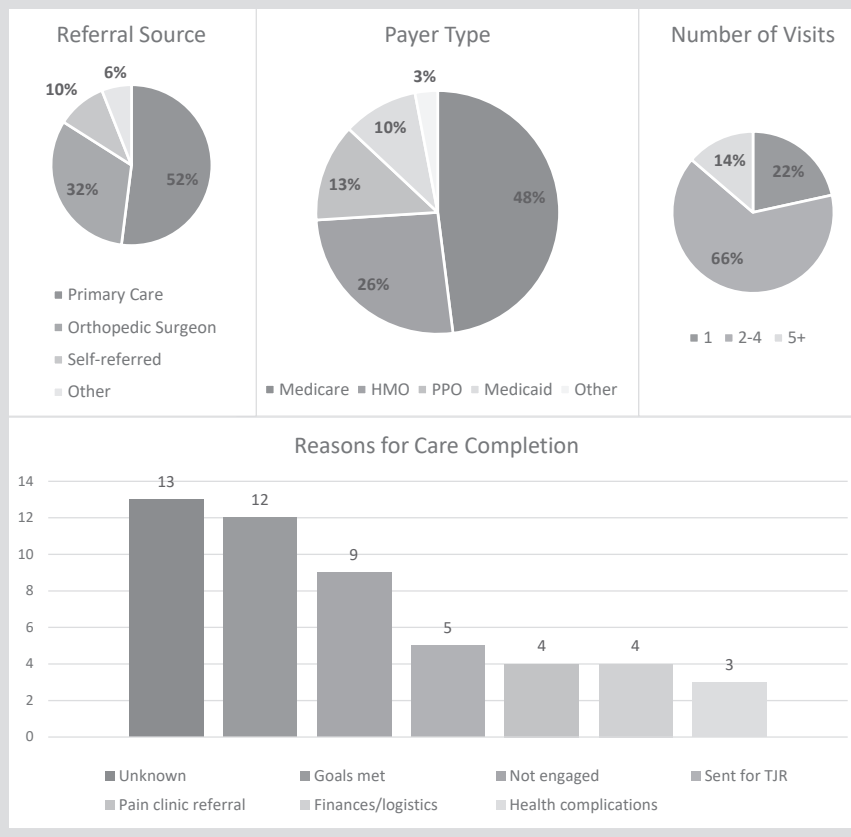


sharing, pharmacologic options, and the role of surgical intervention. These visits were physician-led with support from clinic multidisciplinary team members. A no-cost, 30-minute exercise session was available after each visit.

Outcome Measures

The primary clinic feasibility outcomes were treatment duration, patient adherence, patient satisfaction, and percent of patients receiving all 6 evidence-based core care strategies: (1) disease/self-management education; (2) pain, function, quality of life assessments; (3) nutritional assessment/counseling with weight loss for body mass index (BMI) >25; (4) medication counseling/management; (5) physical activity counseling/management; and (6) coping/mood psychological health assessments. Secondary outcomes included self-reported and objectively assessed patient measures: Pain and Mental Health subscales from the Veterans Rand 12-Item Health Survey (VR-12); Hip Disability and Osteoarthritis Outcome Score (HOOS) and/or the Knee Injury and Osteoarthritis Outcome Score (KOOS); 3 tests of function (Timed Up and Go [TUG], 30-Second Chair Stand, Single Leg

Figure 2. UW KHOA Clinic Operations (Referral Source, Payer Type, Number of Visits Completed, and Reason for Discharge for the First 50 Patients)



Abbreviations: PPO, Preferred Provider Organization; HMO, Health Maintenance Organization; TJR, total joint replacement.

Half of patients (52%) were referred by primary care (Figure 2) and insured by Medicare (48%). The most common visit frequency was 2 to 4 times. The most frequent reasons for clinic discharge were lost to follow-up (26%), goals met (24%), and lack of engagement (18%).

All 50 patients received recommendations and assessments related to the 6 core evidence-based care strategies during their first visit. Patient satisfaction data limited to this cohort of 50 patients are not available; aggregate data for all patients seen through June 2019 indicate that 87.7% would highly/very highly recommend the clinic to a friend. Reasons for dissatisfaction were frustration about not being seen by an orthopedic surgeon or not being a candidate for total joint replacement.

Forty patients (80%) returned 1 or more times for ongoing care, attending 3.8 ± 2.1 visits over a maximum of 18 months (Table). Twenty-three (46%) lost weight over the treatment period; 11 (22%) of these lost more than 5% of initial weight. There were no clinically significant improvements in HOOS/KOOS measures or VR-12 physical subscale scores. VR-12 mental health subscale scores showed a

Stance); and BMI. Outcomes were assessed in person at each clinic visit.

Sample Size and Analysis

Uptake of multimodal care for KHOA has not been assessed. For this pilot project, a convenience sample of the first 50 consecutive patients who completed a visit at the clinic was used. Descriptive statistics described the sample (mean \pm standard deviation). Baseline and follow-up variables were compared using paired 2-tailed *t*-tests. A 2-sided *P*-value <0.05 was used to determine statistical significance.

RESULTS

Baseline characteristics for the first 50 patients (Table) indicate that most were female (64%) and middle-aged (59 ± 10.5 years). Nearly half (44%) were active or former tobacco users, and 44% had ≥ 5 coexisting conditions. Multi-joint osteoarthritis was prevalent, with 48% reporting pain in more than 1 hip and/or knee. One-third (32%) were taking chronic opioid medications. Average weight was 256 pounds and most (82%) had a BMI ≥ 30 kg/m². VR-12 scores reflected moderate to high disease severity and pain, and moderate to low general health and functional status.

statistically significant ($P=0.022$) but not clinically important improvement. Functional status improved. At baseline, 15% of patients completed the benchmark of at least 14 chair stand rises; at end of treatment, 35% reached this goal. At baseline 35% achieved the TUG benchmark of less than 12 seconds to complete the activity; this increased to 50% by treatment end.

SUMMARY

This pilot-level quality improvement project assessing multimodal care for KHOA suggests 2 principal findings. First, this clinic appears feasible based on patient receipt of guideline-recommended care, their willingness to attend multimodal care clinic visits over time, and a report of high satisfaction with such care. Second, the clinic was able to assess self-reported and objectively assessed outcomes as part of routine clinic function, and some of these outcomes improved. While this pilot-level project is not powered to detect pre-post differences in these outcomes, our findings provide a rationale for expansion of clinic hours and suggest the need for formal outcomes assessment and dissemination work.

These findings are consistent with the limited data on multimodal care for osteoarthritis and other conditions. Somewhat similar care models are reported to be feasible and acceptable

outside of the United States; 1 study reported that patients receiving multimodal osteoarthritis care had significantly higher patient satisfaction scores than usual care.¹⁰ Limitations to the current QI study include those inherent to a QI study, a small sample size, and lack of patient satisfaction data for this specific cohort.

Concomitant multimodal care may offer advantages over serial strategies due to synergy between elements of care.⁹ Each of the six evidence-based core treatment strategies for KHOA partially addresses the underlying constellation of factors associated with pain and functional limitation. Removing the barriers to receipt of comprehensive care by offering all core treatment strategies in a single clinic may mitigate barriers for patients. A supportive multidisciplinary team may enhance patients' self-efficacy by reinforcing evidence-based self-management strategies across disciplines.

Implications for Clinical Care and Research

The positive aspects we report here have been matched by subsequent UW KHOA Clinic experience. There is a 3-month wait for an initial appointment. Future plans include expanding clinical operations to better address patient needs, including implementing daily operation, expanding the current clinic offerings through shared medical visits, and using an online platform to asynchronously support patients between visits. Plans also include robust research efforts to assess patient outcomes and program costs, and conduct of formal efficacy and effectiveness research.

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Table. Pilot Outcomes From the First 50 Patients in the UW KHOA Clinic

Outcome	First 50 Patients	40/50 Patients (80%) Completing 2+ Visits		
		Baseline (n=50)	Baseline (n=40)	Final (n=40)
		Average Number of Visits 3.83 (±2.21) Average Duration of Treatment 12.24 Months (±7.79)		
Female sex	32 (64%)	25 (62.5%)		
Age (years)	59±10.5	61±8.25		
Tobacco use				
Current	6 (12%)	4 (10%)		
Former	16 (32%)	14 (35%)		
Coexisting conditions				
0	6 (12%)	3 (7.5%)		
1	4 (8%)	2 (5%)		
2-4	18 (36%)	16 (40%)		
5+	22 (44%)	19 (47.5%)		
Joint involvement				
1 Knee	15 (30%)	13 (32.5%)		
1 Hip	11 (22%)	8 (20%)		
Multi-joint	24 (48%)	19 (47.5%)		
Chronic opioid use	16 (32%)	13 (32.5%)		
Body weight (lbs)	256 (±68.22)	251.05 (±69.23)	241.30 (±67.22)	0.006
BMI (m/kg ²)	39.11 (±9.56)	39.77 (±9.52)	38.19 (±9.24)	0.005
VR 12 mental subscale ^a	45.44 (±13.77)	42.69 (±12.30)	44.92 (±13.23)	0.022
VR 12 physical subscale ^a	28.98 (±9.57)	28.49 (±9.74)	30.25 (±9.10)	0.101
30 sec chair rise (#no. rises)	9.58 (±4.23)	9.43 (±4.94)	11.51 (±4.56)	<0.001
30 second chair rise (no. of patients completing ≥14)	8 (16%)	6 (15%)	14 (35%)	
TUG (seconds)	12.56 ± 6.78	11.48 (±5.35)	10.93 (±4.92)	0.296
TUG (no. of patients completing in <12 seconds)	12 (24%)	14 (35%)	20 (50%)	

Abbreviations: BMI, body mass index; VR, Veterans Rand; TUG, Timed Up and Go.
^aUS population norm of 50; lower scores denote more symptoms.

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Trends in Hip Fracture Mortality in Wisconsin and the United States, 1999-2017

Samantha Pabich, MD; Neil Binkley, MD

ABSTRACT

Introduction: Hip fracture affects >300,000 Americans each year, and the mortality rate following these fractures is high.

Methods: Authors searched the Centers for Disease Control and Prevention Wide-Ranging Online Database for Epidemiologic Research (WONDER) for incidences of hip fracture as a contributing cause of death and stratified by sex, age, race, ethnicity, state, month of death, and underlying cause of death across the United States and Wisconsin.

Results: Wisconsin has the third-highest age-adjusted death rate for hip fracture in the United States. Those who die from hip fracture are most likely to do so in a nursing home. Hip fracture deaths occur more frequently between October and March and often are associated with respiratory illness.

Conclusion: Hip fracture is a major contributing cause of death. Wisconsin residents are particularly affected by this risk.

INTRODUCTION

Hip fracture is an unfortunately common event, affecting more than 300,000 people annually in the United States;¹ most of these fractures are osteoporosis-related and are caused by a fall. About 30% of people with hip fracture die within the year following the event.²

Hip fracture incidence varies by season in the United States,³ which is possibly attributable to the following:

1. Vitamin D deficiency—During winter months, there is inadequate sunlight for cutaneous production of Vitamin D north of the 37th parallel.⁴

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2. Icy conditions—In colder states, icy conditions create increased risk for falls.

3. Seasonal infections—Afflicted patients are more likely to fall; conversely, patients who have fallen are more likely to be institutionalized/exposed to pathogens.

Many hip fractures are preventable. One of the most effective strategies to prevent hip fracture is simply to prevent falls.⁵ There are also several pharmaceutical agents approved for treatment of those at high fracture risk that can significantly reduce risk of hip fracture.⁶ High-risk patients include those with history of fragility fracture, osteoporosis by T-score, or osteopenia with FRAX-predicted 10-year risk of major fracture >20% or hip fracture >3%.

The US hip fracture incidence, which had been declining for years, recently plateaued.⁷ Hip fracture-associated mortality followed a similar pattern as hip fracture incidence in the late 1990s and early 2000s.² However, hip fracture incidence trends in Wisconsin have not been characterized. Thus, the purpose of this report is to examine the epidemiology of hip fracture-associated mortality in Wisconsin and the United States, including temporal/geographic trends and underlying causes of death associated with hip fracture.

METHODS

The Centers for Disease Control and Prevention Wide-Ranging Online Database for Epidemiologic Research (WONDER) is a data hub and query system containing deidentified information from US death certificates for 1999-2017, for use in analysis of public health data. We searched the WONDER Multiple Cause

of Death Database for hip fracture as a “Contributing Cause of Death” (CCOD) on death certificates using diagnostic codes S72.0 (fracture of the femur), S72.1 (fracture of the femur, peritrochanteric fracture), and S72.2 (fracture of the femur, subtrochanteric fracture). The death rate associated with hip fracture was calculated using the number of deaths containing mention of one of these diagnostic codes per 100,000 people in the live population at the time queried.

We stratified deaths in Wisconsin and the United States by age, sex, race, and Hispanic status—the latter 3 were age-adjusted—and looked at trends over time. Age-adjustment compares the proportion of the population in each state to the 2000 US standard population and allows for comparisons of similar age groups across states that might have varying age demographics. Microsoft Excel was used to create a map display wherein states with higher death rates are displayed in darker color. We characterized the 15 leading underlying causes of death (UCOD), the incidence of influenza/pneumonia as co-contributors to death (ICD-10 codes J09-J18 for UCOD or CCOD), and the location where the death occurred (ie, home, institution) for those who had a hip fracture as a contributing cause.

Deaths were analyzed by month for the United States, Wisconsin, and Florida. Florida was chosen for comparison in order to identify variation in seasonal trends between a state with freezing winter temperatures and inadequate sunlight exposure for vitamin D synthesis (Wisconsin) and a state with winter temperatures predominantly above freezing and increased sunlight exposure (Florida).

The number of deaths in each month over the 19 years surveyed was summed to create a count of the total number of deaths in each calendar month (ie, January 1999 deaths + January 2000 deaths + January 2001 deaths, etc). The number of deaths in each month was normalized to a standard 28-day month by dividing the number of days in the month by 28 and multiplying this by the number of deaths that occurred. Over the 19 years surveyed, there were 5 leap years; thus, February was considered to have 28 and 5/19 days. Deaths associated with hip fracture between

Figure 1. Hip Fracture Age-Adjusted Death Rate (AADR) by State

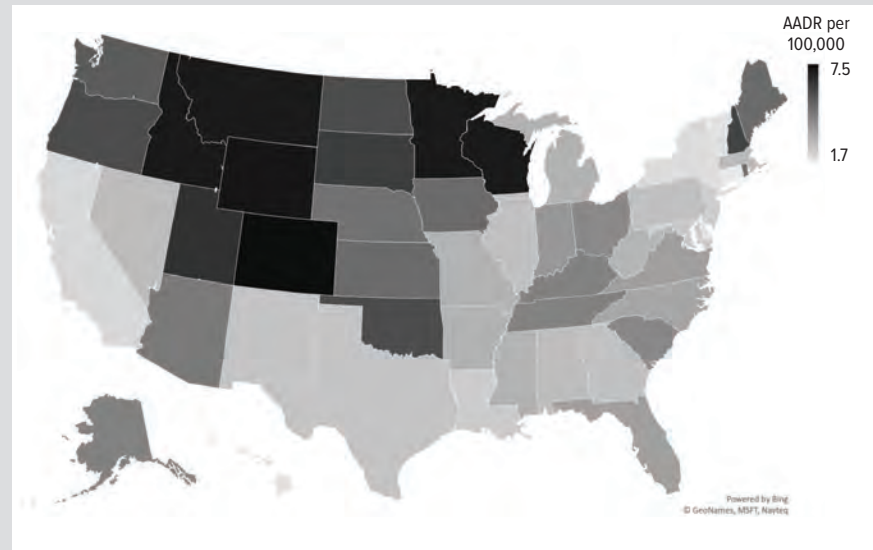


Table. Demographics of Hip Fracture-Associated Mortality, 1999-2017

	Wisconsin		United States	
	No. Deaths	AADR (95% CI)	No. Deaths	AADR (95% CI)
Total	9,749	7.6 (7.4-7.7)	264,356	4.3 (4.3-4.3)
Sex				
Females	6,158	7.4 (7.2-7.6)	167,562	4.2 (4.2-4.3)
Males	3,591	7.9 (7.6-8.1)	96,794	4.3 (4.3-4.3)
Race/Ethnicity				
Hispanic	36	3.1 (2.1-4.3)	6882	1.9 (1.9-2.0)
Non-Hispanic American Indian/Alaska Native	23	6.1 (3.8-9.3)	955	4.0 (3.7-4.2)
Non-Hispanic Asian/Pacific Islander	11	unreliable	2092	1.1 (1.1-1.2)
Non-Hispanic Black	79	2.9 (2.3-3.6)	8175	1.7 (1.7-1.7)
Non-Hispanic White	9,600	7.7 (7.6-7.9)	24,5793	4.8 (4.8-4.8)
	No. Deaths	CDR (95% CI)	No. Deaths	CDR (95% CI)
Age				
<1 year - 44 years	10	unreliable	480	unreliable
45 - 54 years	32	0.2 (0.1-0.3)	1,243	0.2 (0.1-0.2)
55 - 64 years	121	1.0 (0.8-1.2)	4,757	0.7 (0.7-0.8)
65 - 74 years	581	7.5 (6.9-8.1)	1,8014	4.3 (4.3-4.4)
75 - 84 years	2,455	49.6 (47.6-51.6)	73,389	29.3 (29.1-29.5)
85+ years	6,550	304.3 (297.0-311.7)	166,469	167.0 (166.2-167.8)

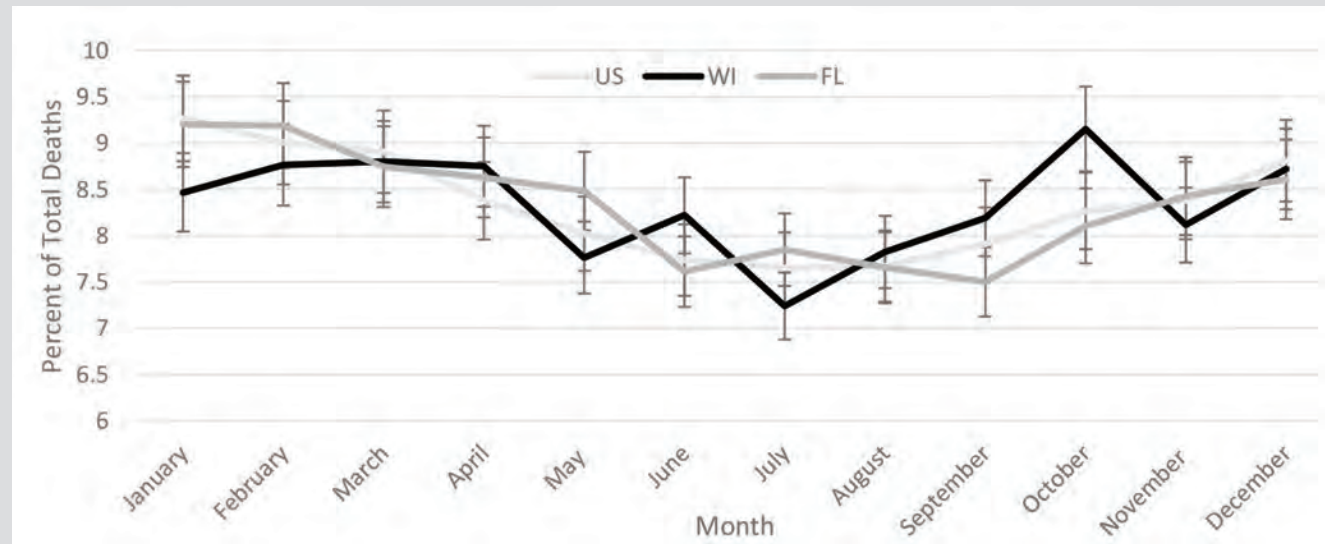
Abbreviations: CI, confidence interval; AADR, age-adjusted death rate; CDR, crude death rate.

October and March were compared to deaths between April and September by 2-tailed paired *t*-test using Microsoft Excel for all 3 geographic areas.

RESULTS

The 1999-2017 age-adjusted death rate (per 100,000 people) for hip fracture as a contributing cause of death is much higher in Wisconsin (7.6; CI, 7.4-7.7) than in the United States as a whole (4.3; CI, 4.3-4.3). Because Wisconsin’s population is older than the standard population, its crude death rate is even higher at

Figure 2. Percent of Deaths with Hip Fractures as a Contributing Cause, by Month



9.1 (CI, 9.0-9.3). Among all states in 2017, Wisconsin was tied for the third-highest age-adjusted death rate for hip fracture as a contributing cause of death, behind only Colorado and Wyoming (Figure 1). Over the years surveyed, the age-adjusted death rate associated with hip fracture was relatively steady in Wisconsin at 7.4 in 1999 and 7.1 in 2017, respectively. In the United States, the rate has decreased: in 1999 it was 4.8 and by 2017 it was 3.4.

The Table demonstrates the actual number of deaths and the age-adjusted death rate for both Wisconsin and the United States by sex, race, and ethnicity for all deaths between 1999 and 2017. The age-adjusted death rate of hip fracture as a contributing cause of death was similar between men and women in both Wisconsin and in the United States. The rate was higher among non-Hispanic whites compared to Hispanics, non-Hispanic blacks, and Asian American/Pacific Islanders. The age-adjusted death rate of hip fracture as a contributing cause of death for people under the age of 44 was negligible but increased significantly with each decade thereafter.

Fifty-one percent of people who died with hip fracture as a contributing cause had an underlying cause of death coded under “Accidents (V01-X59, Y85-86).” The remaining deaths came from underlying causes generally comparable to the leading causes of death in the population at large. The underlying cause was “Diseases of the Heart” (ICD-10 I00-I09, I11, I13, I20-I51) in 19%, “Chronic Lower Respiratory Disease” (ICD-10 J40-J47) in 3.9%, and “Alzheimer’s Disease” (ICD-10 G30) in 3.7%. These same causes of death, respectively, were responsible for 25.6%, 5.4%, and 3.1% of deaths among the general population.

Nearly 10% of nursing home deaths across the United States had hip fracture as a contributing cause. Nursing homes were the most common location of death for Wisconsinites with hip fracture as a contributing cause (38.4%), followed by deaths that

occurred in an inpatient setting (37.2%). Across the United States, 47% of these deaths occurred in an inpatient facility, followed by 32% in nursing home facilities.

More people died related to hip fracture in colder months (Figure 2). In the United States, 52.7% of deaths occurred between October and March, versus 47.3% between April and September ($P < 0.05$). In Wisconsin, 52% of deaths occurred in the cooler months vs 48% of deaths in warmer months ($P < 0.05$), and in Florida, these timeframes represented 52.2% and 47.8% of deaths ($P < 0.05$), respectively. The 15 leading causes of death (which capture about 90% of the deaths with hip fracture as a CCOD) did not change with respect to the season; however, the incidence of influenza as a co-contributor to death (UCOD or CCOD), was considerably higher in the cooler months. Over the survey period, there were 2,970 deaths from hip fracture + influenza/pneumonia in excess of those reported in warmer months. This explains about 22% of the variance between the periods.

DISCUSSION

Hip fracture is a common contributor to death in Wisconsin. While hip fracture-associated mortality has been decreasing across the United States, Wisconsin has not made major strides in reducing deaths from these preventable events.

Effective nonpharmacologic and pharmacologic interventions exist to reduce osteoporosis-related fractures but are not commonly utilized, even after an individual has sustained a fragility fracture.⁸ The STEADI (Stopping Elderly Accidents, Deaths, and Injuries) Toolkit was pioneered in 2015 by the CDC to facilitate detection and prevention of falls by medical providers but has not been maximally implemented in many health systems. Successful implementation has required strong champions, coordination of team member roles/responsibilities, and codification into the

electronic health record.⁹ Additionally, many patients eligible for pharmaceutical therapies are not receiving them, due either to medical oversight or a patient's conscious choice due to misguided beliefs about their adverse effects.¹⁰

Further research could assess whether Wisconsin has excess mortality due to higher numbers of hip fractures or worse outcomes from hip fractures and could also elicit information on intervenable risk factors that predated fracture. Such data could then inform targets for intervention, such as encouraging clinicians to adopt the STEADI toolkit to reduce falls incidence or campaigns to change patients' perception of osteoporosis medications.

Our data also support the importance of considering vaccination for influenza and pneumonia, as hip fracture-associated mortality increases when these infections are present.

Many older adults fear loss of mobility and independence.¹⁰ A high proportion of deaths from hip fracture occur in nursing homes. When disseminating information regarding prevention of hip fracture, it could be useful to appeal to peoples' preference to maintain independence and live at home.¹¹

A limitation of this study is that data from death certificates are only as good as the knowledge of the physician entering this information. If a hip fracture 3 months prior spurred a chain of health decompensation events, by the point of death, that inciting event may not even be recognized. Therefore, a significant number of deaths with hip fracture as a contributing cause may be missing from these data. Additionally, data from patients in Wisconsin are limited by small size; therefore, it was not possible to assess demographic trends over time.

CONCLUSION

Overall, the high death rate from hip fracture and the lack of improvement over the past 2 decades support the need for action in Wisconsin. By intervening on the at-risk population, preventing falls, and preventing fractures, it is likely we can make significant progress in preventing deaths.

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Trends in Smoking During Pregnancy in Wisconsin, 2011-2016

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ABSTRACT

Background: Smoking during pregnancy remains a significant public health concern with widespread social, economic, and health effects.

Objective: To describe the epidemiology of maternal smoking in Wisconsin over time and by county, age, race/ethnicity, education, and other characteristics.

Methods: Cigarette smoking during pregnancy in 2011-2016 was evaluated using Wisconsin Interactive Statistics on Health data.

Results: Maternal smoking rates declined from 14.4% in 2011 to 11.4% in 2016. Rates are highest among women aged 20-24 and those with less education. American Indians had the highest rates of smoking during pregnancy at all education levels.

Conclusion: Despite continued declines in the rates of smoking during pregnancy in Wisconsin, disparities exist for American Indians, young, and less-educated women. Physicians should continue to encourage cessation throughout pregnancy and support evidence-based community programs and policies.

In 2016, one in 14 women (7.2%) who gave birth in the United States smoked during pregnancy.³ Women aged 20-24 had the highest prevalence of smoking at 10.7%. By race, American Indian/Alaskan Natives had the highest smoking prevalence at 16.7%, compared to 10.5% for whites, 6.0% for blacks, 1.8% for Hispanics, and 0.6% for Asians. There were significant differences by state, with a high of 25.1% in West Virginia and a low of 1.6% in California.

The purpose of this study was to describe current trends in smoking rates among different populations of pregnant women in Wisconsin in order to better target tobacco cessation interventions.

BACKGROUND

Smoking during pregnancy can have vast implications for mothers and children, including preterm delivery, low birth weight, sudden infant death syndrome, and preterm-related deaths.¹ There is no safe smoking threshold, and women should be encouraged to stop smoking before becoming pregnant. However, many women face barriers to smoking cessation before or during pregnancy. Those who continue to smoke are more likely to be low income, have partners who smoke, have higher degrees of addiction, and have multiple prior pregnancies.²

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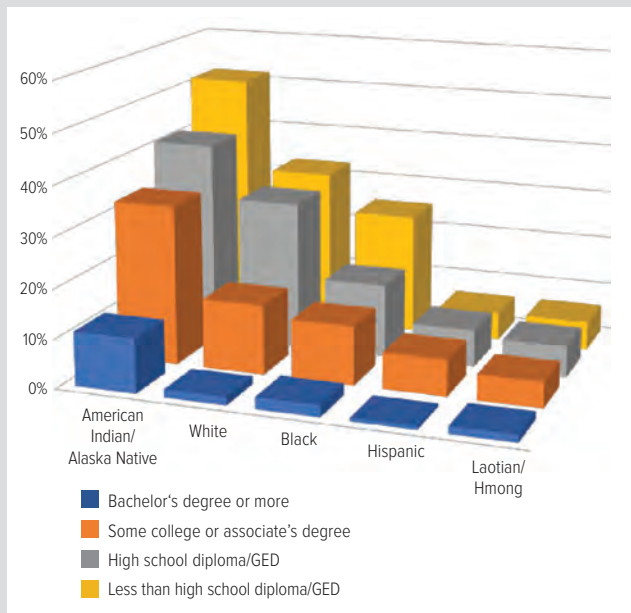
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METHODS

Data on smoking during pregnancy in Wisconsin were obtained from Wisconsin Interactive Statistics on Health, 2011-2016. Trends by age and race/ethnicity were further assessed for 2001-2016. Smoking data are self-reported by mothers on birth certificates in response to questions about cigarette use. The data were analyzed by county, age, race/ethnicity, education, marital status, number of previous pregnancies, maternal body mass index (BMI), trimester during which prenatal care was initiated, medical payment type, infant birthweight, and breastfeeding status. We restricted the analysis by education to women 25 years of age and older, since younger women may not have completed their full education.

We used the following formula to estimate the 95% confidence limits (CL): $95\% \text{ CL} = 1.96 * (\text{rate}/\sqrt{n})$, where n = births with maternal smoking during pregnancy in 2011-2016.⁴ Rates

Figure. Smoking During Pregnancy by Race/Ethnicity and Education, 2011-2016



Abbreviations: GED, general education diploma.

were considered significantly different if their 95% CL did not overlap.

RESULTS

There were 402,252 births in Wisconsin from 2011 to 2016, of which 52,631 mothers smoked during pregnancy (13.1%). The smoking rate has declined over time, from 15.8% in 2001 to 14.4% in 2011 and 11.4% in 2016.

Smoking during pregnancy varies by a number of demographic characteristics depicted in Table 1. Women aged 20-24 years were the most likely to smoke, followed by those aged 18-19 and 25-29, respectively. American Indians/Alaska natives (American Indians) had a 38.6% smoking prevalence—2.8 times higher than the rate among whites (13.8%). Women with some high school but no diploma or general education diploma (GED) had the highest smoking rates. Compared to women with a doctorate/professional degree, they were 73 times more likely to smoke (29.3% vs 0.4%). When controlling for age, this increased to an 83 times difference (33.2% vs 0.4%).

Analysis by race/ethnicity suggests that American Indians had the highest rates of smoking during pregnancy in all educational categories and Hispanics and Laotian/Hmong had the lowest (Figure). Of American Indians with less than a high school diploma/GED, 51.6% smoked during pregnancy, compared to 41.2% of those with a diploma/GED, 32.7% with some college/associate degree, and 11.2% with at least a bachelor's degree. Among mothers without a high school degree, 32.5% of whites, 24.7% of blacks, 5.8% of Laotian/Hmong, and 5.7% of Hispanics smoked during pregnancy. Among those with at least a bachelor's

Table 1. Smoking During Pregnancy by Characteristics, 2011-2016

Maternal Characteristics	Total No. Births	% Smoke During Pregnancy (95% CL)
All births	402,252	13.1 (13.0 - 13.3)
Age		
< 15 years	229	5.2 (2.3 - 8.2)
15 - 17 years	5,461	11.5 (10.6 - 12.4)
18 - 19 years	16,109	19.8 (19.1 - 20.5)
20 - 24 years	80,386	20.9 (20.6 - 21.2)
25 - 29 years	127,091	13.5 (13.3 - 13.7)
30 - 34 years	117,303	9.0 (8.8 - 9.2)
35 - 39 years	46,506	8.3 (8.0 - 8.6)
40 - 44 years	8,627	8.2 (7.6 - 8.8)
45+ years	535	4.9 (3.0 - 6.7)
Race/ethnicity		
White	292,845	13.8 (13.6 - 13.9)
Black	38,349	15.5 (15.1 - 15.9)
American Indians/Alaska natives	4,423	38.6 (36.7 - 40.4)
Hispanic	38,982	6.2 (6.0 - 6.5)
Laotian or Hmong	9,297	5.2 (4.7 - 5.7)
Education (restricted to women aged 25 and older)		
8th grade or less	10,980	3.4 (3.0 - 3.7)
9th - 12th grade, no diploma	13,427	33.2 (32.2 - 34.2)
High school graduate or GED	53,023	24.3 (23.9 - 24.7)
Some college credit, no degree	53,722	17.3 (17.0 - 17.7)
Associate degree	39,040	8.3 (8.0 - 8.6)
Bachelor's degree	86,975	1.9 (1.8 - 2.0)
Master's degree	32,291	0.8 (0.7 - 0.9)
Doctorate or professional degree	9,326	0.4 (0.3 - 0.5)
Marital status		
Married	251,958	5.7 (5.6 - 5.8)
Not married	148,153	25.8 (25.5 - 26.1)
Number of previous pregnancies		
0	118,940	10.8 (10.6 - 11.0)
1	113,334	11.6 (11.4 - 11.8)
2	75,115	13.5 (13.2 - 13.8)
3	43,138	15.9 (15.5 - 16.3)
4	23,187	18.4 (17.9 - 19.0)
5 or more	27,822	20.1 (19.6 - 20.7)
Body mass index		
Underweight (<18.50)	10,013	19.4 (18.5 - 20.3)
Normal (18.50 - 24.99)	169,469	11.5 (11.3 - 11.7)
Overweight (25.00 - 29.99)	103,640	12.7 (12.5 - 12.9)
Obese (≥ 30.00)	112,188	15.4 (15.2 - 15.7)
Trimester prenatal care initiated		
1 - 3 months (1st trimester)	304,972	11.7 (11.6 - 11.9)
4 - 6 months (2nd trimester)	66,151	17.4 (17.1 - 17.8)
7 - 9 months (3rd trimester)	14,562	19.3 (18.6 - 20.0)
No prenatal care	2,504	31.5 (29.2 - 33.7)
Principal source of payment		
Medicaid/BadgerCare	151,429	24.3 (24.0 - 24.5)
Private	224,230	5.8 (5.7 - 5.9)
Self-pay	11,391	7.0 (6.5 - 7.5)
Other	10,701	15.5 (14.8 - 16.3)
Infant Birthweight		
Under 1,000 grams	2,579	19.4 (17.7 - 21.1)
1,000 - 1,499 grams	2,661	17.7 (16.1 - 19.3)
1,500 - 2,499 grams	23,864	22.4 (21.8 - 23.0)
2,500 - 3,999 grams	333,687	13.1 (13.0 - 13.3)
4,000+ grams	39,339	6.9 (6.6 - 7.2)
Infant Breastfed		
Yes	299,450	9.9 (9.8 - 10.0)
No	77,433	25.4 (25.0 - 25.7)

Abbreviation: GED, general education diploma.

The total per category may not sum to the total number of births due to other and missing data.

Table 2. Smoking During Pregnancy by Wisconsin County, 2011-2016

County	Rank	No. Smoke	% Smoke (95% CL)	County	Rank	No. Smoke	% Smoke (95% CL)
Wisconsin	N/A	52,631	13.1 (13.0-13.3)	Marathon	28	1,422	14.8 (14.0-15.5)
Adams	65	219	27.8 (24.1-31.4)	Marinette	61	565	26.0 (23.8-28.1)
Ashland	68	319	30.0 (26.7-33.2)	Marquette	57	205	22.7 (19.6-25.8)
Barron	47	598	19.6 (18.0-21.2)	Menominee	71	185	33.3 (28.5-38.1)
Bayfield	62	195	26.1 (22.4-29.8)	Milwaukee	12	9,437	11.3 (11.1-11.6)
Brown	15	2,577	12.7 (12.2-13.2)	Monroe	40	666	18.1 (16.7-19.5)
Buffalo	31	130	14.9 (12.3-17.4)	Oconto	50	438	20.6 (18.7-22.5)
Burnett	66	230	29.1 (25.3-32.8)	Oneida	55	397	22.1 (19.9-24.3)
Calumet	6	296	9.2 (8.2-10.3)	Outagamie	13	1,574	11.5 (10.9-12.0)
Chippewa	39	748	17.4 (16.1-18.6)	Ozaukee	2	316	6.5 (5.8-7.2)
Clark	7	339	9.9 (8.8-10.9)	Pepin	5	44	9.2 (6.5-11.9)
Columbia	34	594	16.5 (15.2-17.8)	Pierce	11	264	11.3 (9.9-12.6)
Crawford	44	182	18.7 (16.0-21.4)	Polk	49	502	19.9 (18.1-21.6)
Dane	3	2,579	7.1 (6.8-7.3)	Portage	20	543	13.2 (12.0-14.3)
Dodge	42	899	18.2 (17.0-19.4)	Price	53	139	21.3 (17.8-24.9)
Door	33	204	16.0 (13.8-18.2)	Racine	19	1,867	13.0 (12.4-13.6)
Douglas	51	540	20.8 (19.1-22.6)	Richland	32	169	15.9 (13.5-18.3)
Dunn	41	496	18.1 (16.5-19.7)	Rock	38	2,006	17.3 (16.5-18.0)
Eau Claire	30	1,066	14.8 (14.0-15.7)	Rusk	54	190	22.1 (18.9-25.2)
Florence	67	36	29.3 (19.7-38.8)	St. Croix	69	560	8.9 (8.2-9.7)
Fond Du Lac	35	1,082	16.6 (15.7-17.6)	Sauk	45	772	16.8 (15.6-18.0)
Forest	72	221	33.9 (29.5-38.4)	Sawyer	26	307	31.1 (27.6-34.6)
Grant	16	419	12.7 (11.5-13.9)	Shawano	4	493	19.3 (17.6-21.0)
Green	27	333	14.6 (13.0-16.2)	Sheboygan	37	1,066	14.0 (13.5-15.2)
Green Lake	43	221	18.3 (15.9-20.7)	Taylor	23	191	14.0 (12.0-16.0)
Iowa	18	209	13.0 (11.2-14.7)	Trempealeau	24	339	14.1 (12.6-15.6)
Iron	64	46	26.9 (19.1-34.7)	Vernon	10	260	10.3 (9.0-11.5)
Jackson	59	344	23.1 (20.6-25.5)	Vilas	70	338	32.2 (28.8-35.7)
Jefferson	25	752	14.3 (13.3-15.3)	Walworth	14	765	12.4 (11.6-13.3)
Juneau	60	403	24.5 (22.1-26.9)	Washburn	56	198	22.4 (19.3-25.6)
Kenosha	22	1,591	13.7 (13.0-14.3)	Washington	8	804	10.0 (9.3-10.7)
Kewaunee	17	153	12.8 (10.8-14.8)	Waukesha	1	1,428	6.2 (5.9-6.6)
La Crosse	21	982	13.2 (12.4-14.0)	Waupaca	52	646	21.1 (19.5-22.7)
Lafayette	9	128	10.1 (8.3-11.8)	Waushara	46	263	19.4 (17.1-21.8)
Langlade	63	308	26.4 (23.4-29.3)	Winnebago	29	1,668	14.8 (14.1-15.5)
Lincoln	58	368	23.0 (20.7-25.4)	Wood	48	976	19.8 (18.6-21.0)
Manitowoc	36	819	16.8 (15.6-17.9)				

There is a nearly linear positive relationship between the number of previous pregnancies and whether or not women smoke, with a coefficient of determination $r^2=0.982$. Almost a fifth of underweight mothers (BMI < 18.5) smoked during pregnancy. Of low birthweight babies (<2,500 grams), 21.7% were born to mothers who smoked while pregnant. Women who delayed or received no prenatal care had higher rates of smoking than those who sought earlier care. Nearly a quarter of women covered by Medicaid/Badgercare smoked during pregnancy, compared to 5.8% with private insurance.

Smoking rates during pregnancy were ranked by county using 2011-2016 data and ranged from 6.2% in Waukesha County to 33.9% in Forest County (Table 2).

DISCUSSION

Vast differences remain in maternal smoking across the state. In 2016, Wisconsin had a higher percentage of smoking during pregnancy (11.4%) than the United States (7.2%).³ Although the overall prevalence of smoking during pregnancy has decreased in Wisconsin, data suggest this can be attributed largely to decreases among white and black women, while rates among American Indians, Hispanic, and Laotian/Hmong women have remained stagnant. American Indians have a much higher rate than other

groups and have had no real decline since the early 2000s, potentially reflecting socioeconomic and cultural aspects influencing health behaviors.

degree, smoking rates were 7 times higher for American Indians than white women (11.2% vs 1.6%). Trends by race/ethnicity were assessed from 2001 to 2016. Smoking during pregnancy by whites (16.5% in 2001, 15.2% in 2011, 11.4% in 2016) and blacks (19.1% in 2001, 16.4% in 2011, 13.0% in 2016) decreased over time. Smoking by American Indians (37.7% in 2001, 40.7% in 2011, 36.1% in 2016) and Hispanics (5.7% in 2001, 6.5% in 2011, 6.0% in 2016) largely stagnated. Smoking by Laotian/Hmong has fluctuated, from 2.5% in 2001 to a high of 7.1% in 2011, before decreasing to 4.5% in 2016.

All age groups have experienced a decline in smoking from 2001 to 2016; young women, in particular, have had substantial declines since 2011. For ages 15-17 years, smoking declined from 13.9% in 2011 to 8.5% in 2016. The rate declined from 24.8% in 2011 to 15.3% in 2016 among women aged 18-19 and from 23.5% to 16.6%, respectively, among women aged 20-24 years.

Our finding that 11.4% of Wisconsin women smoke during pregnancy is commensurate with the 11.3% rate reported by the Centers for Disease Control and Prevention (CDC), which uses data from the National Vital Statistics System.³ Wisconsin American Indians had a higher smoking prevalence in 2016 than American Indian natives nationwide (36.1% vs 16.7%). This is true for the other racial/ethnic groups in Wisconsin as well. For example, in 2016, the prevalence of smoking in black women in Wisconsin was double that of US black women (13.0% vs 6.0%) and more than triple for Wisconsin Hispanics compared to US Hispanics (6.0% vs 1.8%). These findings are largely consistent with trends from a previous report examining Wisconsin data.⁵

Strengths of our study include that we controlled for confounders of age and education to better understand the effects of

both education and race/ethnicity on our outcome. This report provides the most up-to-date detailed information on maternal smoking in Wisconsin.

A limitation of this study is that the birth certificate asks about cigarettes smoked but does not specify type. The CDC uses this data to evaluate tobacco use during pregnancy and employs the terms “cigarette smoking” and “tobacco use” interchangeably.³ However, data may not reflect other forms of tobacco use during pregnancy (eg, chewing tobacco) and may not reliably capture the use of electronic cigarettes (e-cigarettes), depending on a woman’s interpretation of the question. The dramatic decrease in maternal smoking in younger women since 2011 may, in part, reflect increasing use of e-cigarettes.⁶ E-cigarettes contain nicotine, which can lead to addiction and harm fetal brain and lung tissue development.⁷ Fortunately, pregnant women may be more likely to quit e-cigarettes than conventional cigarettes, possibly because traditional cigarette smokers are established smokers as opposed to more experimental e-cigarette users.⁸

Policy and clinical changes should be considered. The predominance of higher smoking rates in counties in northern Wisconsin and those with tribal lands may reflect both economic and social differences. The Wisconsin Native American Tobacco Network promotes prevention and cessation of commercial tobacco abuse while honoring the cultural heritage of traditional tobacco.⁹ Nuanced understanding of why pregnant Native American women have difficulty quitting is needed to tailor culturally appropriate initiatives. Communities may use the data from Table 2 to better understand how they compare to other counties. As education plays a protective role in smoking, we should focus resources on less-educated mothers who may live in circumstances that make it more likely to start or less likely to quit smoking. Considering a quarter of women covered by Medicaid smoked during pregnancy, policymakers should consider potential long-term savings associated with cessation.

Clinicians can follow counseling guidelines from the American College of Obstetricians and Gynecologists, which include the 5As of Ask, Advise, Assess, Assist, and Arrange,¹⁰ and should be aware of other free resources for patients. First Breath is a statewide program that helps pregnant women, new mothers, and their families quit smoking. In 2017, 84% of First Breath participants abstained, quit, or cut back on tobacco use during pregnancy.¹¹ Another free resource is the Wisconsin Tobacco Quit Line (800-QUIT-NOW), which utilizes a Quit Coach and other materials to help people stop smoking.

CONCLUSION

Despite continued declines in maternal smoking rates during pregnancy in Wisconsin, disparities exist for American Indians, young, and less-educated women. Physicians should continue to encourage cessation throughout pregnancy and support evidence-based community programs and policies. Reducing maternal

smoking will require the joint efforts of public health and clinicians statewide to engage with community partners and develop interventions.

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Social Determinants of Health and Health Outcomes: The Mediating Role of Coping Strategies

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ABSTRACT

Background: Associations between poor health and sociodemographics exist, but the role of coping strategies in this relationship is understudied. Therefore, we examined how adaptive and maladaptive coping affected the relationship between social determinants of health and health outcomes.

Methods: Participants completed survey questions about demographics, health status, and coping strategies. Mediation analyses examined whether education, income, and race affected health status indirectly through coping behaviors.

Results: Maladaptive, but not adaptive, coping strategies, mediated the relationship between income and health and education and health.

Discussion: The use of maladaptive coping strategies plays an intervening role in the relationship between income and health and education and health for some groups. Recommendations for promoting education and policies to reduce the use of maladaptive coping are discussed.

(eg, race, neighborhood poverty, etc). One way to mitigate such challenges may be to address modifiable factors like stress and coping, which might play a role in the link between SDOH and health outcomes.

Stress is associated with both SDOH and poor health outcomes.^{2,3} Mitigating the negative effects of stress on health may be one way to improve health and achieve health equity, but stress resulting from SDOH may not always be modifiable or avoidable, especially for certain sociodemographic groups. For example, race-related vigilance may be an uncontrollable stressor and difficult to eliminate. Although changing the experience of stress linked to various SDOH may not always be feasible, one

can employ effective coping strategies as a means of ameliorating the negative effects of stress on health.

Employing active coping behaviors, such as planning, seeking social support, and exercising restraint (ie, adaptive coping)⁴ is linked with good health outcomes.⁵ Using strategies that employ disengagement or responses that prevent or interfere with active coping (eg, denial of the stressor, giving up, avoidance, and substance use) are considered maladaptive⁴ and have been linked with poor health.⁵ Although diverse forms of coping can be used to address a single stressor,⁴ the degree to which successful coping can be enacted often depends on sociodemographic and socioeconomic (SES) factors. For example, those with low SES and those in the cultural minority often have fewer resources to deal with stressors and, therefore, fewer opportunities to prevent negative health outcomes caused by those stressors.^{6,7} Others argue that those with lower SES and those in the racial minority use more maladaptive strategies to cope and, consequently, report more mental and physical health symptoms.⁸

BACKGROUND

Addressing health disparities by advancing health equity is a primary focus of the Healthiest Wisconsin 2020 state health plan. Yet, in 2016 Wisconsin received a “D” on the Health of Wisconsin Report Card for its all-ages health disparity grade.¹ Promoting health equity requires efforts at both state and local levels, yet it can be challenging to make meaningful changes because some social determinants of health (SDOH) are difficult to modify

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Overall, the mitigating effects of adaptive coping are well established, but less is known about the mediating role that coping might play between SDOH and health outcomes. Risky health behaviors, such as smoking and high alcohol consumption, are sometimes used to cope with stressful events and have acted as mediators between childhood aversive events and adult health.⁹ Consequently, coping—especially maladaptive coping—may have an intervening effect on health behaviors, but more research on the relationship between SDOH and diverse forms of coping behaviors is still needed. For example, those with different sociodemographic backgrounds may employ different coping strategies that may be differentially affecting health outcomes. It also may be possible that those who are more educated have more information about successful coping strategies and can employ more adaptive strategies. These relationships are untested, however.

The purpose of this study is to explore the role of adaptive and maladaptive coping strategies in the relationship between sociodemographic and socioeconomic factors, such as race, education, and income and health. It is hypothesized that adaptive coping strategies will mediate the relationship between SDOH and health status such that those with higher education and higher income and those in the majority with regards to race will be associated with using more adaptive coping strategies and better health. It is also hypothesized that maladaptive coping strategies will mediate the relationship between SDOH and health status such that those with less education and less income and those in the minority race will be associated with using more maladaptive coping strategies and having poorer health.

METHODS

Participants were 161 adults ranging in age from 18 to 78 years mean = 38.24, SD = 12.55). Most participants were women (75.8%), white (91.9%), and had a college degree (32.3%). See Table 1 for additional demographics. After Institutional Review Board approval, participants were recruited via advertisements posted at local businesses and on local social media groups. Invitations to participate were also made at local community events (eg, festival and holiday events) and through the La Crosse County Human Services Department. All interested participants were given an anonymous link to complete the survey online at a time convenient for them. For those who were in the La Crosse

Table 1. Participant Demographics

	N (%)	General Health Status, Mean (SD)	Maladaptive Coping Behaviors, Mean (SD)	Adaptive Coping Behaviors, Mean (SD)
Sex				
Male	38 (23.6)	3.37 (.82)	21.74 (5.60)	35.57 (9.39)
Female	122 (75.8)	3.49 (.96)	19.59 (5.43)	35.92 (9.61)
Race				
White	148 (91.9)	3.49 (.91)	20.24 (5.54)	36.06 (9.40)
Minority ^a	11 (6.8)	3.00 (1.10)	19.67 (7.28)	32.33 (11.11)
Black	4 (2.5)	3.25 (.96)	22.33 (6.03)	39.67 (10.79)
Hispanic or Latino/a	3 (1.9)	2.33 (1.53)	27 (0.00)	31 (0.00)
American Indian/ Alaskan Native	2 (1.2)	2.5 (.71)	12 (NA) ^b	20 (NA) ^b
Asian	2 (1.2)	4.00 (0)	NA ^c	NA ^c
Education				
High school or less	18 (11.2)	2.72 (1.13) ^d	23.08 (5.14)	35.92 (7.29)
Some college or AA degree	52 (32.3)	3.37 (.86) ^e	18.83 (5.16)	34.05 (8.91)
Bachelor's degree	52 (32.3)	3.69 (.78) ^e	20.53 (6.72)	36.38 (9.12)
Post-college degree (MA, PhD, professional)	38 (23.6)	3.63 (.91) ^e	20.36 (4.42)	37.66 (11.37)
Income				
<25,000	37 (23.0)	3.16 (1.01) ^d	21.52 (5.21)	38.15 (7.23)
25,000-49,999	41 (25.5)	3.10 (.77) ^d	21.52 (6.66)	36.17 (9.05)
50,000-100,000	58 (36.0)	3.64 (.74) ^e	18.69 (5.07)	33.78 (10.24)
>100,000	25 (15.5)	4.04 (1.06) ^e	19.63 (4.86)	36.78 (10.95)

Abbreviations: NA, not available; AA, Associate in Arts; MA, master's degree, PhD, doctoral degree.

^aMinority category is comprised of the 4 groups below it.

^bNot available because only one participant had complete data.

^cNot available because participants did not have complete data.

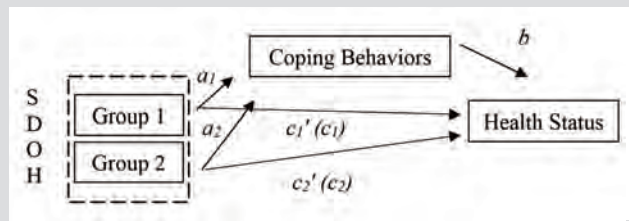
^{d,e}Indicates significant difference between cohorts within category ($P < .05$) based on Tukey's post-hoc comparison tests.

County Human Services Department, paper and pencil surveys were also available. Informed consent was provided as a cover letter for the paper and pencil survey and as the first webpage of the online survey. Completion of the survey was indication of consent. In survey instructions, participants were asked to answer all questions to the best of their abilities, but there were no penalties for skipping questions. Data collection lasted for approximately 9 months, beginning in the summer and ending the following spring. Participants were entered in a drawing for a chance to win one of five \$25 gift cards to a local convenience store.

Measures

Demographics and Health Status. Participants completed questions about age, sex, education, ethnicity/race, income, and general health status. All demographic and health status questions were used from the Behavioral Risk Factor Surveillance System questionnaire. For health status, participants were asked to rate their general health on a scale of 1 (Excellent) to 5 (Poor). Items were reverse scored such that larger values indicated better health. For education, participants identified the highest level of education they completed, with 8 options ranging from "grade school" to "earned doctorate/medical/law degree." For income, participants reported their gross household income by responding to

Figure 1. Conceptual Model of the Hypothesized Intervening Effect of Coping Behaviors on the Relationship Between Social Determinants of Health (SDOH) and General Health Status



that were combined to represent adaptive and maladaptive coping. Subscales used to represent adaptive coping included active coping, use of emotional support, use of instrumental support, positive reframing, planning, humor, acceptance, and religion. Subscales used to represent maladaptive coping included self-distraction, denial, substance use, behavioral disengagement, venting, and self-blame. Scores ranged from 12 to 48 for maladaptive coping and 16 to 64 for adaptive coping. In the current study, Cronbach's alpha for the overall measure was .90, .81 for the maladaptive subscale, and .90 for the adaptive subscale.

Statistical Analysis

Descriptive statistics and frequencies were calculated for all variables. Given the disproportionate number of females in the study, chi-square analyses were conducted to determine if males and females were equally represented in each demographic category (ie, education, income, and race). Independent *t*-tests and 1-way ANOVAs (with Tukey's post-hoc tests) also were calculated to determine if key outcome variables differed depending on survey type and among demographic groups.

Multicategorical mediation analyses¹¹ were conducted to determine the role of coping behaviors (both adaptive and maladaptive coping) in the relationships between SDOH (education, income, and race) and general health status. Mediation analysis is a statistical method to explore the mechanisms through which one variable (X =SDOH) affects another (Y =General Health Status). It is a regression-based path analysis that partitions the effects of X on Y into direct and indirect pathways.¹¹ Figure 1 represents the conceptual model. Path a represents the effects of the SDOH variable on coping behaviors. Because SDOH are categorical, a referent group was created for each SDOH variable (eg, income less than \$25,000 was the referent group for income). Consequently, each a pathway represents the mean difference between the referent group and the identified comparison group of each SDOH variable.¹¹ Thus, statistical significance in pathway a_1 would indicate that compared to the referent group, group 1 had a higher or lower value of the mediator (depending on the positive or negative value of a_1). Path b represents the effects of coping behaviors on general health, controlling for the SDOH variable. Path c' represents the direct effect. The direct effect measures the effect of SDOH on general health, not associated with coping behaviors. Again, given the categorical nature of the SDOH, each group is compared to the referent group and c' represents the relative direct effect of being in that group compared to the referent group. The total effect, the influence of the SDOH variable on general health without the effect of coping behaviors, is labeled as path c . Finally, the indirect effects, which measure the effect and significance of the mediator (ie, maladaptive and adaptive coping behaviors), are found in Table 2. Referent groups were computed as follows: education was having a high school education or less; income was making \$25,000 or less; for race, white was the referent group.

Table 2. Indirect Effects of Mediation Variables

Maladaptive Coping			
Mediation	Indirect Effect	95% BCCI	
Race			
Race » Maladaptive » Health	.04	[-.45, .52]	
Education			
Some college/AA » Maladaptive » Health	.28 ^a	[.05, .54]	
College degree » Maladaptive » Health	.17	[-.08, .45]	
Post-college degree » Maladaptive » Health	.18	[-.04, .41]	
Income			
\$25,000-\$49,999 » Maladaptive » Health	.00	[-.19, .22]	
\$50,000-\$100,000 » Maladaptive » Health	.17 ^a	[.02, .38]	
>\$100,000 » Maladaptive » Health	.12	[-.08, .34]	
Adaptive Coping			
Mediation	Indirect Effect	95% BCCI	
Race			
Race » Adaptive » Health	.03	[-.08, .22]	
Education			
Some college/AA degree » Adaptive » Health	.02	[-.04, .10]	
College degree » Adaptive » Health	-.004	[-.08, .06]	
Post-college degree » Adaptive » Health	-.02	[-.12, .05]	
Income			
\$25,000-\$49,999 » Adaptive » Health	.01	[-.05, .07]	
\$50,000-\$100,000 » Adaptive » Health	.02	[-.07, .12]	
>\$100,000 » Adaptive » Health	.01	[-.06, .07]	

Unstandardized coefficients are reported. Bootstrap sample was 5,000.

^aIndicates a significant value at $P < .05$. For race, white is the comparison group, for education, high school education or less is the comparison group, and for income, \$25,000 or less is the comparison group.

Abbreviations: BCCI, bias corrected confidence intervals, AA, Associate of Arts.

1 of 7 options, ranging from “less than \$15,000” to “\$100,000 or more.” Given characteristics of respondents and to facilitate statistical analyses, ethnicity, education, and income values were recorded. Created categories and frequencies for each variable can be found in Table 1.

Coping. Adaptive and maladaptive coping were measured using the Brief COPE.¹⁰ Participants responded to 28 items on a scale of 1 (I haven't been doing this at all) to 4 (I've been doing this a lot) on the degree to which they have used various behaviors in dealing with problems. Example statements include, “been turning to work or other activities to take my mind off things,” and “I've been learning to live with it.” The Brief COPE has 14 subscales

To determine statistical significance of the indirect effects (ie, the role of maladaptive and adaptive coping behaviors), bootstrapping procedures with bias corrected confidence intervals (BCCI) were used.¹¹ In mediational analysis, bootstrapping procedures estimate the characteristics of a population by sampling, with replacement, a large number of times until an empirical representation of the sampling distribution can be used to generate confidence intervals for the indirect effects.¹¹ This non-parametric bootstrapping method does not assume normality in the sampling distribution and was used because self-reported health behaviors are generally skewed. In this study, the empirical approximation of the sample was created using 5,000 samples, and a 95% BCCI was used to determine significance of the intervening effects. All analyses were conducted using IBM SPSS 24.

RESULTS

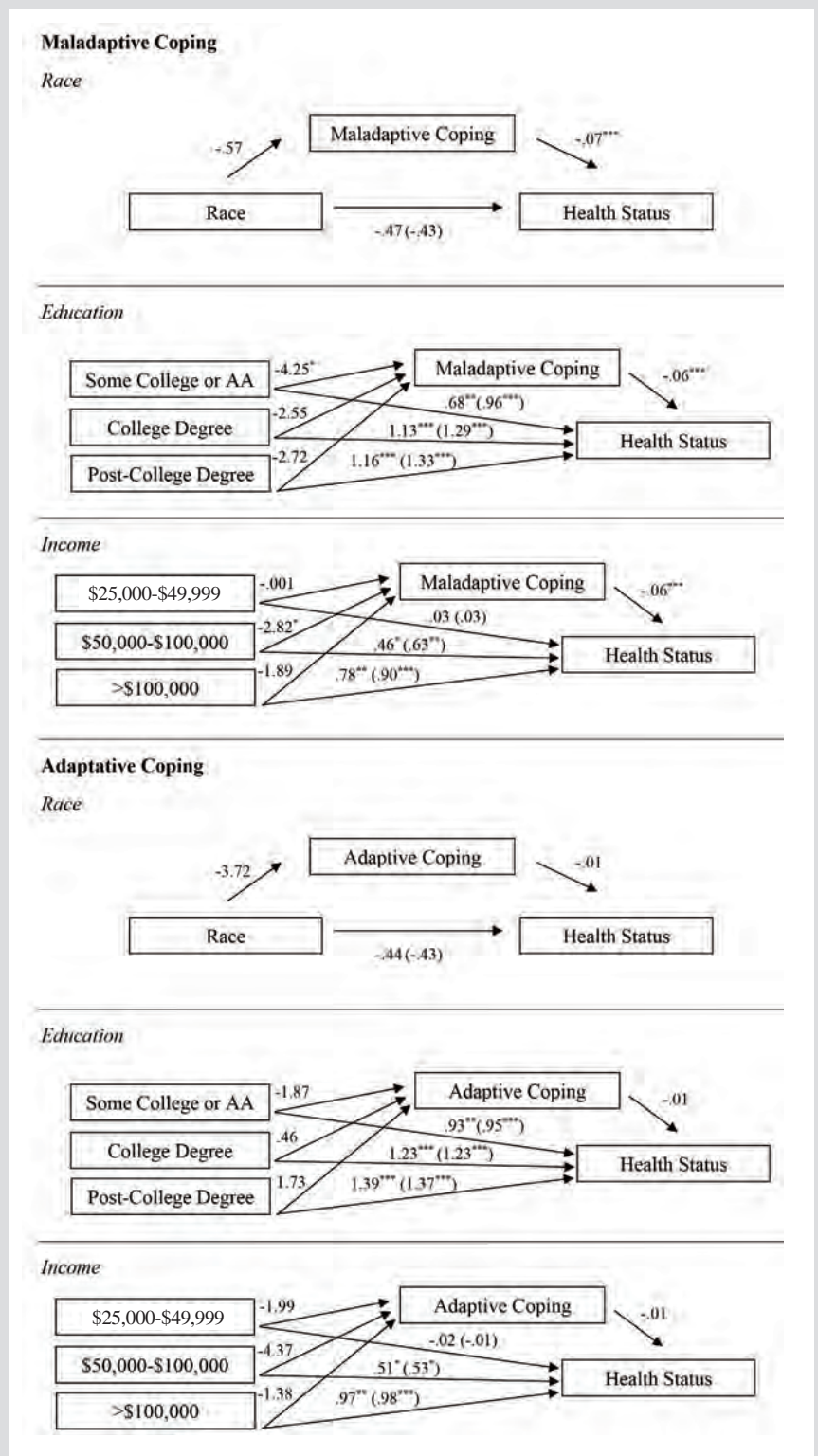
Group Differences by Sex, Survey Type, and Outcome Variable

Males and females were equally represented in education ($\chi^2[3] = 1.81, P = .61$), income ($\chi^2[3] = 1.00, P = .80$), and race groups ($\chi^2[1] = .64, P = .43$). There were also no significant differences found between males and females in general health status ($t[159] = -.63, P = .53$), or maladaptive ($t[112] = 1.78, P = .08$) and adaptive coping behaviors, ($t[112] = -.17, P = .86$).

Only 14 individuals completed the paper and pencil version of the survey. Those who did were less educated ($\chi^2[3] = 36.17, P < .001$) and more likely to be in the minority race ($\chi^2[1] = 4.29, P = .04$). They also employed more maladaptive coping styles (mean = 24.64, SD = 3.96) than did those who completed the survey online (mean = 19.74, SD = 5.56, $t[112] = -2.84, P = .005$), and they reported a significantly lower health status (mean = 2.50, SD = 1.01) than those who completed the survey online (mean = 3.55, SD = .87, $t[160] = 4.25, P < .001$).

Regarding demographic differences on outcome variables, those with a high

Figure 2. Maladaptive and Adaptive Coping Behaviors as Mediators Between Social Determinants of Health (SDOH) and General Health Status



Indirect effects of maladaptive and adaptive coping behaviors on the direct effect of race, education, and income on general health status. Path values represent unstandardized regression coefficients. The value inside the parenthesis represents the total effect. Values outside the parenthesis represent the direct effect, the effect of SDOH on health status controlling for maladaptive and adaptive coping, of race, education, and income on general health behaviors. For race, white is the comparison group; for education, high school education or less is the comparison group; and for income, \$25,000 or less is the comparison group. * $P < .001$, ** $P < .05$, *** $P < .01$. Abbreviation: AA, Associate of Arts.

school education or less reported significantly lower health status compared to those with some college ($t[157] = -2.67, P = .04$), a college degree ($t[157] = -24.06, P < .001$), and a post-college degree ($t[157] = -3.61, P = .002$). Likewise, those making \$25,000 or less reported significantly lower health status compared to those making \$50,000 to \$100,000 ($t[158] = -2.64, P = .04$) and those making more than \$100,000 ($t[158] = -3.91, P = .001$). Those making \$25,000 to \$49,999 also reported significantly lower health status compared to those making \$50,000 to \$100,000 ($t[158] = -3.09, P = .01$) and more than \$100,000 ($t[158] = -4.28, P < .001$). Means and standard deviations are in Table 1.

Mediational Analysis Results

Coefficients for the mediation model pathways can be found in Figure 2, and indirect effects and statistical significance of the mediation variables are in Table 2. Results indicate that maladaptive coping was a significant intervening variable for education and income but not for race. For education, those who had a high school degree or less used, on average, significantly more maladaptive coping strategies compared to those with some college education or an Associate's degree, which was associated with poorer health status. The mean difference in the use of maladaptive coping behaviors was 4.25. For income, those who made \$25,000 or less used, on average, significantly more maladaptive coping strategies than those making \$50,000 to \$100,000, which was associated with poorer health status. The mean difference in use of maladaptive coping strategies was 2.82. All other group comparisons were not statistically significant. Additionally, adaptive coping was not a significant intervening variable for education, income, or race.

DISCUSSION

Results supported hypotheses regarding the role of maladaptive coping strategies in the relationship between education and health and income and health, but only for certain groups. This supports previous research that those with less education and income are likely to have poorer health and use more maladaptive coping strategies.⁶⁻⁸ Moreover, it provides new evidence that maladaptive coping may be associated with some of these disparities in health outcomes because of its role in the relationship between SDOH and general health. Perhaps the use of maladaptive strategies may be more common among those with less education and income because these individuals lack resources to find means other than maladaptive strategies to address their stressors. Furthermore, maladaptive strategies like distraction and disengagement may be a more financially and emotionally feasible solution in the face of certain chronic stressors (eg, cancer diagnosis, neighborhood conditions, etc) that may be more common for those with less education and income. Maladaptive coping like avoidance and distraction is argued to work better to reduce stress than adaptive strategies when the situation is uncontrollable, like in the case of poverty, despite the long-term negative health consequences.⁷

Perhaps those with low income and/or low education may be using more maladaptive strategies because they are effective for immediate needs, despite their negative long-term consequences.

Contrary to our hypothesis, maladaptive coping did not play a role in the relationship between race and health. Our sample was predominately white (92%) and mostly female (76%). The lack of variability in the study may have contributed to a loss of power to be able to detect the hypothesized relationships. Also contrary to our hypothesis, adaptive coping strategies did not play a role in the relationship between any of the SDOH and health status. All education and income groups used similar levels of adaptive coping strategies, thus leaving little variability to detect differences in how it might explain the relationship between SDOH and health status. Our results suggest that when working toward health equity, practitioners and public health workers may need to focus more strongly on addressing differences in the use of maladaptive coping rather than adaptive coping strategies, especially among those with low income and less education.

Implications and Recommendations

Providing services or education to identify and reduce the use of maladaptive strategies, and expand one's repertoire of coping strategies, may be one way to promote health, especially among those with low income or less education. An existing example of such a model has been developed by the Substance Abuse and Mental Health Service Administration with the goal of increasing adaptive coping strategies and reducing maladaptive strategies, such as substance abuse.¹² This approach uses a Screening, Brief Intervention, and Referral to Treatment (SBIRT) model¹³ during a primary care visit, which allows primary care providers to assess alcohol use and misuse while also educating patients about substance use and providing advice on adaptive coping strategies. If needed, referrals to additional treatment and care can be made during this visit. Similar techniques could be used for other maladaptive coping behaviors too, such as behavioral disengagement, venting, and self-blame. Other ways to address maladaptive coping behaviors include facilitating conversations with patients about the use of coping strategies, like denial and behavioral disengagement, and providing additional resources for managing stress and avoiding self-blame for uncontrollable situations. Likewise, implementing public health communication strategies about the detrimental effects of maladaptive strategies, such as self-distraction, venting, and substance abuse, in community health plans or social media and public service announcement campaigns could reduce the use of such maladaptive strategies. Finally, we recommend investing in additional, local- and state-level research aimed at identifying the role of stress and coping in the relationship between SDOH and health disparities.

Limitations and Future Research Suggestions

The population, although representative of the county in which it

took place, was primarily white and female. More research exploring coping strategies and health in men and minority populations is needed. Generalizability is also limited by the use of self-rated measurement tools and a single question about self-rated health. Self-rated responses may be confounded by social desirability among other factors. Although the anonymous nature of the study likely reduced some of these biases, health status and other related factors should be explored in a more comprehensive and objective way (eg, disease states, biological measures of physical fitness, biological measure of vital signs, and blood tests).

There are also likely several confounding variables that were not addressed in the study. Future researchers also could explore how factors like access to health care, social support, employment status, and other confounding variables might affect the relationships examined in this study. The use of experimental methods also would reduce the impact of confounding variables and biases. Study methods, including the use of mediational analyses, were correlational, thus limiting our ability to make causal claims about the relationship between SDOH, coping strategies, and health status. Although it is less likely that health and coping behaviors might determine one's SDOH status, experimental and intervention designs are needed to determine if equipping individuals with strategies for reducing maladaptive coping strategies would eliminate or reduce the health disparities related to education and income.

CONCLUSIONS

Understanding the mechanisms by which sociodemographic and socioeconomic factors affect health status is one way to work toward achieving health equity. We found that the use of maladaptive coping strategies is implicated in the relationship between income and health status and education and health status. Given such findings, addressing the use of maladaptive coping strategies among these populations might be a way to work toward reducing disparities in health and achieving health equity.

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MRSA Septicemia With Septic Arthritis and Prostatic, Intraretinal, Periapical, and Lung Abscesses

Ryan A. Denu, PhD; Deval Patel, MD; Benjamin J. Becker, DO; Thomas Shiffler, MD; Peter Kleinschmidt, MD

ABSTRACT

Introduction: Methicillin-resistant staphylococcus aureus (MRSA) bacteremia is a life-threatening illness and a major global health care problem. It can cause metastatic and complicated infections.

Case Presentation: A 58-year-old man with uncontrolled type 2 diabetes mellitus presented with altered mental status after a fall. He was found to have a hip fracture, diabetic ketoacidosis, and MRSA bacteremia. This was complicated by septic knee arthritis, prostatic abscess, intraretinal abscess, periapical abscesses, and pulmonary abscesses. He was treated with intravenous vancomycin and oral linezolid and eventually recovered.

Discussion: Severe metastatic MRSA infection was likely due, in part, to the patient's uncontrolled diabetes, as he has no underlying immunodeficiency and was HIV negative. Prostatic abscesses are a relatively rare occurrence that typically develop in immunocompromised patients.

Conclusion: This case is an interesting confluence of sequelae of MRSA bacteremia and reinforces the necessity for clinicians to be diligent when evaluating a patient with a suspected prostatic abscess.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major nosocomial and community-acquired pathogen. *S aureus* can become resistant to penicillin by producing β -lactamase gene *blaZ*, and MRSA strains have acquired the *mec* and *fem* genes, which confer resistance to methicillin, penicillinase-resistant penicillins, and

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cephalosporins.¹ Bacteremia is a severe complication from MRSA infection and has a mortality rate ranging from 10% to 30%.² From 2005-2012, the rate of hospital-onset MRSA bacteremia decreased by 17.1% annually while community-onset MRSA declined by 6.9% annually, but this decline slowed from 2013-2016.³

Many risk factors for MRSA bacteremia have been identified. Host factors include advancing age, male sex, African American race, and the presence of comorbidities.^{2,4} Comorbidities most commonly associated with MRSA bacteremia include cirrhosis, congestive heart failure, chronic kidney disease, cancer, and alcohol use disorder.² Other risk factors include the use of multiple antibiotics—particularly fluoroquinolones and cephalosporins, HIV or other

immunosuppression, intravenous (IV) drug use, presence of an indwelling hemodialysis catheter, and residence in a long-term care facility.^{4,5} With bacteremia, MRSA has the potential to seed other sites, including the endocardium, bone, and skin and soft tissues. Herein we report a rare case of MRSA bacteremia in a patient with uncontrolled type 2 diabetes mellitus that seeded his knee, prostate, retina, mouth, and lungs.

CASE PRESENTATION

A 58-year-old man with history of insulin-dependent type 2 diabetes mellitus, stage 3 chronic kidney disease, alcohol use disorder, hyperlipidemia, and chronic right lower leg deep venous thrombosis (DVT) presented with altered mental status after a fall. Initial blood pressure on assessment by emergency medical services was 50/35 and increased to 80/56 after IV fluid administration. Workup for acute coronary syndrome was negative.

His white blood cell count was elevated to 34.9K/ μ L (reference 3.8-10.5K/ μ L), glucose was elevated to 736 mg/dL, hemoglobin A1c was 10.4%, lactate was elevated to 19.0 mmol/L (reference 0-2 mmol/L), pH of 7.3 (reference 7.36-7.44), bicarbonate of 17.7 (reference 22-26 mmol/L), base excess of -7.6 (reference -2.5 to 2.5), and anion gap of 25. In addition, his serum ketones were elevated to 15 mg/dL, and a diagnosis of diabetic ketoacidosis (DKA) was rendered, for which he was treated with IV fluids, insulin infusion, and electrolyte replacement. Computed tomography (CT) of his head showed no acute bleeding but did demonstrate periapical abscesses in the maxilla and mandible. CT of chest, abdomen, and pelvis demonstrated 2 left upper lobe cavitory pulmonary nodules (Figure 1) and right intertrochanteric femur fracture.

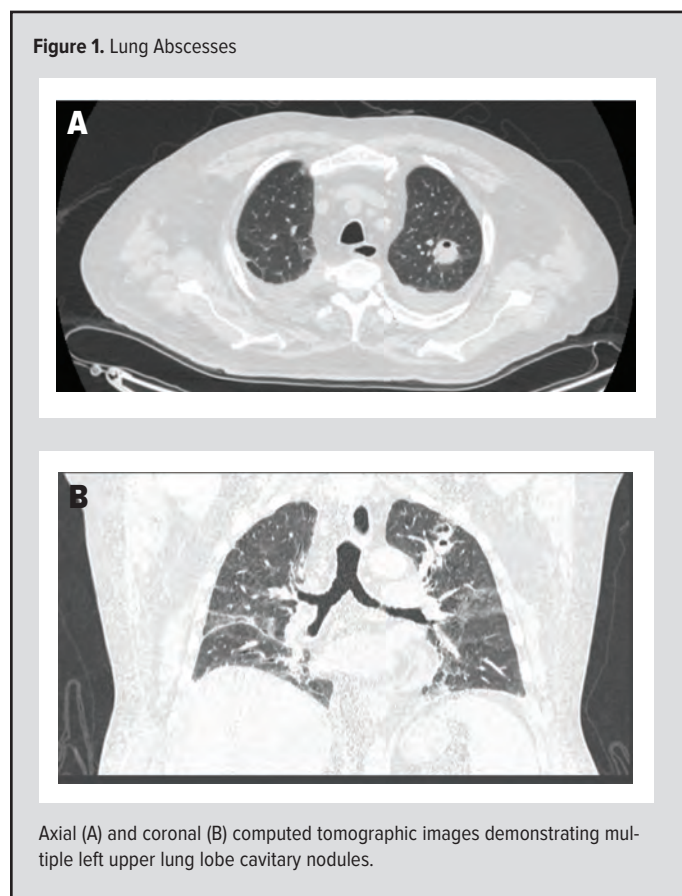
Given concern for sepsis, empiric broad-spectrum antibiotic treatment was started with vancomycin and piperacillin-tazobactam. Blood cultures grew MRSA after 10 hours. As his mental status recovered, he began complaining of right knee pain and was noted to have an erythematous, edematous, and painful right knee. The knee was drained and found to harbor Gram-positive cocci in clusters, which was eventually identified as MRSA. He subsequently underwent surgical drainage (Figure 2).

Urinalysis on admission was positive for bacteria and leukocyte esterase, suggesting a urinary tract infection. Furthermore, magnetic resonance imaging (MRI) for assessing hip fracture incidentally demonstrated diffuse enlargement of the prostate with multiloculated cystic appearance (Figure 3). Digital rectal exam revealed a smooth, nontender prostate. Transurethral deroofing was performed, and the prostate was drained. Both urine and suppurative prostatic fluid grew MRSA.

When his blood pressures normalized and fevers improved, the patient underwent open reduction and internal fixation for his nondisplaced right intertrochanteric femur fracture.

He later reported blurry vision in his right eye, raising concern for septic emboli and ischemia. MRI of his head demonstrated no abnormalities other than the known periapical abscesses. Ophthalmologic exam demonstrated endophthalmitis of the right eye and intraretinal abscess of the left eye. The abscess was drained from his left retina, and his right eye was treated with intraocular injections of vancomycin, ceftazidime, and dexamethasone with subsequent improvement of symptoms.

Upon identification of bacteremia, the infectious disease service was consulted. Systemic antimicrobial coverage initially was directed broadly with vancomycin and piperacillin/tazobactam. Confirmation of MRSA bacteremia and the presence of prostatic and intraretinal abscesses prompted the addition of linezolid. Additional workup included transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE), which were both negative for vegetations. The patient's hospitalization was complicated by ongoing hematuria secondary to his transurethral deroofing procedure and anticoagulation (due to his history of chronic



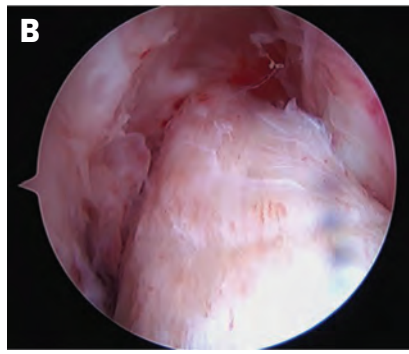
DVT), resulting in anemia and thrombocytopenia that required multiple erythrocyte and platelet transfusions. Linezolid was discontinued due to concerns of exacerbation of thrombocytopenia. He was discharged in stable condition on IV vancomycin, of which he completed a 6 week total course after negative blood cultures were achieved. Periapical abscesses management was deferred until after discharge once his anemia and thrombocytopenia resolved. He is currently doing well.

DISCUSSION

S aureus is a major cause of community- and health care-associated infections. MRSA has long been associated with infections in health care settings, and community-associated MRSA infections emerged in the 1990s.⁷ Approximately one-third of patients with MRSA bacteremia develop a metastatic or complicated infection,⁸ which is associated with increased mortality.⁹ Our patient's specific risk factors for MRSA bacteremia included uncontrolled diabetes (with A1c of 10.4% on admission), alcohol use disorder, and chronic kidney disease. We attempted to identify additional predisposing factors in our patient; his complete blood cell count with differential was unrevealing, and HIV testing was negative.

With regard to treatment of MRSA bacteremia, current guidelines recommend treating with antibiotics for 4 to 6 weeks from the first negative blood culture for MRSA bacteremia and for 6 weeks for endocarditis. Initial antibiotic therapy for MRSA

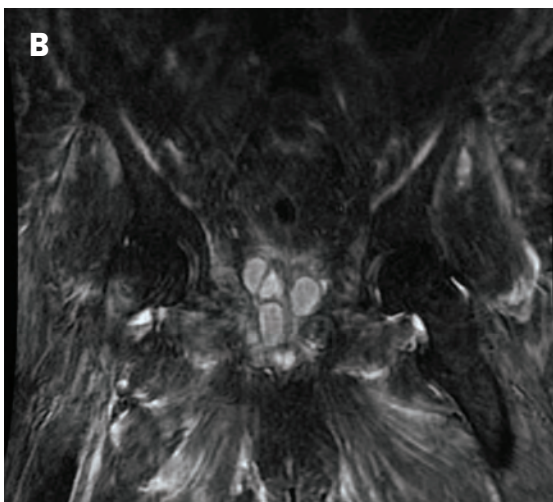
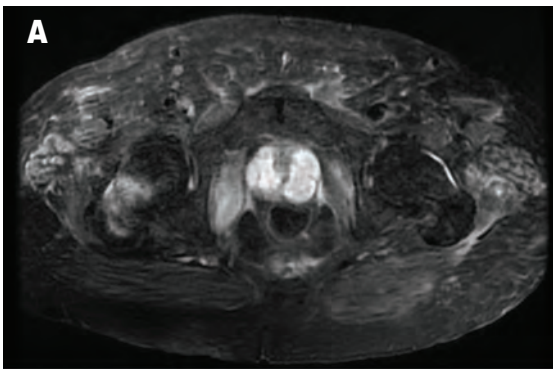
Figure 2. Right Knee Septic Arthritis



(A) X ray of patient's right knee demonstrating a joint effusion. (B) Image taken during right septic knee intra-articular irrigation and debridement showing evidence of septic arthritis.

generally includes vancomycin or daptomycin. Vancomycin typically requires serum concentration monitoring, especially in patients with renal dysfunction. Daptomycin is more costly and is associated with myopathy requiring creatine kinase monitoring and is inhibited by surfactant, limiting its use in pulmonary infections.⁶ Alternative agents include ceftriaxone and linezolid. Infectious disease consultation has been shown to reduce the mortality from MRSA bacteremia.¹⁰ Patients with eradicable foci should have those foci drained or removed, as eradication has been associated with better outcomes and survival.¹¹ In addition, patients should undergo echocardiography to evaluate

Figure 3. Prostatic Abscess



Axial (A) and coronal (B) T1 weighted magnetic resonance imaging demonstrating diffuse enlargement of the prostate with multiloculated cystic lesions.

for presence of endocarditis, with TTE generally performed first followed by TEE, which is superior to TTE for detection of vegetations and cardiac complications, such as intracardiac abscess and valvular perforation.¹² In a study of 103 patients with MRSA bacteremia, 7% had endocarditis established by TTE versus 25% by TEE.¹³

A variety of factors influence mortality from MRSA bacteremia. One major factor is the primary source of infection, with infective endocarditis and primary pulmonary infection associated with the highest mortality rates and peripheral venous catheter-related infections associated with the lowest mortality rate.¹⁴ The presence of an uneradicated focus, septic shock, age over 60, and duration of treatment less than 14 days are also associated with higher mortality in MRSA bacteremia.¹⁵ Development of metastatic foci in the setting of MRSA bacteremia is more likely in cases of unknown portal of entry, treatment delay > 48 hours, and the presence of foreign body material. C-reactive protein is typically higher in metastatic MRSA, with mean values of 74 mg/L for MRSA bacteremia versus 160 mg/L for metastatic MRSA bacteremia. It has been proposed that FDG-PET/CT to detect metastatic infectious foci may lead to improved outcomes.⁹

Prostatic abscess is an infection rarely seen in nonhospitalized patients due to effective antibiotic therapies. The most common causative pathogen of bacterial prostatitis is *E coli*; however, in the reported literature, the most common causative pathogen of prostatic abscesses is MRSA (65% of reported cases).¹⁶ Risk factors associated with the development of *S aureus* prostatic abscess include chronic indwelling catheters, instrumentation of the lower genitourinary tract, diabetes mellitus, HIV and immunosuppression, and chronic hemodialysis requirement.¹⁶ Our case demonstrates a prostatic abscess formed by MRSA in a patient with a history of uncontrolled type 2 diabetes mellitus. Prostatic abscesses generally are treated with either transrectal ultrasound (TRUS)-

guided aspiration or transurethral deroofing. In a small prospective randomized trial, transurethral deroofing was associated with reduced recurrence rate and shorter hospital stay.¹⁷

CONCLUSION

We present an interesting case in which MRSA bacteremia led to septic arthritis, prostatic abscess, intraretinal abscess, periapical abscess, and multiple pulmonary abscesses. This case report reinforces the necessity for clinicians to be diligent when evaluating a patient with suspected MRSA bacteremia. At presentation, the extent of disease may not be obvious. In the setting of metastatic MRSA infection, thorough history and physical, blood and urine cultures, and evaluation of any additional suspicious sites with imaging and cultures should be sought.

Consent: Informed consent was obtained from the patient for publication of this case report.

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Calcium Channel Blocker Toxicity Causing Acute Respiratory Distress Syndrome: A Commonly Used Drug Triggering a Life-Threatening Condition

Fahad Aftab Khan Lodhi, MD; Sophie L. Shogren; Jayanth G. Vedre, MD; Najiya Haque, MD; Martin Reriani, MD; Rashid Ali, MD

ABSTRACT

Introduction: Calcium channel blockers (CCBs) are commonly used but have the potential to cause substantial toxicity. One such underreported toxicity of CCB use is the development of acute respiratory distress syndrome (ARDS).

Case Presentation: A 44-year-old previously healthy woman presented to the emergency department (ED) having taken 60 tablets of 125 mg extended-release verapamil and 90 tablets of 0.25 mg clonazepam with the intent to commit suicide. On presentation to the ED, she was sedated and intubated for airway protection. She received aggressive medical resuscitation and was ventilated using low tidal volume mechanical ventilation. The hospital course was complicated by worsening hypoxia and a chest x-ray demonstrating bilateral patchy geographic areas of airspace opacities consistent with ARDS. On day 5 of hospitalization, the patient's clinical status improved significantly, and she was subsequently weaned off vasopressors and extubated.

Discussion: CCB toxicity can result in profound hypotension, shock, bradycardia, and conduction blocks, as well as hyperglycemia, acidosis and acute kidney injury, and ARDS. It is important for clinicians to understand the signs and symptoms of CCB toxicity, as well as how to treat it.

INTRODUCTION

Calcium channel blockers (CCBs) are classified into 2 categories: dihydropyridine (amlodipine, nifedipine, felodipine) and nondihydropyridine (verapamil, diltiazem). Dihydropyridine CCBs act on L-type channels on the vasculature, whereas nondihydropyridine CCBs act on those on the myocardium. These drugs are commonly used and have the potential to cause substantial toxicity,

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a fact that is often underappreciated. In 2002, 9,500 cases of CCB poisoning were reported to poison centers in the United States.¹ CCBs constitute the leading form of cardiovascular drug overdose and have been implicated in up to 48% of deaths caused by such overdose.²

Dihydropyridine CCB toxicity is caused by arterial vasodilation with reflex tachycardia, and nondihydropyridine CCB toxicity is caused by peripheral vasodilation, bradycardia, and decreased cardiac inotropy.³ The profound hypotension and end-organ ischemia resulting from severe overdose can cause complications such as stroke, seizure, myocardial infarction, renal failure, bowel ischemia, and acute respiratory distress syndrome (ARDS).⁴

CASE REPORT

A 44-year-old previously healthy, ambulatory woman presented to the emergency department having taken 60 tablets of 125 mg extended-release verapamil and 90 tablets of 0.25 mg clonazepam with the intent to commit suicide. Her past medical history included major depressive disorder with previous suicide attempts via intentional ingestion, migraine headaches with aura, and restless leg syndrome. She was taking verapamil for migraine prevention and clonazepam for symptomatic relief from restless leg syndrome; the number of pills she took in attempt to overdose was provided via self-report.

At presentation, the patient was hypotensive and bradycardic with slurred speech and an altered mental state. Physical examination revealed a sedated female with a blood pressure of 80/40, heart rate of 46, respiratory rate of 16 and initial Glasgow Coma

Score of 12/15 (E3, V4, M5). Her pulse was slow and regular without S3 or S4 gallop. Systemic examination of the cardiorespiratory system was unremarkable; she had no new or changed murmurs, and her lungs were clear to auscultation.

The patient was emergently sedated and intubated for airway protection. Poison control was urgently consulted, and their recommendations were followed. Aggressive fluid resuscitation was followed by multiple doses of calcium chloride, calcium gluconate, and atropine. Additionally, insulin and dextrose, glucagon, and lipid emulsion therapy were used to combat CCB overdose. Vasopressor support comprised of epinephrine, norepinephrine, and dopamine was used to overcome resistant hypotension, and a temporary transvenous pacemaker was placed due to unstable bradycardia. The patient was mechanically ventilated with low tidal volume ventilation and permissive hypercapnia; arterial blood gases upon ventilation with 100% fraction of inspired oxygen (FiO₂) were pH 7.37, PCO₂ 32, PO₂ 169.

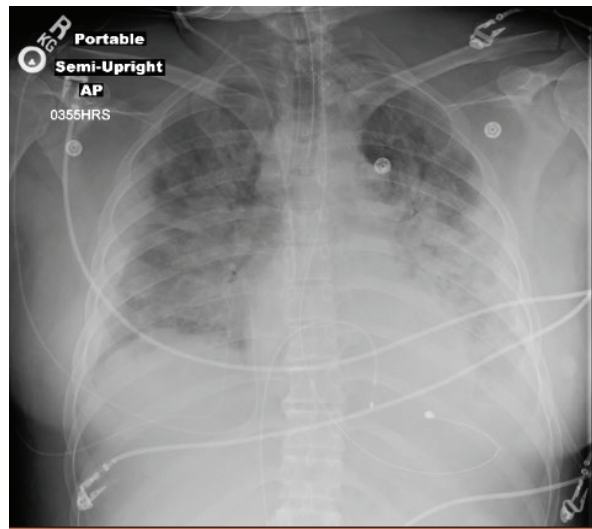
Initial labs revealed a blood glucose of 156 mg/dl, creatinine of 1.05, and an estimated glomerular filtration rate of 57 mL/min. The patient's urine drug screen was positive for benzodiazepines and negative for other drugs, and liver function tests showed mildly elevated aspartate aminotransferase levels. A urine pregnancy test was negative. The complete blood count and inflammatory markers were normal, and blood cultures displayed no growth. The chest x-ray initially showed left basilar atelectasis and on day 3 of her hospitalization revealed the findings depicted in Figure 1. Electrocardiogram (Figure 2) revealed a junctional rhythm with rates of 42, a prolonged QRS of 122 ms, and a corrected QT of 434 ms. Transthoracic 2D echocardiography revealed an ejection fraction of 62%, normal systolic function of both the left and right ventricle, and normal morphology. Mild thickening of the mitral valve with trivial to mild mitral valve regurgitation was detected; however, cardiac output of 3.7 L/min, stroke volume of 58.3 mL, E/e' < 15, and E/A ratio < 0.8 was consistent with normal cardiac function and left atrial filling pressure.⁵

Significant clinical improvement led to weaning of vasopressors and the pacemaker being turned off on day 5 of hospitalization. Ventilator weaning trials were initiated, and the patient was extubated on day 10 of hospitalization. She participated in daily physical therapy sessions and was discharged on day 13 of hospitalization, after she was able to breathe on room air while maintaining her heart rate, blood pressure, and oxygen saturation.

DISCUSSION

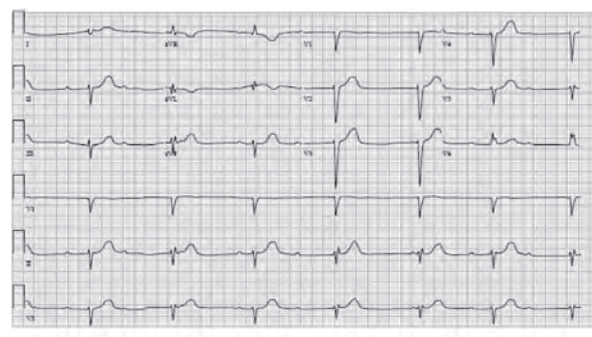
Acting through L-type calcium channels, CCBs cause vasodilation of peripheral vasculature and myocardial depression, which can result in profound hypotension, shock, bradycardia, and conduction blocks.⁶ CCB toxicity also has been associated with hyperglycemia,⁷ acidosis and acute kidney injury,⁸ noncardiogenic pulmonary edema,^{9,10} and ARDS.^{8,10-12} The mechanism behind CCB toxicity causing ARDS is unknown, but 2 mechanisms have been

Figure 1. Patient Chest X-ray



Extensive, patchy geographic areas of airspace opacities throughout majority of the lungs with sparing of apices. Endotracheal tube tip lies 1.7 cm above the carina. Nasogastric tube lies with tip into the gastric body. Right internal jugular central line ends with tip in the high right atrium.

Figure 2. Patient Electrocardiogram



Sinus rhythm with atrioventricular dissociation and wide QRS rhythm.

proposed: one suggests that CCBs inhibit endothelin-1-stimulated surfactant secretion by type II epithelial cells, leading to alveolar collapse,¹¹ while another suggests that selective precapillary vasodilation causes excessive transudation of fluid from pulmonary capillaries into the alveoli.¹³

Although CCB-induced ARDS is a fairly rare occurrence, literature supports the notion that CCB intoxication can increase patient risk of developing ARDS. Siddique et al reported a 40-year-old male who developed ARDS following noncardiogenic pulmonary edema and aspiration pneumonitis from CCB intoxication.⁹ Additionally, ingestion of high-dose verapamil and subsequent development of ARDS has been documented by Izdes et al,¹² and Magdylan et al reported a 22-year-old female developing ARDS after CCB intoxication.¹¹

Though patients ingesting more than the maximum daily dose are at higher risk of developing serious intoxication, toxicity can occur even with therapeutic doses of CCBs in patients with underlying cardiac disease or metabolic derangements.¹⁴ This can be further complicated by the fact that extended-release CCBs—like those the patient in this case took—decrease the rate of clearance via the liver, which ultimately increases duration of toxicity. For this reason, it is important for clinicians to understand the signs and symptoms of CCB toxicity, as well as how to treat it.

First-line therapy for CCB toxicity generally consists of intravenous (IV) calcium to promote calcium influx via unblocked L-type calcium channels, norepinephrine and/or epinephrine when the patient is in shock, and high-dose insulin therapy in the setting of cardiac dysfunction.¹⁵ Both subtypes of CCBs affect the pancreas by reducing insulin secretion, causing insulin resistance in body tissues and inducing a carbohydrate-deficient intracellular state.⁹ As such, lactic acidemia and metabolic acidosis can result. High-dose insulin therapy actively transports glucose into the energy-depleted cells, reverses metabolic derangements, and has a positive inotropic effect on the cardiac myocytes. Additionally, glucagon has been shown to improve heart rate and cardiac output and reverse atrioventricular blocks in animal studies.¹⁶

In patients refractory to first-line therapies, transcutaneous or transvenous pacemaker placement and IV lipid emulsion therapy is recommended.¹⁵ CCBs are lipophilic, highly protein-bound, undergo extensive hepatic first-pass metabolism, and have a large volume of distribution (>2L/kg).⁴ These characteristics make CCB decontamination difficult because at higher doses, clearance via the liver slows; additionally, methods of clearance like hemodialysis are ineffective due to the lipophilic and protein-bound nature of CCBs. Intravenous lipid emulsion therapy is useful in CCB toxicity because the lipid emulsion surrounds the lipophilic CCB, rendering it ineffective. The CCB gets trapped in an expanded plasma lipid compartment, which reduces the volume of distribution.¹⁷ It has also been proposed that intralipids improve overall cardiac function by providing an energy source for the cardiac myocytes, since CCB toxicity shuts down fatty acid transportation to the cardiac myocytes.

CONCLUSION

CCBs are commonly used in clinical practice and have the potential to cause serious side effects if over-ingested (unintentionally or with suicidal intent), used in combination with drugs that have interactions, or even when taken in therapeutic doses by patients with underlying cardiac disease or metabolic derangements. Cautious use of CCBs by clinicians, as well as maintaining awareness that these drugs increase risk of developing ARDS, can help prevent such adverse events from occurring. Additionally, since CCBs have unique metabolic properties that make toxicity challenging to treat, first and second-line treatments must be kept in mind when caring for acutely ill patients.

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Joseph E. Kerschner, MD

Local Efforts Making a Global Impact in the Fight Against COVID-19

Joseph E. Kerschner, MD

Medical schools and teaching hospitals educate the next generation of physicians, conduct cutting-edge research that saves lives, and care for the sickest and most complex patients. Collectively known as “academic medicine” or “academic health systems,” these institutions work together to educate and train the next generation of physicians, biomedical scientists, pharmacists, and other health professionals. In the best of cases, including in Wisconsin, these institutions partner with others in the health arena and the community to provide advantages for populations in the entire region. As major centers of research, they discover and pioneer new and more effective medical treatments that set the standard of care throughout medicine and raise all boats for the care of patients in their local regions and beyond.

Combating diseases and epidemics can only be sustained with continued medical advancements. The nation’s medical schools and teaching hospitals conduct 55 percent of the extramural medical research supported by the National Institutes of Health (NIH). This research has saved lives and improved the quality of life for millions, as well as produced many medical firsts and breakthroughs, including better treatments for heart disease, stroke and diabetes; new techniques such as

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organ, bone and stem cell transplants and minimally invasive surgery; novel discoveries, and cancer treatments that have saved more than 2.4 million lives since 1991; and all

the work at MCW is connected to the Midwest Respiratory Virus Program (MRVP) in MCW’s Department of Pediatrics. This group, combined with the pediatric and clinical practices,

COVID-19 has created substantial loss and suffering already. It is our expectation at MCW that our previous investments and preparation, as well as our current generation of new knowledge as part of the academic medical community, will limit future loss and expedite cures.

210 drugs approved by the US Food and Drug Administration between 2010-2016.¹

In the past few months, the novel coronavirus (COVID-19), its impact, and potential solutions, have occupied the consciousness of nations around the globe. Medical schools, including the Medical College of Wisconsin (MCW), and their associated academic health systems, stand at the front lines in the United States in developing plans, providing systems of care, and investigating potential solutions.

The benefits of a medical school and academic medicine are often felt locally – such as cutting-edge cancer clinical trials or Level 1 Trauma care for seriously injured patients. In important ways, however, local efforts can make a global impact, and this is occurring in the current fight against COVID-19. Much of

is focused on developing a rapid molecular diagnostic approach for COVID-19 that can be used in clinical laboratories, allowing a reduction in turnaround time for diagnosis of the disease from the current three days to less than one hour. We expect to translate our academic development into real-world testing in the near future.

The impact in creating new diagnostic techniques to assist diagnosis and limit disease spread was highlighted during the H1N1 (Swine Flu) outbreak in 2009, when the MRVP developed a specific type of molecular testing that allowed for rapid and highly specific diagnosis of this dangerous infectious disease. Our partnership with health systems throughout the state enabled Wisconsin to rank as one of the only states in the country to provide a large

volume of testing throughout the outbreak. A similar approach would be implemented should the spread of COVID-19 accelerate throughout the United States.

Additionally, experts in our Clinical Microbiology Research group in the department of pathology have spent the last decade working to develop and partner with commercial entities to commercialize rapid respiratory diagnostics. In a patient suspected of being infected with COVID-19, it is critical to rule out other respiratory viruses (including flu) in a timely manner. Through these advancements, the turnaround for both a flu test and comprehensive respiratory profile is less than one hour from the time the specimen is collected bedside without sacrificing test performance.

Beyond testing innovations, epidemiological surveillance (the systematic collection, analysis and dissemination of health data for the planning, implementation, and evaluation of public health programs) and strain characterization (identification of subtypes of microorganisms, such as a “flu strain”) also are critical to fighting COVID-19. An example of progress in this arena has been a program called SMAART, which encompasses a regional partnership across southeast Wisconsin comprising all of the major health systems and a number of long-term care facilities to identify sources of multi-drug-resistant pathogens (infectious agents) and to prevent their spread. Currently, this comprehensive approach includes environmental surveillance and patient surveillance to characterize the origins of the Acinetobacter outbreak (an emerging pathogen capable of causing hospital-acquired infections) and contain it. In SMAART, the epidemiological collaboration of health care systems is supported by a partnership among MCW, the Wisconsin Laboratory of Hygiene at the University of Wisconsin, and Wisconsin Diagnostic Laboratories that uses whole genome sequencing to identify what makes the pathogen resistant to antibiotics.

Also related to COVID-19 are antiviral clinical trials conducted by MCW’s department of medicine’s division of infectious diseases, which have led to multiple new antivirals that have been cleared in recent years – and which ultimately may be the foundation to treatments for COVID-19.

COVID-19 has created substantial loss and suffering already. It is our expectation at MCW that our previous investments and preparation, as well as our current generation of new knowledge as part of the academic medical community, will limit future loss and expedite cures.

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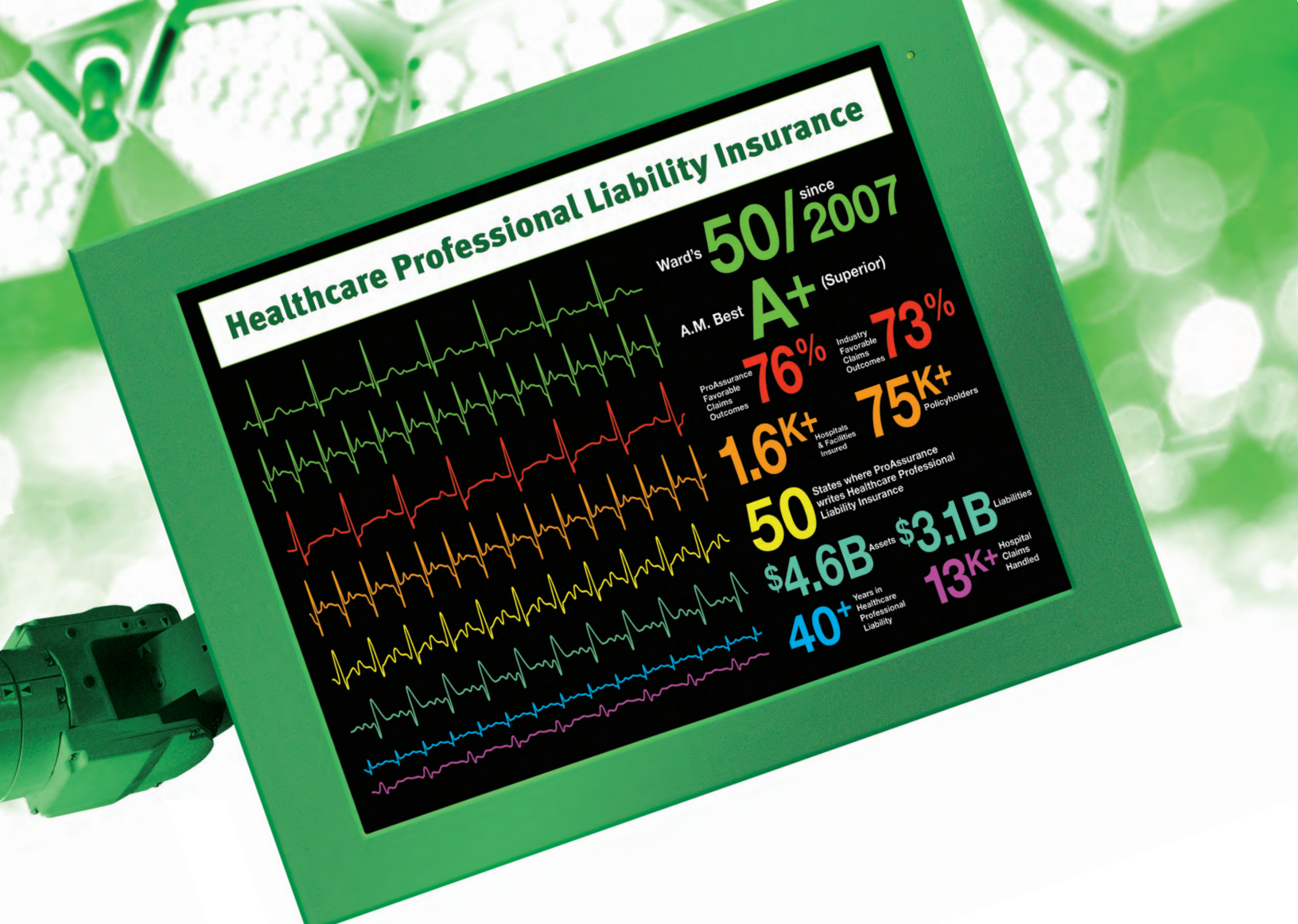
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