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WMJ

2023 • volume 122 • issue 4

IN THIS ISSUE

A closer look at some of the myriad aspects of medical education

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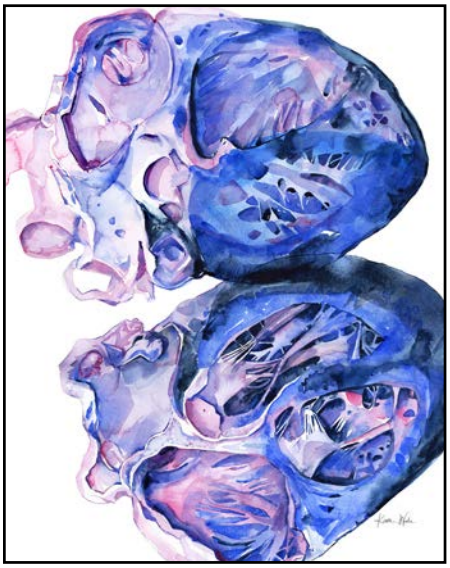

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WMJ

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COVER ART

The Exquisite Heart

Kaitlin Walsh

Watercolor, 22x30

Artist's Statement

"This painting is a part of my series, Exquisite Anatomy. While I used an actual heart dissection as reference, my hope was that through a carefully chosen palette and composition, the viewer would feel appreciation and awe for the sheer beauty and delicate intricacies of our inner workings, rather than distaste at something typically considered unappealing."

About the Artist:

Kaitlin Walsh specializes in abstract anatomical paintings. From a young age, she exhibited a fascination with both art and medicine. She focused her studies on both disciplines with a graduate degree in medical illustration. After graduation, Kaitlin had a child in the NICU for three months. That experience inspired her to showcase the beauty of the inner body. She launched her studio, Lyon Road Art, in 2015 and has now sold over 50,000 prints of her work. She lives in Madison with her family.

EDITORIAL

ORIGINAL RESEARCH

REVIEW

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

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BRIEF REPORTS

CASE REPORTS

Exploring the Feasibility of POCUS Training for Advanced Practice Providers at an Academic Medical Center

Dear Editor:

Over the past few decades, point-of-care ultrasonography (POCUS) has evolved as an integral part of physical examination. Many US medical schools have incorporated POCUS training into their curricula, with over 70% reporting to have an ultrasound curriculum as of 2019.[1] As advanced practice providers (APP) play a significant role in delivering care across various specialties, it is crucial to consider the potential of APP-performed POCUS. In a recent survey involving 59 hospitalist faculty and APPs at the Medical College of Wisconsin, a majority of respondents (80%) expressed interest in pursuing POCUS training.[2]

In June 2023, we conducted a pilot POCUS course for a small group of Medicine APPs. The course was attended by 9 participants and spanned over 5 intensive hours, incorporating both didactic sessions and hands-on training. It encompassed core elements of hospital medicine POCUS, including basic physics and knobology, kidney, lung, and focused cardiac ultrasound. Each topic was presented in concise lectures, lasting no more than 30 minutes. To enhance the understanding of sonographic anatomy, a 10-minute simulation of echocardiographic views was conducted using the heartworks augmented reality simulator. For the hands-on training, 3 scanning stations were set up with ultrasound machines and adult volunteer models.

Following completion of the workshop, an online voluntary anonymous survey was distributed to collect feedback. Out of the 9 attendees, 7 responded to the survey. The respondents were asked to rate their confidence on a qualitative scale of 0 to 10, in interpreting and acquiring images for different sonographic applications before and after the course. For kidney ultrasound interpretation, confidence rose from 1±1.8 to 5.3±1.1, lung from 1.7±2.6 to 6.6±1.5, focused cardiac from 1.2 + 1.9 to 5.2 + 1.3, and familiarity with ultrasound modes and knobs from 2.4±3.1 to 7.9±1.5 (P<.001 for all comparisons). Similarly, the confidence in performing kidney ultrasound increased from 1.4±2 to 5±1.7, lung from 1.4±2.1 to 5.3±1.4, cardiac (excluding inferior vena cava) from 1.1±1.9 to 4.6±1.7, and inferior vena cava from 2.2±2.3 to 5.4±2 (P<.001 for all comparisons). When asked whether they were willing to incorporate POCUS into routine practice, 100% of the respondents answered yes, assuming ultrasound machines are available and expert assistance is readily accessible.

While acknowledging that confidence alone does not guarantee proficiency, we find great encouragement in the enthusiasm displayed by the participants in learning POCUS. We plan to expand this program into a longitudinal curriculum with institutional support. Our upcoming project aims to provide handheld ultrasound devices to APPs for a specified duration, allowing us to analyze the evolution of image quality over time and use this data to develop local certification guidelines.

—Abhilash Koratala, MD; Paige Gioia, PA-C; Devin Madenberg, DO; Anu Taylor, MD

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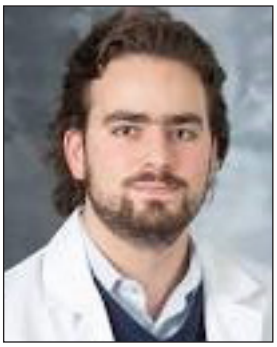
Fahad Aziz, MD, FASN



Kian Samuel Djamali, BA

Providing Feedback Is Essential for Professional Growth

Fahad Aziz, MD, FASN; Kian S. Djamali, BA

This issue of *WMJ* includes several papers that explore various aspects of medical education. For physicians and other health care professionals, however, learning and professional growth continue throughout our careers. A necessary component of this dynamic process is giving and receiving feedback. It not only helps to stimulate learning and uphold professional standards, but it is also one of the most effective ways to improve ourselves and those around us. And given the high stakes and fine margins for error in the medical field, receiving feedback at every stage of one's career is crucial.

The purpose of this editorial is to offer guidance to those working in health care on ways to effectively deliver feedback to peers and colleagues at any point in their career. A future editorial will discuss how to receive feedback.

KEYS TO EFFECTIVE FEEDBACK

When delivering feedback, focusing on the issues rather than the personalities involved is essential. It is easier to have difficult conversations and for individuals to differentiate between criticism and feedback when we foster an environment of respect. Understanding the distinction between direct and subtle or soft feedback is important as well. To be most effective, we should be able to balance the two while tailoring our comments to each individual's personality and learning style.

Benefits of Effective Feedback

Knowledge expansion

Skill improvement

Leadership development

Unfortunately, it is not uncommon for medical professionals to lack formal training in the art of providing effective feedback and constructive criticism. We have found the following principles to be most beneficial:

- **Structure the feedback:** Giving serious thought to any criticism before voicing it is essential. One must remember that the goal of feedback is to promote learning and development for others and to facilitate problem-solving. Critical feedback should not be a zero-sum activity. Instead, we should aim to ensure that everybody wins. Structure successful feedback by deciding when and where to give it, selecting words carefully, and approaching the situation without judgment or bias.
- **Show the impact:** It is important to think about how resolving an issue through feedback will affect those involved and their individual growth. Fixing an issue often requires convincing people to consider how the conflict in question might affect them.
- **Be specific:** Feedback – especially negative feedback – needs to be pinpointed in its concentration and unambiguous in its delivery. Using an indirect, gentle approach may lead to confusion. Conversely, an overly direct method risks being misinterpreted as criticism. It is almost always more beneficial to supply objective data versus subjective information while delivering feedback.
- **Recognize positives:** Even negative feedback should incorporate positive content. One way to help someone improve is by first reviewing their strengths, then discussing areas where they are not as successful. Admire and acknowledge their positive abilities and actions rather than simply criticizing what they have done wrong. When people's strengths are recognized, they are more likely to be receptive to suggestions.
- **Suggest actionable solutions:** Feedback that does not include specific steps to act upon can be misleading and, in many cases,

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counterproductive. One should propose concrete, actionable steps that address specific issues at hand, as well as a road map for personal improvement and growth in the workplace. Without goal-oriented solutions and a follow-up plan, the value of feedback can be diminished significantly.

- **Allow explanation:** Recipients of feedback should have the opportunity to explain themselves and also be permitted to express their opinions about the feedback they receive.
- **Conclude positively:** A feedback meeting should conclude on a positive note, regardless of the topic. People remember what was said at the end of a conversation, so finishing on a positive note lets them focus on practical ways to improve and provides more of an incentive for them to act upon the feedback they received.
- **Always keep calm:** Regardless of the severity or nature of the issue, one must stay calm during feedback dialogues. It is crucial for us in the medical field to be able to strike a balance between being explicit with our comments and avoiding emotionally charged statements. Remember that feedback is vital for personal growth, and losing one's temper will reduce its effectiveness.
- **Be available:** One should always be willing to answer questions regarding the feedback they give. This clarifies any doubts or confusion the recipient may have and demonstrates that we care about their success, thereby increasing the likelihood that they will be motivated to act.

What to Avoid When Providing Feedback

Creating an environment that fosters disrespect

Being judgmental

Providing feedback that is
- overly general,
- overly direct
- overly detailed

Focusing on personality instead of the issue

Giving feedback without
- goals
- actionable items
- a follow-up plan

As medical professionals, when we can successfully provide constructive feedback and work to address our shortcomings, we can create a positive environment where we can learn and succeed together. This, in turn, facilitates leadership development and optimizes the level of care we can deliver to patients.

ALSO IN THIS ISSUE

The cover of this issue of *WMJ* features a watercolor titled, "The Exquisite Heart" by Kaitlin Walsh. This is the first in what we hope will be a series of reader-contributed artwork on the cover that illustrates the art and science of medicine. Readers are invited to submit works in the following media: photography, digital design, or well-rendered photographs of painting, drawing, sculpture, ceramics, printmaking, or textile/fiber art for consideration for future issues. Visit www.wmjonline.org to learn more.

Unmeaningful Work and the Practicing Physician

Joseph Edward Fojtik, MD, MPH

With its goals of improving the experience of care, improving the health of populations, and reducing the per capita cost of health care, the Triple Aim attempts to achieve what Donald Berwick and associates have described as high-value health care.[1] However, since its publication, several factors continue to confound the Triple Aim, including three of primacy: the decline of primary care, physician burnout, and the accumulating amount of unmeaningful work for the practicing physician.[2] These three also may be interdependent and irreducible, and each must be mitigated to facilitate attaining the Triple Aim goals.

The decline of primary care has been persistent and progressive, despite several ongoing interventions by national vanguard organizations. It is predicted to exacerbate future health care gaps in an aging population with a burden of chronic diseases.[3,4] Physician burnout has been well known for over two decades; however, only relatively recently has its downstream sequelae on patients, populations of patients, and the cost of care been better understood.[5-7]

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While these two factors have been well-described, unmeaningful work has not. There is a paucity of extant work defining unmeaningful work, expanding its lexicon beyond simple administrative tasks, or elucidating if it is an independent risk factor to the decline of primary care and physician burnout. Defining unmeaningful work and its taxonomy can facilitate a better understanding of how it relates to the decline of primary care and physician burnout and may act as a synergistic antagonist to the Triple Aim.

Since its publication, several factors continue to confound the Triple Aim, including three of primacy: the decline of primary care, physician burnout, and the accumulating amount of unmeaningful work for the practicing physician.

Any work associated with patient care can be meaningful. However, if that work is not license-level appropriate or does not contribute to direct patient care, it may be perceived as unmeaningful. Unmeaningful work can be further defined as cognitive work demanded upon a physician that is not license-level appropriate but is required to complete a clinical encounter, adds no clinical value for the patient or the physician, and acts as a barrier to care. Unmeaningful work for physicians may also be more than simple administrative tasks or routine workflow interruptions encountered by other professions and disproportionally affects the generalist specialist more so than others.[8,9] Although there are currently no formal categories of unmeaningful work, three can be identified: unmeaningful work units, electronic frustrations, and redundant layers of complexity.

Unmeaningful work units are the miscellaneous, unrelievable clerical tasks now omnipresent within clinical encounters. They may include the requirement of generalist specialists in some systems to perform written clerical referrals for patients to see other specialists due to the persistent and antiquated misinterpretation of the generalist specialist being a clerical gatekeeper versus a specialized coordinator of care.[10,11] Physicians also may be the only health care professionals in some systems allowed to enter computerized physician order entries due to the persistent misinterpretation of regulatory statutes,[12] or perform clinically unnecessary box-checking to document certain arbitrary patient attributes to finalize orders within clinical encounters (euphemistically titled “The Revenge of the Ancillaries”).[13] Unmeaningful work units

are ubiquitous, interwoven within the clinical encounter, and intrude into the cognitive space physicians need to complete that encounter.

Electronic frustrations are unique elements associated with the now widely perceived dysfunctional electronic health record (EHR) ecosystem and are disruptive to patient care. They include the generalized EHR attributes pervasively found within clinical encounters, subversively diverting the physician's attention from the patient to the computer, as repeatedly shown in time-motion studies.[14,15] They also may include the paradoxical EHR window-popups physicians need to navigate during clinical encounters ("popup fatigue"),[16,17] or the excessive mouse movements and mouse clicks needed to complete simple clinical tasks ("click fatigue").[18,19]

Electronic frustrations also include physicians' interactions when searching for clinical data uniquely imbedded within the EHR. Concerns were raised early in the EHR's advent about these interactions,[20,21] centering on the deficiencies of what can be considered the three essential Rs of clinical data: the need for it to be reliable, relevant, and readily available. These concerns persist. Data erroneously entered in the EHR can be difficult to remove, unreliable, may not accurately describe the diagnostic process, and can lead to medical misadventures.[22-25] Clinical notes, generated by an EHR ecosystem complacent with cut and paste techniques,[26] have become so excessively long and "note bloated" that they become irrelevant to subsequent treating physicians.[27,28] Physicians now spend extraneous amounts of time foraging across different electronic platforms within the EHR ecosystem for clinical data not readily available due to the promised EHR interoperability being unmet and incomplete.[29,30] The introduction of the EHR to clinical practice has been correlated to physician burnout;[31] electronic frustrations may also be the added independent risk factors to this relationship.

Redundant layers of complexity may include work required by health care entities for a physician to practice medicine within those entities in addition to state statutes. These statutes, including medical practice acts, ultimately define the requirements and boundaries within which a physician may practice medicine.[32] Redundant layers of complexity may include a requirement for physicians to complete discordant educational activities to work within an entity that are not required by a state's medical practice acts. They also include the disproportionate reliance health care entities place upon proprietary patient surveys, with the subsequent edicts attempting to change physicians' clinical behavior,[33,34] or the requirements for physicians to utilize overly complex or discordant diagnostic codes within the EHR.[35,36]

Unmeaningful work elements also include newly added administrative work burdens historically completed by others that are now presumed upon the physician during the "interstitial time between other work."[37] The unrestricted ability of unmeaningful work elements to enter into a clinical encounter and intrude into the cognitive space needed for the physician to complete that encounter is more worrisome than the elements themselves, and the widespread societal acquiescence of their presence infers that the medical profession has been little-prepared to protect the physician.

Medicine, as with other professions, draws its unity and authority with self-imposed and self-governed rules that over the millennia have evolved into ethics and codes of professionalism.[38,39] These ethics and codes define the profession by defining a high moral standard of conduct and professionalism expected of the physician toward his or her patients, fellow physicians, and society.[40] However, to date, there is no ethical construct that defines its corollary specifically; no ethic conceptualizes a high moral standard of conduct expected of the profession and its associated health care entities toward the physician. An ethic that protects and preserves the physician and the physician's cognitive space relevant to patient care – "The Physician Ethic" – should be considered. Its conceptualization and further development may also mitigate the three confounding elements of the Triple Aim and is long overdue.

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Audit of Sex and Gender Medicine Topics in Preclinical School of Medicine Curriculum

Kendall Trieglaff, BS; Madeline J. Zamzow, BS; Bryn Sutherland, BA; Amy Farkas, MD, MS; Sandra Pfister, PhD

ABSTRACT

Introduction: The importance of the inclusion of sex and gender medicine (SGM) in medical education has been recognized formally by both the American Association of Medical Colleges and the Department of Health and Human Services since 1995. Yet, few medical schools, including the Medical College of Wisconsin, have a standard SGM curriculum. This work mapped the SGM health topics taught in the Medical College of Wisconsin preclinical curriculum.

Methods: Seven medical students audited 16 basic science preclinical courses in 2020-2021. SGM characterizations, including epidemiology, diagnosis, presentation, treatment, prognosis, pharmacology, and disparity, were captured by an online survey tool. Comparisons were made to 38 high-yield topics presented in the textbook "How Sex and Gender Impact Clinical Practice: An Evidence-Based Guide to Patient Care."

Results: Of the 604 preclinical sessions audited, 54% contained some SGM content. Epidemiology was the most common characterization (23% of total). Thirty-four of the 38 high-yield clinical SGM topics received mention in the basic science sessions. Breast cancer, stroke, osteoporosis, sex and gender considerations in therapeutic response, and systemic lupus erythematosus had the most frequent SGM-specific coverage (representation in at least 4 of the 16 preclinical courses).

Conclusions: Utilizing a medical student cohort to thoroughly audit courses was an effective way to document that Medical College of Wisconsin preclinical curriculum introduces many clinically relevant SGM topics. However, the audit also discovered varying levels of detail among the high-yield topics with concern that students may not be adequately prepared to treat all patients. These results establish the groundwork for a more formalized and integrated approach to include SGM in preclinical curriculum.

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INTRODUCTION

Recognition and teaching of sex and gender diversity is an essential component of medical education and critical to providing high-quality medical care to all people.[1,2] Sex as a biological variable affects anatomy, physiology, and pathophysiology. The term gender is considered a social construct and encompasses behaviors individuals use to present themselves in society.[3] Sex and gender both influence aspects of health including, but not limited to, clinical presentation, diagnosis, treatment, and access to health care. For example, cardiovascular conditions are well-studied instances of how sex and gender affect medicine. The anatomy of a female heart has coronary vessels with more branching than those of a male heart, which leads to different patterns of blockage and, thus, different symptoms related to myocardial ischemia.[4] Additionally, the traditional gender role of women as primary caretakers can result in women delaying prevention and treatment of chronic conditions like heart disease.[5,6]

Despite the importance of understanding the differences in sex and gender terminology, there is a concern that undergraduate medical education lacks adequate training of learners in sex and gender medicine (SGM).[7-9] While a national survey[10] indicated that 85.5% of medical students were aware of SGM differences and 94.4% believed that medical education should include teaching about SGM, it is not easily apparent which medical schools (allopathic and osteopathic) have a standard SGM curriculum. The textbook *How Sex and Gender Impact Clinical Practice: An Evidence-Based Guide to Patient Care* by Jenkins and

Newman listed 8 US academic institutions that have educational resources on sex and gender health.[11] Furthermore, the survey reported that 97.9% of faculty and 89.0% of students answered "no" or "not sure," to the question "Does your institution have an identified sex and gender-based medicine curriculum?"[10]

An internal survey of Medical College of Wisconsin (MCW) students and faculty supported the results of the national survey.[12] Of the 210 students (M1-M4 years) surveyed, 84% said their education should include SGM education and that knowledge would improve patient care. Faculty surveyed indicated that they felt strongly that MCW medical education should include the teaching of sex and gender medicine differences (96%), while only 20% said that their own training had prepared them to teach it to medical learners. More importantly, both national and MCW institutional survey data reported that over 50% of students indicated that their curriculum did not prepare them to clinically manage SGM differences.[10,12] This training deficit needs to be addressed in a more systematic manner.

There are some published results of curricular audits of SGM topics taught in either undergraduate or graduate medical education and in learning materials for licensing board examinations.[7,13-15] In general, these studies found content focused more on anatomical and physiological sex differences, with less details on incidence, treatments, and outcomes that are sex- and gender-based. The Sex and Gender Medical Education (SGME) Summits played a major role in raising awareness of teaching SGM in all health professions.[16,17] These summits provided key connections to validate and implement the integration of SGM into education and laid groundwork for content standardization.[3]

The goal of this work was to perform a directed audit to identify and document SGM topics in MCW medical curriculum with intent to inform future curriculum content. The MCW Institutional Review Board deemed this work exempt from review.

METHODS

Organization

MCW enrolls approximately 1000 medical students across 3 campuses, with an approximate distribution of 56% female and 44% male. MCW teaches basic or foundational (preclinical) science over 2 years using mainly didactic lectures and clinical case correlations. M1 courses are Clinical Human Anatomy I and II, Molecules to Cells, Physiology, Infectious Agents and Host Immunity, Principles of Drug Action, Medical Neuroscience, and Foundations of Human Behavior. M2 courses are arranged by organ system units and include Foundations of Pathological Processes and Musculoskeletal Skin, Cardiovascular, Renal-Respiratory, Heme-Lymph, Gastrointestinal-Nutritional, Endocrinology-Reproduction, Neurology-Psychiatry, and Symptoms.

Curriculum Review

The MCW Curriculum and Evaluation Committee (CEC) is charged with oversight of the undergraduate medical curriculum. In 2019, the CEC discussed a curricular thread review of sex and gender topics in current courses and clerkships. To meet its goal, the CEC funded this work through a learning resource grant to engage students in identifying sex and gender topics in the MCW curriculum. Details of methodology are included below.

Recruitment of Student Auditors and Training

Student auditors were recruited to provide real-time assessment of the preclinical lecture content. Open positions were advertised during orientation for M1 and M2 students during the start of the 2020-2021 academic year. Ultimately, 7 student auditors were recruited to the project: 6 women and 1 man. Each student auditor received a stipend for their work and met with the faculty leader to review the project's objective, time commitment, and design. Additionally, they were provided with asynchronous training on SGM resources pertaining to the historical context of SGM, recent studies on sex and gender in medical education, and correct use of SGM terminology. A Microsoft Teams page was used for further communication and sharing content. The faculty leader (SP) did monthly face-to-face check-ins with students to get updates and address concerns.

Survey Development and Real-Time Audit

The Qualtrics survey platform was used to capture these data: course, session title, SGM terminology, SGM coverage, and comments. When it was noted that terms relating to sex (male or female) and/or gender (man/boy or woman/girl) were used in a lecture, the survey expanded to capture additional details of how SGM topics were characterized using the following categories: pharmacology, prognosis, treatment, disparity, diagnosis, presentation, and epidemiology. Additionally, training emphasized that student auditors include more distinct facts about a lecture in the comments section.

Data collection began in October of the 2020 fall semester and continued through the end of the 2021 spring semester. M1 and M2 students audited their respective enrolled courses. Only large group didactic lectures were audited given the variability inherently present in small group, clinical skills, and laboratory-based sessions. Due to the COVID-19 pandemic, all students were limited in their ability to attend class in-person. Because the large group sessions were recorded, student auditors had the option to either attend class in person when appropriate according to institutional policies, stream the lecture in real time, or watch recorded lectures later. The recorded lectures and slide decks were reviewed to retrospectively evaluate those lectures from August to October that took place before the real-time audit began. All student auditors were expected to complete a survey after every lecture. There were multiple auditors for each session to decrease any auditor bias. M1 lectures had up to 3 different student entries, and M2 lectures had up to 4 different

student entries. Additional details recorded as comments were specific to each student. To avoid the observer effect, faculty lecturers were unaware of the project.

Data Analysis

Data analysis was carried out during the summer following the 2020-2021 academic year. All survey data were combined into a final dataset, with 1 entry per lecture session. Any discrepancies between auditors were resolved by group consensus using survey comments, lecture slides, and lecture recordings. Most of the inter-auditor variance was attributed to the use of sex and/or gender terminology in clinical case examples without adequate context of sex and/or gender in lecture material (eg, "a 62-year-old female presents to the emergency department"). Auditors agreed that SGM was not covered if the lecture session only used sex and/or gender terminology in clinical case examples but did not discuss SGM topics in the lecture. Session presentation of SGM content focused on the categorical characterizations of pharmacology, prognosis, treatment, disparity, diagnosis, presentation, and epidemiology. Curriculum characterization content was then mapped to current practices in medicine for comparison.

A variety of sources exist to identify and map sex and gender topics to include in medical education curriculum.[18] With input from faculty, the students chose the textbook *How Sex and Gender Impact Clinical Practice: An Evidence-Based Guide to Patient Care,*[11] which was highlighted in presentations and workshops at the most recent Sex and Gender Education Summit (2021) to provide an authoritative source for use in the education of learners about sex and gender differences.

Using section 2 in the textbook, "Sex and Gender Evidence in Health and Disease," a comprehensive template was created to include 38 SGM topics (Table 1). Approximately 74% of lecture sessions included additional student comments, which were used to compare the depth of topic coverage by scoring for several distinct facts. This process was verified by a second rater for randomly selected topics at each coverage level. Table 2 shows an example of comment scoring.

RESULTS

Session Presentation of SGM Content

All 604 basic science sessions delivered in large group didactic lectures were audited across the M1 and M2 preclinical years. Fifty-four percent (330/604) of sessions contained SGM characterization content, which further divided into 45% (132/294) of M1 sessions and 64% (198/310) of M2 sessions. Of the sessions covering SGM content, 60% (198/330) were from the M2 year. The breakdown of topics by sex and gender across the 7 characterizations is shown in Figure 1. Coverage of 6 out of 7 characterizations was greater in M2 courses compared to M1 courses. Only pharmacology had less coverage in M2 courses compared to M1 courses. Epidemiology and disparity characterizations were used

Table 1 . Topics Selected From *How Sex and Gender Impact Clinical Practice: An Evidence-Based Guide to Patient Care*

Topic	M1	M2
Access to care	—	En-Rep
Acute ischemic syndrome	—	CV
Alcohol use disorder	PDA	GI-N, Sym
Alzheimer's dementia	Phys	Sym
Ankylosing spondylitis	—	FPP-MSS, CV
Anterior cruciate ligament injuries	—	—
Asthma		R-R, Sym
Breast cancer	PDA, CHA, MTC	En-Rep, FPP-MSS, GI-N, CV
Chronic obstructive pulmonary disease	—	R-R, Sym
Colorectal cancer	—	GI-N
Diabetes	Phys	GI-N, En-Rep
Dyslipidemia	—	CV, En-Rep
Effect of sex and gender in disease states on drug therapy outcomes	—	CV
Gastroesophageal reflux disease and Barrett's esophagus	—	—
Generalized anxiety disorder	—	Neu-Psy
Heart failure	—	CV
History of sex/gender in drug therapy	PDA	—
Importance of sex/gender in pharmacologic research	PDA	CV
Inflammatory bowel disease	—	—
Intimate partner violence	CHA	En-Rep, Neu-Psy
Liver lesions	—	GI-N
Lung cancer	PDA	R-R
Major depressive disorder	M-Neu	Neu-Psy
Migraine	M-Neu	Neu-Psy, Sym
Myocardial infarction from obstructive coronary artery disease	FHB	CV, Sym
Nonobstructive ischemic heart disease	—	CV
Obesity	—	CV, GI-N
Opioid use disorder	PDA	—
Osteoarthritis	CHA	FPP-MSS
Osteoporosis	Phys, PDA	FPP-MSS, En-Rep
Rheumatoid arthritis	—	FPP-MSS, CV
Sex/gender considerations in therapeutic response	PDA	CV, GI-N, En-Rep
Schizophrenia	M-Neu	Neu-Psy
Sleep apnea	—	—
Stroke	Phys, PDA	CV, Neu-Psy, Sym
Systemic lupus erythematosus	—	FPP-MSS, CV, R-R, Sym
Tobacco use and nicotine addiction	—	CV
Vaccination	IAHI	GI-N

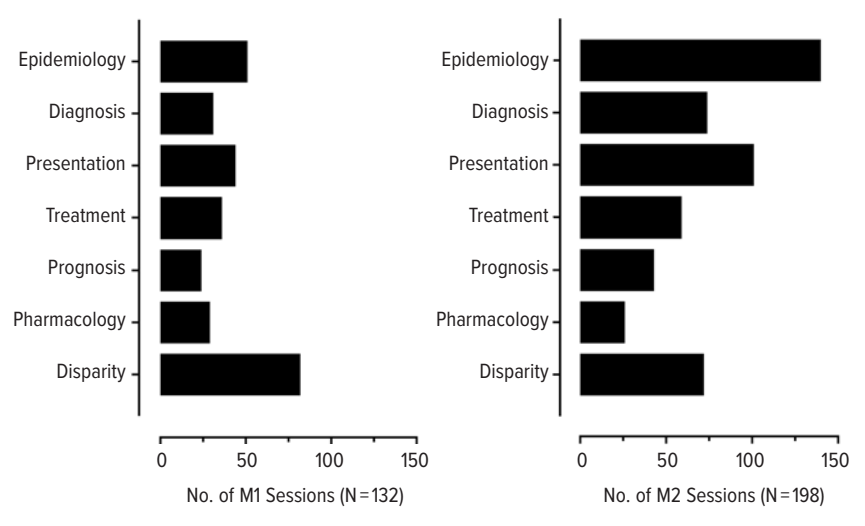
Abbreviations: MTC, molecules to cells; Phys, physiology; CHA, clinical human anatomy; IAHI, infectious agents and host immunity; FHB, foundations of human behavior; PDA, principles of drug action; M-Neu, medical neuroscience; FPP-MSS, foundations of pathological processes and musculoskeletal skin; CV, cardiovascular; R-R, renal-respiratory; H-L, Heme-Lymph; GI-N, gastrointestinal-nutrition; En-Rep, Endocrine-Reproduction; Neu-Psy, neurology-psychology; Sym,a symptoms.

Table 2. Example of Student Comments Matched to Sex and Gender Medicine (SGM) Topics

Coverage Level	SGM Topic	Student Survey Comments
Brief (1-2)	Rheumatoid arthritis	Rheumatoid arthritis is more common in women than men, approximately 2.5:1
Moderate (3-5)	Major depression disorder (MDD)	Women more likely than men to have a diagnosis of depresion depression after an ischemic event Discussed prevalence of depression in males vs females Women are 70% more likely than men to experience depression Men are less likely to seek help for MDD
In depth (6+)	Myocardial infarction from obstructive coronary arrtery disease	Women have a harder time quitting smoking and increased cardiovascular risk due to sex- and gender-based differences There are traditional and nontraditional atherosclerotic cardiovascular disease risk factors in women Session included difference in men (50%) vs women (15%) dying from ischemic heart disease related to hyperlipidemia type 2a. Session discussed aspirin originally being tested in men or cardiovascular disease secondary prevention and later tested (and comparable) in women Prevalence of coronary artery disease in "men and women" Also discussed the greater prevalence of autoimmune disorders in women, which increases the risk for atherosclerosis and heart disease

Student comments from the survey were mapped to the SGM topics. Each unique comment was added to score each topic and assign a coverage level. For example "brief" coverage included topics with 1-2 discrete comments.

Figure 1. Breakdown of Sex and Gender Medicine Characterizations by M1 and M2 Year



The number of times each characterization was used in a lecture is plotted, along with the total number of M1 and M2 sessions containing SGM content.

most often in the presentation of SGM topics in M2 and M1 courses, respectively.

Curriculum Content Comparison

When the preclinical course characterization content was compared to the 38 SGM topics from the Jenkins and Newman textbook, 34 topics were covered (Table 1). The M1 curriculum covered 18 of 38 (47%) topics, while the M2 curriculum covered 32 topics (84%). The 4 topics not covered from SGM perspective included inflammatory bowel disease, sleep apnea, anterior cruciate ligament injuries, and gastroesophageal reflux disease/Barrett's esophagus. Regarding the depth of coverage (Table 3), 14 topics were covered briefly with 1 to 2 distinct facts, 11 were covered moderately with 3 to 5 distinct facts, and 9 were covered in-depth with 6 or more facts. The median SGM topic coverage was 3 facts (Table 3). Topics receiving the most SGM-specific coverage were breast cancer (3 M1courses, 4 M2 courses), stroke (2 M1 courses, 3 M2 courses), osteoporosis (2 M1 courses, 2 M2 courses), sex and gender considerations in therapeutic response (1 M1 course, 3 M2 courses), and systemic lupus erythematosus (4 M2 courses) (Figure 2). Ten topics were mentioned in only 1 course across both preclinical years (Table 1).

Overlap across the 2 preclinical years was noted. While 2 topics were covered only in the M1 year, most topics covered in the M1 year were repeated in the M2 year (16/18). Although M2 courses are organ systems based, SGM topics from other organ systems had overlapping coverage among courses. For example, the M2 cardiovascular unit covered 15 topics, ranging from addiction and autoimmune to metabolic and neurological (Table 1). Only 5 topics are primarily cardiovascular-specific (acute ischemic syndrome, myocardial infarction from obstructive coronary artery disease, nonobstructive ischemic heart disease, heart failure, dyslipidemia).

DISCUSSION

Learning sex- and gender-based medicine during the preclinical years sets a foundation for young clinicians to "improve diagnosis, disease management, and health outcomes"[11] for all. It was notable that the SGM content in MCW curriculum expanded on sex-based anatomical and/or physiological differences and made connections to clinical evidence of sex- and gender-based differences. In contrast, a report from the Texas Tech Health University Health Sciences Center School of Medicine found that most SGM content was focused on anatomical and physiological sex differences, while incidence, prevalence, treatments, and outcomes that were more clinically sex- and or

Table 3. Summary of Number of Distinct Facts Matched to Sex and Gender Medicine Topic List

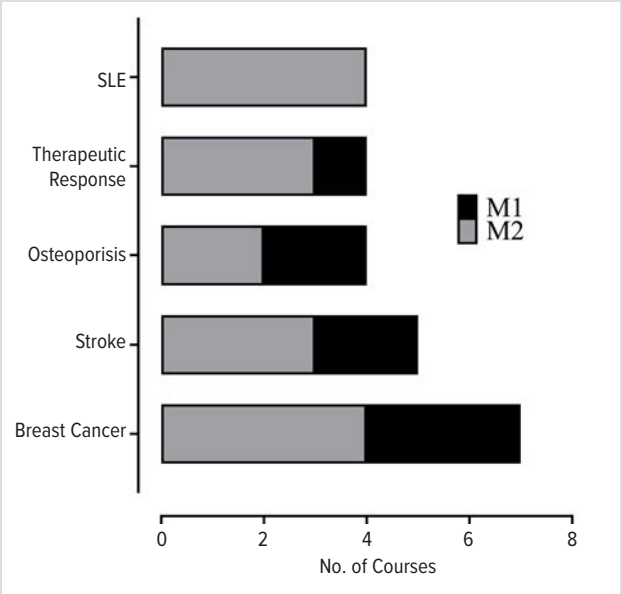
	No Coverage (0)	Minimal Coverage (1-2)	Moderate Coverage (3-5)	In-Depth Coverage (6+)
Topics	Gastroesophageal reflux disease and Barrett's esophagus Inflammatory bowel disease Anterior cruciate ligament injuries Sleep apnea	Opioid use disorder Rheumatoid arthritis Ankylosing spondylitis Colorectal cancer Heart failure The effect of sex and gender in disease states on drug therapy outcomes Tobacco use and nicotine addiction Nonobstructive ischemic heart disease Generalized anxiety disorder Dyslipidemia Obesity Osteoarthritis Alzheimer's dementia The history of sex and gender in drug therapy	Systemic lupus erythematosus Liver lesions The importance of sex and gender in pharmacologic research Vaccination Asthma Major depressive disorder Schizophrenia Access to care Alcohol use disorder Diabetes Stroke	Acute ischemic syndrome Myocardial infarction from obstructive coronary artery disease Osteoporosis Chronic obstructive pulmonary disease Breast cancer Migraine Lung cancer Intimate partner violence Sex and gender considerations in therapeutic response
TOTAL	4	14	11	9

Student comments indicated more distinct details about sex and gender medicine topics (Table 2). The number of distinct facts were summated across both the M1 and M2 curriculum as no coverage, minimal coverage (1-2), moderate coverage (3-5) and in-depth coverage (6+).

gender-based were obscure.[7] The dual approach used by the current study of first identifying session presentation of SGM terms linked to characterizations and then doing a more in-depth comparison to relevant SGM clinical content was key to gaining more insight into strengths and gaps in curriculum content.

While SGM characterizations were covered in the M1 and M2 curriculum, it was clear that many were taught in an inconsistent manner. Sessions described only minimal epidemiological differences between sex and gender. It is speculated that faculty lecturers relied more heavily on incidence and prevalence to demonstrate a sex and/or gender-based difference because these are well known and widely reported. The apparent lack of SGM characterization related to pharmacology is also a concern, given the known differences in pharmacology between the sexes, but not necessarily unexpected, as a similar finding was reported by Miller et al[19] in a case study of SGM at Mayo Medical School. Reasons for pharmacology deficits are varied, but one possibility is the continued lack of inclusion of women in clinical drug trials. The work also showed that most clinical content topics from the Jenkins and Newman textbook were covered, and this is acknowledged as an asset to the preclinical MCW medical education. It will be an important framework on which to continue to build a more robust clinically relevant SGM curriculum. It is notable that of the 38 topics used to index the sex and gender clinical content in the M1 and M2 courses, only 4 topics were not covered from SGM perspective. It is predicted that fewer SGM topics will be missed, as research and clinical studies continue to include and report on sex as a biological variable and/or gender identity in health conditions.[8] A challenge remains how to keep faculty knowledgeable and how to easily incorporate new information into existing lectures.

Figure 2. Topics Receiving the Most Sex and Gender Medicine Coverage



Bar graph shows topics that had most coverage across the M1 and M2 courses compiled from Table 1. Therapeutic response = sex and gender considerations of therapeutic response. Systemic lupus rrythematous (SLE) from a sex and gender medicine perspective was not taught in the M1 year.

The overlap of SGM topic coverage across the 2 preclinical years and between individual courses also demonstrates the achievability of further integration. This is important because it means no additional lecture time needs to be pulled from other founda-

tional topics to make room for SGM. Instead, our data support the conclusion that coverage needs to be formalized, intentional, and presented at a greater depth. A necessary next step of current work is to develop ways to engage faculty to integrate SGM more completely into future curriculum. Most recently, a set of 4 sex and gender health educational tenets were developed by an interprofessional group of educators based on work of the 2020 Sex and Gender Health Education Summit.[3] Adaptation of these tenets by curriculum leaders will ensure that educational materials are continually updated as the knowledge base of sex and gender medicine continues to expand.

Study Limitations

This study had some limitations. One was a lack of common language across faculty lecturers to define and discuss sex and gender. While this added to the complexity of describing and analyzing SGM topics within the curriculum, it also demonstrates additional need to educate faculty lecturers on both importance of these discussions and the use of clear and appropriate terminology.

Not auditing small groups and clinical skills sessions is another limitation of this work, particularly as many in medical education work to transition away from large lecture formats toward smaller group sessions. In the future, such small groups could be audited for SGM topic coverage using a similar method with more auditors or with more qualitative methods, such as focus groups or interviews.

Additionally, utilizing a single textbook to define the SGM topics for analysis could potentially limit what SGM topics were deemed important. However, as accomplished leaders in both the practice of SGM and education of medical students, Jenkins and Newman took a comprehensive and foundational approach to sex and gender health and disease. The outline of the book was systems-based and correlates well with the course structure of many medical schools, including the current MCW curriculum.

Another limitation was the qualitative approach to analyze the curriculum content as it was based on the feedback provided in the survey's optional comments section. However, because sessions were viewed by multiple students, the comments—while completed to varying degrees by individual students—allowed compilation from all the student observations.

Study Strengths

Strengths of the study include the real-time audit approach being time efficient and comprehensive. The survey audit form was completed shortly after the lecture session, took a few minutes to complete, and considered both written and spoken content contained in the lecture. Additionally, using medical student auditors authentically captured the student perspective on the discussion of SGM topics in the curriculum.

Like other SGM curriculum audits, our work provides a meaningful baseline of SGM teaching. The MCW CEC encouraged and supported this work with the additional caveat that the results be used to inform current and future curriculum changes. These methods also could be adapted to audit other elements of the curriculum, such as race, ethnicity, mental health, substance use, and social determinants of health, to ensure their inclusion in appropriate contexts. While it is inherent that this study was performed on a single medical school's curriculum, it joins a growing number of such audits that could, and should, be used in the future to begin to examine on national and international levels how SGM is taught in medical education. This is important, particularly when considering curriculum redesign and integration of SGM.

CONCLUSIONS

Previous survey data from both national and local levels reported that medical students recognize the importance of SGM while acknowledging a lack of preparedness, demonstrating the need for institutions to approach SGM integration into the curriculum in a formalized and consistent way. The defined dual approach of this study to identify SGM characterization content in lectures and compare it to topics presented in an evidence-based book on SGM is novel and can be a model for other medical schools.

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The Impact of a Scholarly Concentration Program on Medical Student Research in Pediatrics

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ABSTRACT

Introduction: To promote scientific inquiry, medical schools encourage medical students to participate in scholarly concentration programs (SCP). Manuscript publishing, a proxy of productivity, enhances medical student understanding of scientific inquiry. To evaluate an elective medical SCP offered between the first two years of medical school, the pediatrician authors' primary aim was to study the publishing productivity of the program participants in the University of Wisconsin (UW) School of Medicine and Public Health Department of Pediatrics compared to other departments. Secondary aims were to study whether productivity was influenced by the following predictors: (1) self-identified medical student gender, (2) working with a frequent mentor, (3) mentor degree, (4) funding source, and (5) area of research.

Methods: PubMed joint publications from 2002 through 2017 were searched using both medical student and mentor names through 2 years post-graduation.

Results: From all UW School of Medicine Public Health departments, 1108 medical students self-selected projects and mentors. One hundred two (9.2%) students chose the Department of Pediatrics. The majority of these students were female (61%) compared to female medical student participation (42%) in other departments ($P = 0.0004$). The majority of projects were clinical (53%), with basic science (26%) and public/global health (21%) following, though with more public/global health projects chosen in the Department of Pediatrics ($P = 0.002$) versus other departments. Overall, frequent mentors improved publication rates (P=0.0008), though frequent mentors ($P = 0.45$) and publication rates ($P = 0.60$) did not differ between pediatrics and other departments.

Conclusions: Medical students' SCP manuscript productivity benefitted from working with frequent mentors, but productivity in the Department of Pediatrics did not differ from other departments.

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INTRODUCTION

Scholarly concentration programs (SCP) are offered to medical students with the goal of benefiting from: (1) faculty mentoring experience, (2) scholarly knowledge and skills gained in scientific methodology, and (3) communication of scholarly research.[1] SCPs vary between elective to mandatory and a summer project to a 4-year longitudinal project.[2-5] A critical aspect of SCPs is medical student and faculty mentor collaboration on the project.

Data from the Association of American Medical Colleges indicate that medical student participation in scholarly endeavors is increasing.[6] Both allopathic and osteopathic medical schools have deemed SCPs beneficial to medical students,[7] and school administrations encourage participation as supported by the US medical schools' national accreditation body, the Liaison Committee on Medical Education.[8,9] SCPs are found to influence medical students' decisions for both clinical specialty and future careers in academic medicine, while improving medical student research and dissemination skills through conference presentations and manuscript publications.[1,10] Participating medical students tend to value goals that lead to both skill acquisition (ie, learning the process of manuscript writing) and accomplishments (ie, manuscript publication).[3] With this knowledge, evaluating the factors that play a role in manuscript publication can provide guidance to SCPs, medical students, and faculty mentors.

Successful SCPs require strong mentorship and administrative

support.[2] Mentorship from faculty and more senior medical students can benefit junior medical students.[11] Substantial mentor resources have been recommended to promote physician scientist training,[2] with strategies to provide optimal SCP administrative and financial support currently under discussion nationally.[5] SCPs allow medical student participation in different research fields and disciplines. Clinical/translational fields, as well as public/global health (PGH), are particularly critical to child health. Medical students' participation in child health research may promote academic research careers in pediatrics. Little is understood, however, about how SCP project selection and productivity in pediatrics differs from other departments.

In 2002, the University of Wisconsin School of Medicine and Public Health (UWSMPH) allopathic undergraduate medical education organized and offered an 8- to 12-week SCP fellowship for interested single-degree MD students in the summer between the first two years of medical school. The elective SCP fellowship participation increased from 17% of medical students in 2002 to 63% of medical students in 2017.

Our objective was to better understand factors influencing scientific manuscript publication as a proxy to better understanding the impact of SCPs on medical student research in the University of Wisconsin School of Medicine and Public Health (UWSMPH) Department of Pediatrics (DoP) and other departments in the summer SCPs during 2002-2017. Our primary aim was to study the dependent variable of manuscript publication from SCP medical students who choose the DoP versus other departments. Secondary aims examined the impact of these independent predictors on manuscript publication in pediatrics versus other departments: (1) self-identified medical student gender, (2) working with a frequent mentor, (3) mentor degree, (4) funding source, and (5) area of research.

METHODS

Scholarly Concentration Program

The Institutional Review Board (IRB) quality improvement tool determined IRB review was not required because, in accordance with federal regulations, the project does not constitute research as defined under 45 CFR 46.102(d). Potential project ideas submitted by UWSMPH faculty mentors were offered to medical students. Medical students either self-selected these projects or generated their own projects and mentorship from any UWSMPH faculty member. Medical students and mentors further developed their proposal and applied for SCP grant funding. Departmental or Medical Student Research Committee faculty then reviewed projects and either accepted or suggested revision before acceptance. After summer SCP completion, all participating medical students were expected to submit a research abstract for presentation (poster or podium) at an annual medical student research forum the next semester. Medical students were not required to submit manuscripts.

Dataset

We reviewed data from a prospectively collected cumulative SCP dataset with medical student enrollment from 2002 through 2017. In addition to self-identified medical student gender and area of research, we collected from proposals primary mentor department and mentor's primary/secondary degrees, including MD, PhD, master's degrees, and combinations of the aforementioned. We then grouped mentors (1) into a single MD degree group, (2) into a MD-masters group, and (3) those with MD-PhD or single PhD into a PhD group. We combined the PhD and MD-PhD mentored students into one group because: (1) research training was more extensive in these mentors than other groups, (2) the PhD mentor group was the smallest group. If missing, we collected mentor degrees from departmental websites. We defined frequent mentors as mentoring more than 3 medical students in the SCP before the current student, because it was the geometric mean of mentee/mentor in the dataset, while also ensuring that the mentor had experience with the SCP and had previous experience working with medical students. Each mentor, however, was only identified once, regardless of number of mentees within the time period. We collected specific funding sources for each medical student in the SCP, including the Herman and Gwen Shapiro Foundation, predoctoral training grants, mentor grants, and departmental-supported funding. From the student's proposal title, we demarcated the SCP projects into either clinical, basic science, or PGH fields (categorized by authors AB and PK).

Dependent Variables

We determined the dependent variables of any and first author joint research publication through a PubMed search that included any publications jointly authored by both primary mentor and medical student for a duration that included the year of the SCP fellowship until 2 years after student medical school graduation (5-year window). We did not include publications with a different mentor either before or during the 5-year window. The final PubMed search occurred on June 20, 2020, after medical students enrolled in the summer 2017 SCP graduated. We discriminated students as either first author or any author. We chose this discrimination because we assumed as first author, the student contributed more significantly to the work, whereas if the student was listed elsewhere in the author order, the contribution may be less significant. We analyzed publications within the 5-year window for 898 medical students, 4-year window for 87 medical students, and 3-year window for 114 medical students.

Data Analysis

Data were analyzed by STATA 15 (StataCorp, LLC, College Station, Texas). We observed a natural inflection point with relatively higher student participation in 2010 and demarcated both an early 2002-2009 and a late 2010-2017 student epoch to deter-

Table 1. Comparisons of Self-identified Medical Student Gender, Frequent Mentorship, Mentor Degree, Type of Funding, and Type of Research in the Department of Pediatrics vs Other Departments

Variable	Subvariable	N (%)	DoP MS n (%)	Other Dept MS n (%)	χ^2	Cramer's V	*P* value
Self-identified MS gender		1108 (100%)	102 (9%)	1006 (91%)	13.31	-0.11	0.0004
	Female	485 (44%)	62 (61%)	423 (42%)			
	Male	623 (56%)	40 (39%)	583 (58%)			
Frequent mentor >3 mentees		360 (33%)	37 (36%)	321 (32%)	0.76	0.026	0.45
Mentor degree					14.04	0.0611	0.2
	MD only	609 (55%)	58 (57%)	551 (55%)			
	MD + Master's	167 (15%)	16 (16%)	151 (15%)			
	PhD ± MD	332 (30%)	28 (27%)	304 (30%)			
Had training grant		118 (11%)	5 (5%)	113 (11%)	4.03	-0.06404	0.07
Type of research					14.07	0.1134	0.002
	Clinical	582 (53%)	41 (40%)	542 (54%)			
	Basic science	288 (26%)	25 (24%)	264 (26%)			
	Public/global health	233 (21%)	36 (36%)	197 (20%)			

Abbreviations: DoP, Department of Pediatrics; MS, medical student.

mine if publication rates changed over time with χ^2 and Cramer's V to estimate effect size. Because 4 authors are affiliated with the DoP, we compared data in pediatrics to other departments. We defined any publication and any first author publication as the 2 categorical dependent variables. χ^2 testing and Cramer's V were used to estimate effect size. We did not model interactions between independent and dependent variables by multivariable logistic regression because the test of independence showed that multiple variables were not independent from frequent mentorship. A P value < 0.05 was deemed significant.

RESULTS

Demographic Characteristics

From 2002 through 2017, 1108 of approximately 2800 enrolled medical students (40%) participated in SCP fellowship projects, with 415 individual primary mentors. The ratio of female/male medical students was higher in pediatrics than in other departments ($P = 0.0004$) (Table 1). Most medical students (n = 1025, 93%) selected projects within clinical departments: 490 students (48%) chose medical and 539 students (52%) chose surgical specialties. The Department of Internal Medicine supported the largest percentage of medical students (n = 308, 28%), followed by the departments of general surgery (n = 236, 21%), orthopedics (13%), and pediatrics (9%).

Of primary mentors, we identified 358 (86%) as frequent (>3 mentees). Selection of frequent mentors in pediatrics did not differ from other departments (Table 1). Mentor degrees or funding sources did not differ between the DoP and other departments (Table 1). However, for the DoP, the ratio of medical students who chose PGH research was higher than in other departments ($P = 0.002$) (Table 1).

Joint Publications With Mentor: Primary Aim

In the later epoch of the program (2010-2017), both any publication (36.7% vs 23.5%, $\chi^2 = 12.8$, Cramer's V = 0.11, $P < 0.0001$)and first author publication rates were higher (18.4% vs 9.8%, $\chi^2 = 8.8$, Cramer's V = 0.089; $P = 0.003$) as compared to the earlier epoch. In the whole cohort, we found that 380 medical students (34%) in the SCP fellowship produced a joint manuscript with their summer project mentor, including 186 (17%) as first authors. Overall, any or first author joint publication rates did not differ between self-identified male and female medical students (Table 2). Rates of any and first author publications were higher with frequent mentors, mentors with a single MD degree, and training grants, with effect size greatest with training grants (Table 2). Publication rates did not differ by type of research ($P = 0.057$) but differed slightly ($P = 0.041$) by first author (Table 2).

Joint Publications With DoP Mentor vs Other Departments: Secondary Aims

The joint publication rate for any and first author publications in the DoP did not differ from other departments based on gender, frequent mentorship, mentor degree, mentor training grant, or type of research ($P > 0.05$ for all comparisons) (Table 3).

DISCUSSION

Over time, graduation surveys from UWSMPH, as well as summary data from United States medical schools, report rising rates of research participation by medical students during medical training.[6] It is important to better understand what makes concentrated SCPs effective in both enhancing medical school education and opening up career opportunities. We found that publication rates were higher in the later cohort, perhaps due to organized training grants, more experienced mentors, and maturation of training resources within the departments and school-sponsored fellowship programs. Previous work found that publication productivity increased after better-defined SCP expectations, along with increased financial and administrative support.[4] In the current study, training grants showed the largest effect size, followed closely by both frequent mentorship and the mentor having a single MD degree, although frequent mentorship was not independent from training grants and mentor degree. While research in the Department of Pediatrics exhibited some differences from

other departments, with relatively greater rates of PGH research and more female students, publication rates were comparable.

Reported publication rates in SCPs for other medical schools range from 5% to 75%, with 45% on average for any publication and one-third as first author.[2,4,12-15] The publication rate of 34% in our study may be lower than average because we only searched PubMed (and residency applications generally include papers not indexed on PubMed[16]), and because we examined only medical student-mentor collaborations, excluding publications with other mentors who were not within the SCP fellowship. We searched PubMed for 2 years after medical student graduation to allow for (1) project maturation, (2) medical students participating in research electives during their fourth year, and (3) delays in submission-to-publication. In support of our strategy, it was previously found that two-thirds of manuscripts listed as "submitted" or "in press" in radiology electronic residency applications were published 2 years post-graduation.[17]

Scientific writing is beneficial by engaging students in the research process apart from clinical care, providing in-depth learning about a singular interest, and increasing skills in interpreting the medical literature. Medical students report improved self-efficacy in research methodology and communication of study findings following completion of a SCP fellowship.[18] Writing in a field of interest promotes both collaboration and contacts and, thus, career mentorship. Many medical school graduates report that SCP both influenced career choice and ongoing interest in the project's topic,[1] especially because our projects were self-selected. In addition, medical students participating in clinical research are more likely to enter residencies in that specialty, though it is unclear if the choice of residency influenced the research area or vice versa.[19,20]

Physician-scientist numbers are declining.[21] Early exposure to SCP fellowships or specific research experience increases a medical students' interest in entering an academic career.[10,12,14] Three aspects of medical student research previously were found to be associated with an intent for career-long research: (1) SCP satisfaction, (2) female medical students gender, and (3) publication rates.[14,22] Publishing SCP projects may be a potential strategy to increase the physician-scientist workforce,[14] especially with relatively less emphasis on research than volunteerism for acceptance to medical schools.[23] Pediatric-specific data support this, with about 58% of already published medical students publishing during residency compared to only one-third during residency if they did not publish as a medical students.[24,25]

SCP publication rates have not previously been shown to differ based on sex, consistent with our findings.[26] Our study noted there was increased female medical student participation in pediatric research compared to male medical students, consistent with a greater proportion of female physicians in the field of pediatrics. However, publication rates did not differ among self-identified gender in medical students participating in SCP overall or between the DoP and other departments, despite the overall differences in

Table 2. Overall Whole Cohort Rates of Medical Student Any and First Author Publication by Self-identified Medical Student Gender, Frequent Mentorship, Mentor Degree, Type of Funding, and Type of Research

Publication	Variable	Overall N (%)	χ^2	Cramer's V	*P* value
	Self-identified MS gender	485 female, 623 male			
Any[a]	Female	32%	1.97	0.04	0.16
Any[a]	Male	36%			
1st[b]	Female	16%	0.31	0.017	0.31
1st[b]	Male	23%			
	Mentorship	360 frequent, 749 infrequent			
Any[a]	Frequent	57%	11.44	0.102	0.001
Any[a]	Infrequent	31%			
1st[b]	Frequent	24%	17.90	0.127	0.0001
1st[b]	Infrequent	14%			
	Mentor degree	MD only 609, MD + Master 167, PhD ± MD 332			
Any[a]	MD only	39%	13.94	0.112	0.001
Any[a]	MD + Masters	32%			
Any[a]	PhD ± MD	36%			
1st[b]	MD only	19%	9.61	0.093	0.008
1st[b]	MD + Masters	7%			
1st[b]	PhD ± MD	13%			
	Funding	118 training, 990 no training			
Any[a]	Training grant	50%	15.04	0.114	0.0001
Any[a]	No training grant	32%			
1st[b]	Training grant	33%	25.39	0.152	0.0001
1st[b]	No training grant	15%			
	Type of Research	583 clinical, 288 basic science, 233 public/global health			
Any[a]	Clinical	38%	5.74	0.072	0.057
Any[a]	Basic science	30%			
Any[a]	Public/global ealth	31%			
1st[b]	Clinical	19%	6.37	0.076	0.041
1st[b]	Basic science	13%			
1st[b]	Public/global health	16%			

Abbreviation: MS, medical student.
[a]Rate of any publication between medical student and mentor.
[b]Rate of first author publication between medical student with mentor.

Table 3. Rates of Any and First Author Publications Based on Self-identified Medical Student Gender, Frequent Mentor, Mentor Degree, Use of Training Grant, and Type of Research Between Department of Pediatrics Medical Students and Other Departments

Variable	Authorship	Category	Dept of Pediatrics n (%)	Other Departments n (%)	χ^2	Cramer's V	*P* value
Publication Rate	Any[a]		38 (37.3%)	380 (34.1%)	0.43	0.020	0.52
	1st[b]		16 (15.6%)	186 (16.9%)	0.11	0.010	0.74
Self-identified medical student gender			62 female, 40 male	423 female, 583 male			
	Any[a]	Female	38.7%	31.1%	1.43	0.054	0.23
	Any[a]	Male	35.0%	36.3%	0.03	0.0065	0.63
	1st[b]	Female	17.7%	15.9%	0.13	0.017	0.72
	1st[b]	Male	12.5%	17.7%	0.73	0.034	0.39
Frequent mentors >3 mentees			37 frequent, 65 infrequent	321 frequent, 685 infrequent			
	Any[a]	Frequent	48.6%	40.0%	0.91	0.050	0.35
	Any[a]	Infrequent	30.7%	31.0%	0.002	0.0016	0.97
	1st[b]	Frequent	13.5%	24.9%	2.41	0.082	0.12
	1st[b]	Infrequent	16.9%	13.2%	0.69	0.030	0.41
Mentor degree			58 MD only, 16 MD+Master's, 28 PhD ± MD	551 MD only, 151 MD+Master's, 304 PhD ± MD			
	Any[a]	MD only	41.4%	38.7%	0.16	0.016	0.67
	Any[a]	MD+Masters	31.3%	32.5%	0.01	0.0076	0.92
	Any[a]	PhD±MD	32.1%	26.5%	0.41	0.035	0.53
	1st[b]	MD only	17.2%	19.3%	0.150	0.016	0.70
	1st[b]	MD+Masters	19.8%	12.5%	0.50	0.269	0.48
	1st[b]	PhD±MD	11.3%	16.6%	0.22	0.026	0.64
Mentor training grant			2 yes, 100 no	102 yes, 902 no			
	Any[a]	Yes	40.0%	50.9%	0.23	0.044	0.63
	Any[a]	No	37.1%	31.9%	1.065	0.033	0.30
	1st[b]	Yes	20.0%	33.9%	0.41	0.060	0.52
	1st[b]	No	15.4%	14.8%	0.026	0.005	0.87
Type of research			41 clinical, 25 basic science, 36 public/global health	201 clinical, 76 basic science, 62 public/global health			
	Any[a]	Clinical	39.0%	37.5%	0.04	0.008	0.85
	Any[a]	Basic Science	45.8%	29.0%	2.96	0.102	0.09
	Any[a]	Public/global health	30.5%	31.5%	0.012	0.007	0.91
	1st[b]	Clinical	19.5%	19.4%	0.0003	0.0007	0.97
	1st[b]	Basic Science	12.0%	12.5%	0.001	0.002	0.99
	1st[b]	PGH	13.9%	16.2%	0.13	0.023	0.72

[a]Rate of any publication between medical student and mentor
[b]Rate of first author publication between medical student with mentor.

gender participation between pediatrics and other departments.

Publication rates were improved overall among medical students who worked with frequent mentors. The increased exposure in frequent mentors to SCP and to medical student researchers may explain this higher rate of publications. Other confounders such as faculty member productivity, rank, and academic track, were not collected or included in analysis but may influence medical student productivity. It is unclear if frequent mentors were overall more productive (as defined by publication rate), had a higher rank, or were on different research tracks that may have tilted the publication rates in favor of the frequent mentors.

In this study, most mentors held single MD degrees. Higher publication rates were seen among mentors with a single MD degree than those with more than one degree or a PhD. Although the reason for this finding is unclear and was not reported in previous SCP cohorts, many medical student projects studied existing datasets, which may publish at higher rates than other pilot projects or preliminary basic science. Our SCP guidelines supported research projects with scholarly methodological approaches, including systematic reviews and scholarly quality projects.

Publication rates were increased overall if the medical student had a training grant from their mentor, though no differences were noted between the DoP and other departments. The infrastructure and requirements for a training grant may push more medical students toward publishing, as evident in our findings. The lack of differences between pediatrics and other departments

suggest that the training grant opportunities exist in all departments providing improved resources for medical students to publish their work.

Interestingly, there was a higher percentage of medical students participating in PGH research in the DoP than in other departments, though no difference in publication rates were noted. This difference in project selection is not well understood, though could be related to a general pediatric focus on public health policy and improving the care of all children.

Strengths of this study include a large, growing SCP in a medical school with strong research infrastructure and support systems. There are a few weaknesses, however. Although annual data were collected prospectively, some data points were missing. Data were limited by less granularity about student experience, including our inability to track presentations from regional or national meetings. We did not track name changes or preferred name for manuscripts, potentially leading to underrepresenting manuscripts from medical students who changed their last name between the SCP fellowship and eventual manuscript publication. While medical students self-identified their gender on the survey, options at the time of dataset origination were only binary and not inclusive of transgender or nonbinary individuals. Additionally, mentors did not self-select gender data on the fellowship application and, thus, medical student and mentor gender was not compared. The definition of frequent mentorship did not include potential mentorship of other medical trainees, such as residents and/or fellows, and, therefore, could be underestimating a mentor's experience with medical trainees.

CONCLUSIONS

Having a structured and funded SCP summer fellowship facilitated medical student and mentor participation in research. Overall, training grants and frequent mentors improve publication rates--often a desired medical student outcome of the SCP fellowship. Identifying and supporting improved faculty mentorship may allow for the improved mentorship of medical students, leading to increased productivity and publications. Financial resources and administrative support going towards this faculty mentoring has the potential to increase the likelihood that faculty mentors may be willing to work with more and more students. Relatively more women medical students select pediatrics projects, including more PGH projects, but medical students in the Department of Pediatrics publish at rates comparable to other departments.

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Teaching Students to Care (Coordinate): A Randomized Controlled Trial

Lara Voigt, MD; James McCarthy, MD; Ankur Segon, MD, MPH

ABSTRACT

Introduction: Interdisciplinary rounds are a vital part of discharge planning; however, medical students receive little training in how to contribute effectively. Many existing discharge planning curricula are either prohibitively time consuming or narrowly focused. Addressing this gap can help improve interdisciplinary care and enhance the role of medical students on inpatient teams.

Methods: We developed a 30-minute curriculum on the purpose of interdisciplinary rounds, expected presentation content, and team members' roles and conducted a randomized controlled trial among medical students on their inpatient internal medicine rotation. Outcomes were measured using pre- and post-curriculum surveys and comparison of evaluations of student participation in interdisciplinary rounds.

Results: Eighty-six medical students participated in the study (59 intervention, 27 control), and we received 142 presentation evaluations (91 intervention, 51 control). There was significant post-curriculum improvement in all students' understanding of and comfort presenting in interdisciplinary rounds and knowledge of team members' roles. Presentation evaluations did not show a significant difference; however, students in the intervention group were better able to answer questions about their patients, with a difference approaching statistical significance (70% vs 57%, $P = 0.069$).

Conclusions: A brief, just-in-time curriculum improved learners' knowledge of interdisciplinary discharge rounds and showed a trend towards improvement in their ability to answer questions during rounds. Our curriculum can empower medical students to help their inpatient teams by participating in discharge rounds and can be integrated into existing curricula with minimal disruption.

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INTRODUCTION

Medical students receive rigorous training in pharmacology, physiology, pathology, and physical exam techniques, but preparation for transitioning patients between phases of care is often lacking.[1] Many students are not exposed to the various factors that influence length of hospital stay and readmissions or the interdisciplinary teams involved in discharge planning until the start of their clinical rotations. Even during their clinical years, few students receive any formal training on planning transitions of care or participating in interdisciplinary care.[1]

Interdisciplinary rounds have become a vital part of planning transitions of care from the inpatient setting. O'Mahony et al demonstrated that interdisciplinary rounds improved quality outcomes and led to better efficiency and communication among team members.[2] Subsequent studies by O'Leary et al reinforced that interdisciplinary rounding improved communication and reduced adverse event rates.[3-5] These results have led to the proliferation of interdisciplinary rounds to improve patient care and discharge planning. At our large Midwestern institution, interdisciplinary care coordination rounds (CCR) take place daily, with input from physicians, nursing staff, physical and occupational therapists, pharmacists, speech therapists, social workers, case managers, and dieticians. The medical teams are represented by attending physicians, advanced practice providers, resident physicians, or medical students. Physicians or their

representatives provide a brief summary of the patient's readiness for discharge and anticipated discharge needs. Each member of the interdisciplinary team then provides their input on discharge planning. Presentations and discussions must be succinct and discharge focused as each medical/surgical unit discusses up to 32 patients in a span of 60 minutes or less. Third- and fourth-year medical students on internal medicine clerkships and acting internships are expected to be able to present the team's patients at CCRs. Student participation in CCRs is a key part of their educational experience that also helps teams spread over multiple units engage with CCRs. However, nurses at our hospital reported that students were unable to deliver succinct discharge planning patient presentations at CCRs and were ill prepared to answer discharge-related follow-up questions from the interdisciplinary team.

In reviewing the existing curricula for interdisciplinary discharge planning, two major approaches emerged. On one side, comprehensive curricula aim to educate learners on all aspects of the discharge process. These programs may cover several sessions and often involve direct interact between members of the interprofessional team.[6-12] Other models take a more focused approach, going into greater depth on a particular patient population or aspect of the discharge process.[13-16] These methods both have proven successful, but challenges in teaching appropriate discharge planning remain. Many of these curricula are delivered in the beginning of the third year of medical school as part of transitioning to clerkship-type courses and students may not recall the content taught several months later when they start their internal medicine rotation. The time commitment and coordination between teams required of the more comprehensive programs are significant barriers to implementation, and although more focused curricula are easier to integrate into existing structures, they may only partially fill the educational gap.

With rising medical school enrollment across the country, 84% of medical student deans are concerned with finding a clerkship site for their medical students.[17,18] One strategy to encourage facilities to accept medical students is to train students so they can lighten the workload for their clinical teams.[19] Addressing the lack of training students receive in interdisciplinary care and discharge planning in the inpatient setting can empower students to take the lead in presenting their patients at CCRs and participating in the discharge process and making a concrete contribution to the patient care team. We developed a succinct, just-in-time curriculum designed to familiarize third- and fourth-year medical students with the discharge planning process, increase their knowledge of the roles played by interdisciplinary team members, and improve the quality of their presentations at CCRs. We used Kern's 6 steps of curriculum design as our framework for curriculum development and studied the impact of our curriculum in a randomized, controlled design. The objective of our study is to describe the impact of our care coordination curriculum on cognitive and psychomotor outcomes in third- and fourth-year medical students on general internal medicine wards.

METHODS

Curriculum Development

We performed a targeted needs assessment by surveying interdisciplinary team members, including case managers and charge nurses (27 responses), and physicians, including hospitalists, internal medicine clerkship directors, and acting internship directors (25 responses). This needs assessment guided course objectives, curricular content, and evaluation questions. Based on the needs assessment, we developed a brief, in-person presentation (Appendix A) that included the purpose of CCRs, the expected content of student presentations, and the roles played by the different members of the interdisciplinary team. We designed this introductory material to require no prior knowledge beyond terminology covered in the first 2 years of medical school and followed it with discussion of example cases to provide practice in identifying both discharge needs and which interdisciplinary team members would be most helpful in implementing various aspects of the discharge plan. We intentionally created complicated sample cases to expose students to multiple facets of the care coordination process.

Study Design and Participants

We conducted a randomized controlled trial from March 2019 to October 2019 among third- and fourth-year medical students on their internal medicine rotation at our institution, a major multihospital Midwestern medical center. All students who rotated at the primary teaching hospital during the study period were eligible to participate, and those who rotated only at other sites were excluded. During their rotation, 1 to 3 students were assigned to one of 13 inpatient medical teams, and we randomly assigned each team to either the intervention or control group. The intervention group received the curriculum during the first week of their 1-month rotation, while the control group received it during the last week. Participation in the study was voluntary, and our protocol was evaluated and approved by the Medical College of Wisconsin (MCW) institutional review board.

Metrics

Our needs assessment identified understanding of the purpose of CCRs, lack of familiarity with interdisciplinary team members' roles, and expectations for presentation content as educational gaps; this data were used to develop our assessment tool (Appendix B). We used 5-point Likert scale questions to evaluate students understanding of CCRs, their familiarity with participants' roles, and their comfort presenting at CCRs. We also included a series of questions in which students were asked to identify the team member best suited to help with a given discharge need. Pretests were given at the beginning of the session and posttests were dis-

tributed immediately after the curriculum was delivered. We did not collect data on students' or teachers' perceptions of the curriculum.

To measure behavioral change, charge nurses completed a standardized checklist of medical students' performance at CCRs, with questions covering both the quality and content of presentations (Appendix C). Charge nurses were asked to include the students' team number on the evaluation but were blinded as to which teams were in the intervention or control groups.

Data Analysis

For Likert scale survey questions, we converted responses to numerical scores (ie, strongly disagree, very poor, or very unimportant = 1; strongly agree, very good, very important = 5) and calculated mean scores and standard deviations for each question. We used a *t* test to compare pre- and post-curriculum responses. We compared pre- and post-curriculum quiz scores using either a chi-square test or Fisher exact test based on the total number of responses. We used Fisher exact test to compare charge nurses' evaluations of intervention and control group presentations. Statistical significance thresholds for all comparisons were set at $P < 0.05$.

Table 1. Familiarity With Care Coordination Rounds (1 = Strongly Disagree to 5 = Strongly Agree)

	Intervention			Control		
	Pretest n = 59 Mean (SD)	Posttest n = 50 Mean (SD)	*P* value	Pretest n = 27 Mean (SD)	Posttest n = 25 Mean (SD)	*P* value
I understand the purpose of care coordination rounds (CCR)	3.66 (0.28)	4.7 (0.13)	< 0.001	4.19 (0.31)	4.72 (0.18)	0.006
I am familiar with the composition of the multidisciplinary team	3.19 (0.30)	4.73 (0.12)	< 0.001	3.81 (0.37)	4.72 (0.18)	< 0.001
I am familiar with the roles of various members of the multidisciplinary team	3.08 (0.31)	4.6 (0.15)	< 0.001	3.85 (0.32)	4.68 (0.19)	< 0.001
I am aware of what is expected of me when I present at CCRs	2.80 (0.31)	4.62 (0.14)	< 0.001	3.48 (0.4)	4.68 (0.19)	< 0.001
I feel comfortable presenting at CCRs	3.12 (0.31)	4.24 (0.22)	< 0.001	3.74 (0.34)	4.48 (0.2)	< 0.001
CCRs are valuable for patient care	4.17 (0.20)	4.76 (0.13)	< 0.001	4.07 (0.31)	4.56 (0.28)	0.027
CCRs are a valuable learning experience for medical students	3.90 (0.25)	4.58 (0.21)	< 0.001	3.63 (0.34)	4.44 (0.30)	< 0.001

Table 2. Familiarity With Roles of Team Members (1 = Very Poor to 5 = Very Good)

	Intervention			Control		
	Pretest n = 58 Mean (SD)	Posttest n = 50 Mean (SD)	*P* value	Pretest n = 27 Mean (SD)	Posttest n = 25 Mean (SD)	*P* value
Case management	3.28 (0.27)	4.24 (0.18)	< 0.001	3.37 (0.32)	4.48 (0.20)	< 0.001
Social work	3.79 (0.22)	4.34 (0.17)	< 0.001	3.85 (0.27)	4.52 (0.20)	< 0.001
Physical and occupational therapy	4.16 (0.20)	4.66 (0.16)	< 0.001	4.41 (0.24)	4.76 (0.17)	0.023
Respiratory therapy	3.76 (0.25)	4.32 (0.21)	0.001	4.19 (0.31)	4.56 (0.26)	0.076
Dietitian	3.83 (0.22)	4.48 (0.18)	< 0.001	4.19 (0.23)	4.76 (0.17)	< 0.001
Speech therapy	3.76 (0.23)	4.42 (0.19)	< 0.001	4.07 (0.32)	4.72 (0.18)	0.001
Pharmacy	4.22 (0.18)	4.64 (0.17)	0.001	4.56 (0.20)	4.76 (0.17)	0.124

RESULTS

Out of 146 eligible students, 86 (59%) participated in the study, with 59 randomized to the intervention group and 27 to the control group. Some students were called away for clinical duties prior to or during the curriculum session, leading to a lower participation rate and a lower number of post-curriculum surveys. We received a total of 142 charge nurse evaluations: 91 for the intervention group and 51 for the control group.

Following the curriculum, we found a statistically significant improvement in all students' understanding of and comfort with CCRs (Table 1). Both groups improved most in their awareness of the expected content of CCR presentations, followed by their familiarity with the composition of the interdisciplinary team and the roles of various interdisciplinary team members. We observed a larger difference between the two groups when students were asked about their familiarity with individual team members' roles (Table 2). The intervention group showed a significant improvement in their understanding of all team members' roles, except for the pharmacist, which had the highest pre-curriculum score. Students in the control group only showed significant improvement in their familiarity with the roles of case managers, social workers, and dietitians.

In the quiz portion of the survey, intervention group members improved significantly in their ability to identify the appropriate role for case management, physical therapy, and the charge nurse (Table 3). The control group also showed significant improvement in 3 areas, improving their scores on questions related to the role of social work, case management, and pharmacy (Table 3). Our pre- and post-curriculum results show evidence of a Kirkpatrick Level 2 (knowledge gain) impact.

Charge nurse evaluations did not reveal a significant difference in presentation quality between the intervention and control groups (Table 4). A majority in both groups were familiar with their patients' reason for admission, potential discharge date, and barriers to discharge. Students in the intervention group were better able to answer questions regarding their patients' plan of care

Table 3. Quiz Results Matching Role to Task (% Correct Responses)

	Intervention			Control		
	Pretest n=57	Posttest n=50	*P* value	Pretest n=27	Posttest n=25	*P* value
Guardianship	71.9	82.0	0.2194[a]	55.6	92.0	0.0044[b]
Home health care	45.6	58	0.2009[a]	29.6	80.0	<0.001[b]
Durable medical equipment	19.3	44.0	0.0058[a]	11.1	64.0	<0.001[b]
Out of bed mobility	84.2	96.0	0.0581[b]	81.5	100.0	0.0515[b]
Discharge huddle	54.4	90.0	<0.001[b]	55.6	68.0	0.3567[a]
Patient with hand weakness	43.9	58.0	0.1444[a]	59.3	76.0	0.1985[a]
Home intravenous medications	61.4	76.0	0.1057[a]	63.0	92.0	0.0201[b]
Poor oral intake	82.5	88.0	0.4224[a]	77.8	84.0	0.7289[b]

[a]Chi-square test.
[b]Fisher exact test.

Table 4. Charge Nurse Evaluation of Presentations

		Intervention (n=51)	Control (n=90)	*P* value
Familiar with patient's hospital course and reason for admission	Yes	79%	78%	1
	Partial	21%	22%	
	No	0%	0%	
Identified potential discharge date	Yes	70%	59%	0.3424
	Partial	27%	37%	
	No	3%	4%	
Identified barriers to discharge	Yes	64%	69%	0.8679
	Partial	31%	27%	
	No	5%	4%	
Presentation was succinct	Yes	75%	74%	0.2248
	Partial	24%	20%	
	No	1%	6%	
Able to answer questions appropriately	Yes	70%	57%	0.0697
	Partial	29%	35%	
	No	1%	8%	

appropriately, with the difference between groups approaching statistical significance (70% vs 57%, $P = 0.069$).

DISCUSSION

This brief, just-in-time curriculum on interdisciplinary rounds showed a Kirkpatrick Level 2 impact by improving learners' knowledge of the composition of the interdisciplinary team and the roles played by each of its members. Although the difference did not rise to the level of significance, students in the intervention group were better able to answer questions about discharge planning during rounds, suggesting that a larger study may have found a Kirkpatrick Level 3 (behavioral change) impact. These results are promising in that they show that discharge planning education can be implemented efficiently and can allow medical students on inpatient teams to effectively assist in the daily task of care coordination without major disruptions to existing curricula.

Our institution has encouraged residents and faculty to better prepare students to participate in CCRs, but students' education had been inconsistent due to variations in educators' approaches to CCRs and difficulty finding time on busy medical services to focus on an additional topic. This inconsistency prompted the development of our curriculum. Students in the control group received the curriculum at the end of their rotation and had higher pre-curriculum scores for comfort level with and knowledge of CCRs compared to students in the intervention group, but the improvement in their scores on the post-curriculum assessment suggests our intervention added value beyond the existing informal instruction that occurs on medicine wards.

The primary limitation of our study was a small number of participants, particularly in the control group. We delivered the curriculum to the intervention group at the beginning of the rotation during other orientation sessions, which appears to have improved attendance. By contrast, sessions for the control group were scheduled at the end of the month when students had transitioned away from the orientation setting and were more involved in the day-to-day functions of their medical teams. Although it was the most feasible option in terms of logistics, our randomization process likely also introduced bias into our results, as all students on each team were in the same experimental group. Because of variability in teaching provided and emphasis placed on CCRs by different attending physicians and residents, it is possible that not all the difference seen between groups was attributable to the curriculum.

The low number of charge nurse surveys returned was another limitation that may have affected our ability to find a behavior-level change. It is impossible to determine how many surveys theoretically could have been filled out due to the fact that not every student would present at CCRs every day; however, considering that hundreds of CCR meetings occurred over the course of the study, 141 student evaluations likely represents a low response rate. Given the many responsibilities charge nurses have during CCRs, evaluating medical student participation was likely low on their list of priorities. Designating a separate evaluator may have improved our response rate.

Despite these limitations, our study showed that a succinct curriculum on interdisciplinary rounds improves both students' knowledge of discharge planning and their contributions to patient care. While details of the curricula, such as the specific

roles of case managers and social workers, were specific to our institution, the content would be adapted easily to fit other interdisciplinary rounding models, and the overall concept of introducing a brief discharge planning curriculum is readily generalizable. A short curriculum can be seamlessly integrated into orientation and could be delivered by nearly any faculty member. Given the increased use of asynchronous and virtual sessions, future studies should investigate the impact of an interdisciplinary rounding curriculum delivered as an online module to further facilitate its implementation. Dedicated education on interdisciplinary rounding should become a core part of medical training as we prepare learners to provide safe and efficient transitions of care for their patients.

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Age-Appropriate Cancer Screenings Through a Dermatology Lens

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ABSTRACT

Background: Primary care physicians are often the first to identify signs and symptoms concerning for cancer. An important aspect of cancer screening is thorough skin examinations and subsequent referral to a dermatologist for atypical cutaneous presentations, which may be associated with an underlying visceral malignancy. Diagnostic considerations for pruritus without dermatitis ("itch without rash") in adults include senile pruritus, medication reaction, and paraneoplastic syndrome. Recognition of cutaneous manifestations of cancer should prompt cancer screening by primary care providers.

Objective: To update practicing physicians on current cancer screening guidelines with a specific focus on cutaneous clues to prompt further workup.

Methods: American Cancer Society and United States Preventive Services Task Force guidelines were systematically reviewed using PubMed and organizational websites during August and September, 2021, with review of Task Force Guidelines during October, 2022.

Results: Colorectal, cervical, breast, lung, skin, prostate, ovarian, hematologic, pancreatic, thyroid, testicular, bladder, oral, and gastric cancer screening guidelines are summarized.

Conclusions: Primary care physicians can recognize atypical cutaneous conditions and facilitate referral to a dermatologist for evaluation and/or directly order tests themselves to initiate appropriate cancer screening.

BACKGROUND

Primary care physicians are often the first to identify signs and symptoms concerning for cancer. An important aspect of cancer screening is thorough skin examinations and subsequent referral to a dermatologist for atypical cutaneous presentations, which may be associated with an underlying visceral malignancy. Diagnostic considerations for pruritus without dermatitis ("itch without rash") in adults include senile pruritus, medication reaction, and paraneoplastic syndrome. Recognition of cutaneous manifestations of cancer should prompt cancer screening by primary care providers.

With this review, we sought to update practicing physicians on current cancer screening guidelines with a specific focus on cutaneous clues to prompt further workup.

METHODS

American Cancer Society (ACS) and United States Preventive Services Task Force (USPSTF) guidelines were systematically reviewed using PubMed and organizational websites during August and September, 2021, with review of Task Force Guidelines during October, 2022.

Colorectal, cervical, breast, lung, skin, prostate, ovarian, hematologic, pancreatic, thyroid, testicular, bladder, oral, and gastric cancer screening guidelines are summarized (Tables 1 and 2).

CANCER SCREENING GUIDELINES

Colorectal Cancer Screening

As of May 2021, the United States Preventive Services Task Force (USPSTF) recommends colorectal cancer (CRC) screening in all adults aged 45-49 [Grade B] and 50-75 [Grade A].[1] Screening can be discontinued for patients aged 76-85 based on health status, prior screening results, or individual preference [Grade C].[1]

Notable risk factors include personal/family history of

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Table 1. Age-Appropriate Cancer Screening Recommendations

Type of Cancer	Gender	Age	USPSTF Grade	Recommendation
Bladder	Female/Male	All ages	I	Insufficient evidence to recommend screening
Breast	Female	40-49	C	Screening per patient status/preference
Breast	Female	50-74	B	Screening mammography every 2 years
Breast	Female	75+	I	Insufficient evidence to recommend screening
Cervical	Female	21-65	A	Cervical cytology testing alone is recommend for women ages 21-29. High-risk human papilomavirus testing in combination with cervical cytology (co-test) is recommended for women ages 30-65
Colorectal	Female/Male	45-49	B	Screening recommended (annual HSgFOBt or FIT, DNA-FIT every 1-3 years, CT colonography every 5 years, flexible sigmoidoscopy every 5 years, flexible sigmoidoscopy every 10 years plus annual FIT test, or colonoscopy every 10 years)
Colorectal	Female/Male	50-75	A	Screening recommended (annual HSgFOBt or FIT, DNA-FIT every 1-3 years, CT colonography every 5 years, flexible sigmoidoscopy every 5 years, flexible sigmoidoscopy every 10 years plus annual FIT test, or colonoscopy every 10 years)
Colorectal	Female/Male	76-85	C	Screening per patient health status/preference
Gastric	Female/Male	All ages	N/A	USPSTF does not discuss
Hematologic	Female/Male	All ages	N/A	USPSTF does not discuss
Lung	Female/Male	50-80	B	Annual screening with LDCT for patients who currently smoke with history of smoking 20 packs of cigarettes/year or quit in past 15 years. Continue screening until patient has not smoked for 15 years or develops health complication that limits potential lung cancer intervention or life expectancy.
Oral	Female/Male	All ages	I	Insufficient evidence to recommend screening
Ovarian	Female	All ages	D	Recommend against screening in healthy individuals
Pancreatic	Female/Male	All ages	D	Recommend against screening in healthy individuals
Prostate	Male	55-69	C	Screening per patient status/preference
Prostate	Male	70 and older	D	Recommend against screening in healthy individuals
Skin	Female/Male	All ages	I	Insufficient evidence to recommend screening
Testicular	Female/Male	All ages	D	Recommend against screening in healthy individuals
Thyroid	Female/Male	All ages	D	Recommend against screening in healthy individuals

Abbreviations: USPSTF, United States Preventive Services Task Force; CT, computed tomography; FIT, fecal immunochemical test.

CRC adenomatous polyps, inflammatory bowel disease, increased red meat intake, decreased fiber intake, inherited syndromes (such as Lynch syndrome), male sex, obesity, diabetes, smoking, or excess alcohol use.[1] Additionally, Black adults across all age groups have a higher incidence and mortality from CRC than White adults.[1]

Table 2. United States Preventive Services Task Force Grade Definitions[1]

Grade	Definition	Suggestions for Practice
A	High certainty that the net benefit of screening is substantial	Offer this service
B	High to moderate certainty that the net benefit of screening is substantial	Offer this service
C	Moderate certainty that the net benefit of screening is small	Offer this service for select patients depending on professional judgement and patient preference
D	Moderate to high certainty that this service has no net benefit, or that the harms outweigh the benefit	Screening is discouraged
I	Evidence is insufficient to assess the balance of benefits and harms of this service	If the service is offered, patients should understand the uncertainty about the balance of harms and benefits

There are several described cutaneous associations with underlying CRC. Leser-Trélat, dermatomyositis, acanthosis nigricans, tripe palms, Cronkhite-Canada syndrome, extramammary Paget's disease, and tripe palms are well-described associations and should prompt immediate colonoscopy.[2] Patients with Muir-Torre syndrome should begin CRC screening with colonoscopy every 1 to 2 years starting at age 25 (or 5 years prior to the youngest age of CRC diagnosis in the family) and annually at age 40.[3] A diagnosis of Peutz-Jeghers syndrome should prompt an esophagogastroduodenoscopy (EGD) and colonoscopy beginning at age 8, followed by a 1- to 3-year screening interval with colonoscopy if polyps are detected on baseline endoscopy.[4] Screening for CRC in patients with Gardner syndrome begins annually at ages 10-12, and proctocolectomy is indicated upon detection of 30 to 50 polyps in a single colonoscopy.[2]

Screening options include high-sensitivity guaiac fecal occult blood test (HSgFOBt) or fecal immunochemical test (FIT) every year, stool DNA-FIT test every 1 to 3 years, computed tomography (CT) colonography every 5 years, flexible sigmoidoscopy every 5 years or every 10 years plus an annual FIT test, colonoscopy every 10 years, or colonoscopy every 5 years with a family history of CRC or previous removal of adenomatous polyps.[1]

When stool-based tests, flexible sigmoidoscopy, or CT colonography reveal abnormal results, follow-up colonoscopy is needed for validation.[1]

Cervical Cancer Screening

Cervical cancer screening is recommended every 3 years for women ages 21-29 via cervical cytology alone, regardless of sexual history or human papillomavirus (HPV) vaccination status [Grade A].[5] The USPSTF recommends cervical cancer screening every 5 years for women ages 30-65 with high-risk HPV testing in combination with cervical cytology (co-test) [Grade A].[5] Cervical cancer screening may be discontinued for women who had a hysterectomy with removal of the cervix or are over 65 years of age with negative results of screening on 3 consecutive tests or 2 negative co-testing results in the past 10 years.[6,7]

High-risk groups for cervical cancer include women with persistent HPV infections, a compromised immune system (HIV infection, organ transplant, and long-term steroid use), lack of health care access or health insurance coverage, cigarette smoking, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer.[5,7] New onset nodular skin lesions on the abdomen or vulva in patients with a history of cervical cancer should prompt referral to a dermatologist for biopsy to rule out metastasis.[7] Additionally, non-Hispanic Black women across all age groups have a higher incidence and mortality rate of cervical cancer than non-Hispanic White women.[8]

Breast Cancer Screening

The USPSTF recommends breast cancer screening with mammography every 2 years in women ages 50-74 [Grade B] and based on patient preference in women ages 40-49 [Grade C]; there is insufficient evidence to provide a recommendation for screening in women age 75 years and older [Grade I].[9] In contrast, the American Cancer Society (ACS) recommends screening with mammography annually in women ages 45-54, biennially in women ages 55 and older, and based on patient preference in women ages 40-44.[10] All major societies recommend screening with mammography every 1 or 2 years in women ages 50-74.[11] Notable risk factors include family history, early age radiation therapy to the chest, dense breast tissue, BRCA1 and BRCA2 gene mutations, inherited syndromes and existing but benign breast proliferative lesions with atypia. Men with BRCA1/2 mutations who have gynecomastia also should be screened.[12]

Dermatologic manifestations with links to breast cancer include mammary Paget's disease, Cowden syndrome, carcinoma en cuirasse, carcinoma erysipeloides, alopecia neoplastica, Sweet's syndrome, hypertrichosis lanuginosa acquisita, multicentric reticulohistiocytosis, dermatomyositis, acquired ichthyosis, erythema gyratum repens, and intralymphatic histiocytosis.[13,14]

Digital mammography is the gold standard for breast cancer screening. Adjuvant screening via ultrasonography, magnetic resonance imaging (MRI), and/or digital breast tomosynthesis may be considered in women identified to have dense breasts on an otherwise negative screening mammogram.[9]

Lung Cancer Screening

The USPSTF recommends screening patients ages 50-80 who have a history of smoking 20 packs/year and have quit smoking within the last 15 years or who currently smoke [Grade B].[15] The ACS recommends screening patients ages 55-74 who have a history of smoking 30 packs/year and have quit smoking within the last 15 years or who currently smoke.[16] Low-dose computed tomography (LDCT) without contrast is recommended for lung cancer screening.[15]

The greatest risk factors for lung cancer are older age and smoking history.[15] Other high-risk populations include Black males relative to White males and White females relative to Black females.[17] Dermatologic manifestations of lung cancer that should prompt screening include dermatomyositis, erythema gyratum repens, hypertrichosis lanuginosa, superficial thrombophlebitis (Trousseau syndrome), tripe palms, and Leser-Trélat.[18]

SKIN CANCER SCREENING

Screening for skin cancer via total body skin exam is among the safest and most cost-effective medical tests available, but data to inform consistent guidelines are lacking.[19] The paucity of studies demonstrating mortality benefit and potential for sequelae of overdiagnosis led the USPSTF to conclude that evidence is insufficient [Grade I] to recommend for or against screening.[19] Alternatively, the ACS recommends periodic visual examination of the skin for general cancer prevention but does not specify frequency or age range.[19] Concerns over these guidelines include omission of disease morbidity and high-risk populations,[19] earlier detection of thinner melanomas with screening,[20] and overdiagnosis by primary care providers rather than experienced dermatologists.[21]

Some dermatologists suggest screening be considered for adults ages 35-75 who have at least 1 skin cancer risk factor.[19] Patients at highest risk are those with CDKN2A mutations, a personal history of skin cancer, greater than 100 common nevi, greater than 4 atypical nevi, indoor tanning use or excessive ultraviolet light exposure, fair skin, history of sunburns, geographic proximity to the equator, living at higher elevations, and weakened immune systems.[19] Organ transplant and immunocompromised patients also have a particularly increased burden with overall incidence and risk of invasive nonmelanoma skin cancer.[22] Though rare, it has been well documented that melanoma has associated paraneoplastic syndromes, including generalized melanosis[23] and dermatomyositis.[24] Additionally, adult-onset vitiligo has been reported both prior to and after the diagnosis of melanoma.[25]

Prostate Cancer Screening

The USPSTF states that prostate-specific antigen (PSA)-based screening is optional for males aged 55-69 years old [Grade C] and recommends against PSA-based screening in men 70 years and older [Grade D].[26] The association of prostatic malignancies with extramammary Paget's disease[27] and dermatomyositis[28] justifies screening beyond USPSTF recommendations. Since there is currently no consensus on prostate cancer screening guidelines for patients with extramammary Paget's disease and dermatomyositis, shared decision-making should incorporate known prostate cancer risk factors as well as risks and benefits of prostate cancer screening.[26]

Prostate cancer risk factors include older age, African American race, family history, BRCA1 and BRCA2 gene mutations, and Lynch syndrome.[26,29] PSA-based screening has a false-positive rate of approximately 1 in 6.[26] Transrectal ultrasound, MRI, and magnetic resonance spectroscopic imaging are less common screening modalities.[26] Other paraneoplastic dermatoses associated with prostate cancer include migratory thrombophlebitis, pityriasis rotunda, erythema gyratum repens, and acquired ichthyosis.[30]

Ovarian Cancer Screening

The USPSTF recommends against ovarian cancer screening in asymptomatic women [Grade D].[31] Screening is recommended for women with the following risk factors: personal or family history of breast cancer, BRCA gene mutation, pelvic inflammatory disease, endometriosis, ovarian cysts, Lynch syndrome, and smoking a pack of cigarettes daily for the past 20 years.[32] Though dermatological manifestations of ovarian cancer are uncommon, manifestations include dermatomyositis, acanthosis nigricans, secondary Raynaud's phenomenon, and palmar fasciitis with polyarthritis.[33] A complete pelvic exam, CA125 blood test, and transvaginal ultrasound are the recommended screening modalities for ovarian cancer.[34]

Hematologic Cancer Screening

Data is lacking for the USPSTF to offer screening recommendations for these cancers, but screening should be individually tailored to paraneoplastic dermatoses with well-established associations.[30] The strongest associations include paraneoplastic pemphigus with B-cell lymphoproliferative disorders; Sweet's syndrome and pyoderma gangrenosum with acute myelogenous leukemia; necrobiotic xanthogranuloma, POEMS syndrome, follicular hyperkeratotic spicules with plasma cell dyscrasias;[35,36] and acquired ichthyosis with Hodgkin's lymphoma.[30]

Pancreatic Cancer Screening

The USPSTF recommends against screening for pancreatic cancer in asymptomatic adults [Grade D] due to low incidence of disease and lack of available screening tests proven to reduce mortality or morbidity of disease.[37] For symptomatic individuals, CT with intravenous contrast is the preferred initial imaging modality,[38] along with blood tests and biopsy for definitive diagnosis.[39] For patients with suspected necrolytic migratory erythema, a serum glucagon level should be checked for glucagonoma diagnosis.[40] Additional cutaneous signs that have been reported with pancreatic cancer include migratory thrombophlebitis, hypertrichosis lanuginosa acquisita, palmar fasciitis and polyarthritis syndrome, dermatomyositis, pityriasis rotunda, palmoplantar keratoderma, and papular mucinosis.[41]

Thyroid Cancer Screening

The USPSTF recommends against screening for thyroid cancer in healthy asymptomatic adults [Grade D]. The task force found inadequate evidence to support the accuracy of neck palpation or ultrasound as a screening test. High-risk individuals (family history, inherited syndromes, history of radiation exposure to the head and neck) were not included in the review. For symptomatic individuals, ultrasound and fine-needle aspiration biopsy can detect thyroid cancer.[42]

Dermatologic manifestations of thyroid cancer are rare and usually occur from metastatic disease. New onset flesh-colored skin nodules, particularly in the scalp area, should raise clinical suspicion for metastatic thyroid carcinoma. While cutaneous metastasis predominantly occurs in patients with a known history of thyroid cancer, there are reports of such lesions leading to detection of occult thyroid cancer.[43]

Testicular Cancer Screening

Due to rare occurrence and favorable treatment outcomes of testicular cancer, the USPSTF recommends against routine testicular cancer screening in healthy adolescent or adult males [Grade D].[44] Clinical physical examination of the testicles may be indicated with the following risk factors: cryptorchidism, personal/family history of testicular cancer, HIV infection, Peutz-Jeghers syndrome, or carcinoma in situ of the testicles.[45] An ultrasound is recommended if clinical examination suggests testicular cancer.[44] There do not appear to be strong associations of paraneoplastic dermatoses with testicular cancer.[45]

Bladder Cancer Screening

The USPSTF does not recommend routine bladder cancer screening in healthy adolescents or adults [Grade I].[46] Screening may be indicated with the following risk factors: smoking, occupational carcinogen exposure, male sex, older age, White race, bladder parasitic infections, or personal/family history of bladder cancer.[46] Additionally, patients with extramammary Paget's disease or Muir-Torre syndrome should be screened for bladder cancer.[47] Urinalysis/cytology are the recommended screening tools as they are most efficient, noninvasive, and inexpensive.[47]

Oral and Gastric Cancer Screening

The USPSTF has determined that evidence is insufficient [Grade I] to provide guidelines for oral cancer screening,[48] though inspec-

tion and palpation of the oral cavity is reasonable for patients presenting with Bazex (acrokeratosis paraneoplastica) or Sweet's syndromes.[49] Similarly, there are no consensus statements for gastric cancer screening, but rare, yet strong associations exist with acanthosis nigricans—including tripe palms and Leser–Trélat.[30] Endoscopic workup for patients presenting acutely with these dermatoses may be warranted.[30]

CONCLUSIONS

Performing skin examinations is a crucial component of routine cancer screening because numerous skin conditions are associated with internal malignancies. Delays in accessing recommended malignancy screenings for paraneoplastic dermatoses can lead to more advanced and potentially metastatic/fatal disease. Pruritus without dermatitis ("itch without rash"), often described as a "paraneoplastic itch," is associated with several types of underlying solid and hematologic malignancies.[50] Patients with a suspected paraneoplastic dermatosis should obtain all age-appropriate cancer screenings and be referred to dermatology for any history, physical, or review of system concerns.

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Trends in Adult Suicide Rates in Milwaukee County, Wisconsin, 2002 through 2020

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ABSTRACT

Background: Monitoring suicide rates is an important public health strategy to inform prevention efforts. We describe rates of adult suicide in Milwaukee County, Wisconsin, over a 19-year period.

Methods: Data on all adult suicides from 2002 through 2020 (n = 981) were obtained from the Milwaukee County Medical Examiner's Office. Subpopulation rates were identified using the Wisconsin Interactive Statistics on Health System.

Results: Suicide rates increased significantly over the study period, with disproportionate increases among Black and Latinx residents.

Discussion: Expanded prevention efforts are needed to reverse this concerning trend. Further research should guide development of culturally relevant interventions, provide data for the equitable allocation of limited resources.

BACKGROUND

Surveillance of county-level suicide rates is key to understanding the evolving nature of this public health problem within local communities. A recent statewide report cites a 40% increase in all Wisconsin suicides from 2000 to 2017, with significant variability across rural and urban counties.[1] We sought to build upon these state-level findings by describing adult suicide rates over time in Milwaukee County, the largest and most diverse urban county in the state.[2]

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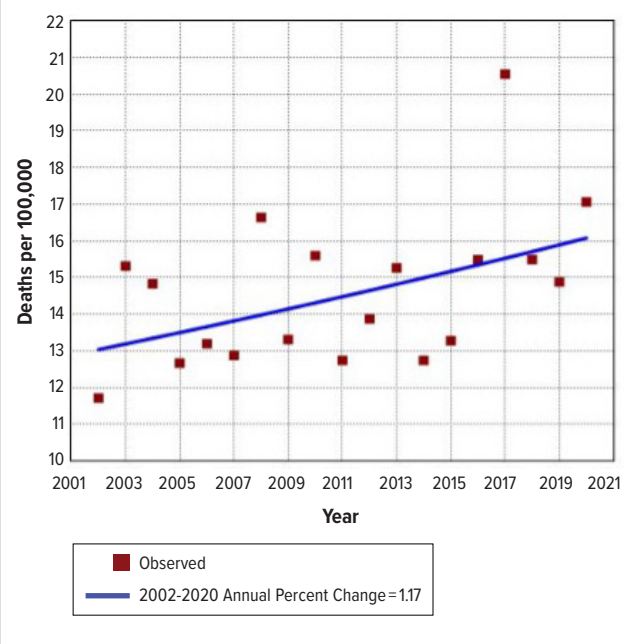
METHODS

Study Design

Data were obtained from the Milwaukee County Medical Examiner's Office (MCMEO) on all deaths determined to be suicides by the MCMEO from 2002 through 2020. Variables included name, date of birth, date of death, race, sex, cause of death, and location of injury. Text variables (eg, mechanism of injury, sex) were recoded into numerical, categorical variables to allow for statistical analysis (eg, sex was coded as 0 = male, 1 = female). Race categories included Hispanic ethnicity and were recoded according to the categories used by the MCMEO (White, Black, Asian/Pacific Islander, American Indian/Alaska Native, Hispanic, Eastern Indian, and multiracial). A variable for racial/ethnic minority status also was created (0 = nonminority/White, 1 = minority). Cause of death was recoded into 9 categories based on the most prevalent causes (firearm; asphyxia, suffocation, hanging; poisoning; fall from heights; motor vehicle crash; drowning; burns; cut with sharp object; and "other," which included all causes not represented in other categories). Finally, population-level data from the Wisconsin Interactive Statistics on Health (WISH) query system's Population Module were used to calculate county-level annual suicide rates per 100 000 as there were significant increases in the Milwaukee County population from 2002 through 2020 ($r^2 = .91$, $P < .001$).[3]

Frequency tabulations were conducted to summarize demographic information and rates of suicide by year. Logistic regression was utilized to calculate odds ratios based on sex and race to examine associations with relevant factors, such as cause of death. Probability values of $P < .05$ were considered statistically significant. Finally, joinpoint regression models were estimated to

Figure. Number of Suicides per Year and Results of Joinpoint Regression Analyses



Annual percent change = 1.17 is significantly different from zero at the alpha = 0.05 level.

Table 1. Demographic Characteristics and Descriptive Statistics, N = 1,981

	n	% Total
Race		
White	1541	77.8
Black	265	13.4
Asian/Pacific Islander	37	1.9
American Indian/Alaska Native	12	0.6
Hispanic	105	5.3
Eastern Indian	11	0.6
Multiracial	9	0.5
Not recorded	1	0.05
Immediate cause of death		
Firearm	811	40.9
Asphyxia/hanging/suffocation	632	31.9
Poisoning	305	15.4
Fall from heights	102	5.1
Motor vehicle crash	31	1.6
Drowning	30	1.5
Burns	11	0.6
Cut from sharp object	55	2.8
Other	0	0
Not recorded	4	0.2
Year of death		
2002	82	4.1
2003	107	5.4
2004	104	5.2
2005	89	4.5
2006	92	4.6
2007	91	4.6
2008	117	5.9
2009	94	4.7
2010	111	5.6
2011	91	4.6
2012	100	5.0
2013	110	5.6
2014	92	4.6
2015	96	4.8
2016	124	5.7
2017	149	7.5
2018	112	5.7
2019	108	5.5
2020	124	6.3

identify changes in the number of suicides in Milwaukee County from 2002 through 2020 using the Joinpoint Regression Software, Version 4.9.0.0 (Surveillance Research Program, National Cancer Institute). This analytic method uses counts or rates of occurrence for a given phenomenon of interest to isolate subsets of the data with distinct linear trends. (For a detailed description of this analytic approach, see Kim et al and the methodological guidelines cited here).[4,5]

RESULTS

A total of 1981 deaths from 2002 through 2020 were determined to be suicides by the MCMEO. The average age at the time of death was 45 years (SD = 16.8). As displayed in the Figure, the greatest number of suicides occurred in 2017 (n = 149, rate = 20.54) and the fewest occurred in 2002 (n = 82, rate = 11.73). Descriptive statistics are displayed in Tables 1 and 2. Suicide decedents were most commonly White, non-Hispanic (77.8%; n = 1541), and 76.7% (n = 1520) of decedents were male. However, results indicate an increase in the proportion of suicides among Hispanic decedents (almost half of whom were women) over time (from 4.9% of all suicides in 2002 to 8.9% of all suicides in 2020), and an increase in the proportion of suicides among Black decedents was noted in later years (from 6.3% in 2015 to 15.3% in 2020). This trend in suicides by race mirrors overall population trends for the county between 2002 and 2020. The proportion of White residents decreased from 70% in 2002 to 65% in 2020, while the proportion of Black residents rose from 26% in 2002 to 29% in 2020. Proportions of Asian and American Indian residents remained stable over time. Similarly, the proportion of non-Hispanic residents decreased from 90% in 2002 to 84% in 2020, while the proportion of Hispanic residents increased from 10% to 16% over the same time period.[6]

The three most common suicide methods were self-inflicted gunshot wound (40.9%; n = 811); asphyxiation, suffocation, or hanging (31.9%; n = 632); and poisoning (15.4%, n = 305). Logistic regression (Table 3) revealed that Black decedents were significantly less likely than White decedents to have died from self-inflicted gunshot wounds versus other methods. White, Latinx, and female decedents were significantly more likely use a firearm as a method of suicide.

Table 2. Wisconsin Suicide Rates by Year

	White		Black		Hispanic	
	Milwaukee County	Other Counties	Milwaukee County	Other Counties	Milwaukee County	Other Counties
2002	11.6	12.1	5.7	6.5	4.3	3.8
2003	12.4	11.9	8.4	*	5.3	3.5
2004	13.3	12.1	8.0	6.9	5.1	5.9
2005	11.7	11.8	5.2	4.7	5.8	4.9
2006	11.8	12.2	7.9	7.2	3.7	4.6
2007	12.2	13.6	6.1	5.2	4.4	4.9
2008	15.8	13.4	5.4	4.1	6.0	5.1
2009	12.2	13.5	8.4	9.6	3.3	5.9
2010	15.1	14.3	5.2	11.0	4.0	3.8
2011	14.0	13.8	1.9	9.1	3.9	6.4
2012	13.5	13.7	5.2	*	4.6	3.1
2013	14.5	16.1	4.1	6.5	5.2	2.6
2014	12.4	14.5	4.5	4.2	6.6	8.9
2015	13.2	16.9	3.3	*	4.3	5.8
2016	14.2	15.8	6.7	6.1	5.7	7.3
2017	21.0	16.2	7.4	6.6	10.4	5.9
2018	15.6	16.1	6..3	9.0	3.4	7.4
2019	13.6	15.3	6.3	6.9	8.8	7.5
2020	16.6	15.4	8.1	9.1	9.2	8.0

Suicide rates by year are displayed for White residents, Black residents, and Hispanic residents only, as numbers by year were <5 for other race groups and are suppressed to protect confidentiality.
Values of * indicate that rates are not available due to numbers <5.

Table 3. Association Between Demographic Characteristics and Use of Firearm as Suicide Method

	Odds Ratio	SE	*P* value	95% CI
Race (White is referent)				
Black	0.67	0.09	0.002[a]	0.51-0.86
Asian/Pacific Islander	1.27	0.44	0.50	0.64-2.51
American Indian/Alaska Native	3.44	2.67	0.10	0.75-15.75
Hispanic	2.45	0.59	<0.001[a]	1.53-3.94
Eastern Indian	3.10	2.42	0.10	0.67-14.37
Multiracial	0.34	0.24	0.10	0.09-1.38
Sex (Male is referent)				
Female	3.71	0.47	<0.000*	2.89-4.77

[a]*P*< 0.05.

In order to identify trends over time, we utilized joinpoint regression. Models were estimated using 0, 1, 2, or 3 joinpoints. The final model selected had 0 joinpoints, suggesting that the best fitting model did not contain any breaks in the trend of suicides between 2002 and 2020 (Figure). Using a Monte Carlo Permutation method, the annual percentage change/average annual percentage change was significantly different than zero, with a 1.17% increase in suicide rates throughout the timeframe. Based on the methodology for characterizing trends set forth by the Cancer Trends Progress Report, an annual percentage change greater than 0.5 is considered rising as opposed to stable.[7] Thus, the trend in Milwaukee County suicides has increased steadily and significantly since 2002, without any shifts in direction or magnitude.

DISCUSSION

The purpose of this study was to evaluates trends in suicide rates over time from 2002 to 2020 in Milwaukee County, Wisconsin. We found that the annual rate of adult suicides increased significantly during this timeframe. This increase was disproportionately greater among Black and Latinx decedents than White decedents. This raises concern over the factors driving this finding, which is an important area for future research. Although suicidology research has identified the importance of culturally relevant suicide prevention initiatives for specific subpopulations (eg, veterans; lesbian, gay, bisexual, transgender, queer or questioning, and more individuals; farmers; and racial/ethnic minorities), development of such approaches has been limited.[8]

Our results call attention to the need for suicide prevention initiatives tailored for people living in more densely populated communities. Population-level data (WISH Data Query System) indicate that in Wisconsin, Black American and Latinx individuals are more likely to reside in urban rather than rural counties. Therefore, prioritizing the development of culturally responsive suicide prevention approaches for Black American and Latinx individuals is an important step toward eliminating health disparities in urban settings. This is a health equity issue that demands our attention.

Milwaukee County and the city of Milwaukee contained within are highly segregated across race and ethnicity.[9] Systemic and structural racism – drivers of segregation – heighten the risk for suicide among people of color.[10] Our identification of growing rates of suicides among Black and Latinx individuals in Milwaukee County underscores the multifaceted health effects of racism on historically marginalized communities.

Limitations

While the data source is a strength of this study, it also came with limitations. There were several demographic variables that we would have liked to include to better characterize the sample (eg, socioeconomic status). However, these were unavailable because they are not a standard part of the medical examiner's death investigation reports. Future research should seek to include this infor-

mation where possible to provide more information about the generalizability of the findings. Additionally, there is not a standardized process used to determine manner of death as a suicide. For example, it is possible that some drug overdoses that were made with suicidal intent were not labeled suicides due to insufficient evidence available to the medical examiner. This is a known issue in forensic science in light of research showing, for example, that cognitive bias may influence individual decisions around manner of death.[11] Although beyond the scope of the present study, future research on factors influencing manner of death classification is needed to elucidate these effects and identify solutions.

Implications

Our finding that suicide rates have risen significantly in Milwaukee County over the last 19 years, especially among Black and Latinx residents, has important implications for policy, clinical practice, and research endeavors. Data-informed policy is key to the equitable allocation of resources across the state. Evidence of the expanding scope and disparities of this public health issue reflect the urgent need to develop culturally relevant suicide prevention initiatives in urban settings, particularly for marginalized communities. Additionally, clinicians should be aware that suicide rates are trending upward in Milwaukee County and that this increasing risk disproportionately affects their Black and Latinx patients.

Future research and suicide prevention programming should leverage community-based partnerships to examine unique factors that contribute to suicide risk among racial/ethnic minorities. Cultural context is an important consideration in suicide prevention efforts; however, many suicide prevention strategies are framed by White, non-Hispanic paradigms. A qualitative research approach could elucidate how experiences of racism and discrimination in the community contribute to suicide risk. Future studies should evaluate suicide rates relative to proportion of each race in the population. In addition, it is imperative to continue quantitative surveillance of suicide trends in both urban and rural counties to improve community health across Wisconsin.

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Medical Student Well-being Outcomes After a Novel Shared Meal and Resiliency Skills Course

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ABSTRACT

Introduction: Medical student well-being is a major problem. The authors aimed to assess well-being outcomes 6-months after a novel extracurricular shared meal and resiliency course.

Methods: We implemented the course during 3 academic years (2018-2020). Participants received surveys assessing resilience, perspective-taking, self-compassion, and empathy at 4 timepoints. We used linear mixed effects models to assess changes from baseline to post-course assessments for the 3-year aggregate and pre-COVID and early-COVID time periods.

Results: One week and 6 months post-course, resilience, perspective-taking, and self-compassion scores improved ($P < 0.01$). Notably, resilience changed significantly only during early-COVID ($P < 0.01$), not pre-COVID ($P = 0.16$). For scores with evidence-based interpretation cut-offs, no clinical changes occurred.

Discussion: Several well-being measures statistically improved post-course but did not change clinically. Qualitative studies may better capture meaningful well-being outcome impact.

INTRODUCTION

Emotional distress among medical students presents serious challenges. Meanwhile, resiliency skills, including perspective-taking, empathy, and self-compassion, bolster medical student well-being.[1,2] While required resiliency training has not shown improved well-being outcomes,[3] elective resiliency skills courses have offered promise.[1,2]

The Oregon Health Sciences University (OHSU) Resiliency Skills Curriculum is an innovative course that previously demonstrated encouraging immediate post-course improvements in mindfulness, perceived stress, and positive affect.[4] In the course, students and facilitators share a warm, healthy meal, then practice resiliency skills.[4] At our institution, we recognized a gap in providing resiliency training. We aimed to pilot the OHSU course over 3 years (2018-2020), assessing select well-being skill outcome measures 6 months post-course.[5-7] When the coronavirus-19 (COVID) pandemic interrupted the 3rd course-year, we also aimed to compare outcomes pre-COVID (2018, 2019) versus early-COVID (2020).

METHODS

The University of Wisconsin Social Science/Education Institutional Review Board certified this study as program evaluation.

Setting, Format, Approach

The 8-session extracurricular course was delivered each year during February to May. Sessions occurred in a medical school classroom or wellness lounge. The final 4 sessions in 2020 were conducted virtually. The group shared a meal, practiced resiliency skills, then debriefed. Facilitators used reflective listening, nonjudgment, and compassion. During exam weeks, the course director emailed participants, offering encouragement and resiliency skill reminders.

Enrollment, Recruitment

Yearly enrollment was limited to 15 students. An enrollment

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lunch talk occurred 4 weeks pre-course for students to learn about the course and attendance expectations (6 of 8 sessions). Although the course schedule was tailored to first-year schedules, all medical students were eligible to participate in the course and study.

Surveys, Measurements

Students received online surveys at 4 timepoints: T1 (1-4 weeks pre-course); T2 (1 week post-course, 1 week before final exams); T3 (6 weeks post-course); T4 (6 months post-course). We assessed 4 outcome measures: Brief Resilience Scale,[5] Interpersonal Reactivity Index Perspective-Taking and Empathic Concern scales (IRI-PT, IRI-EC),[6] and Neff Self-Compassion Scale.[7] These variables, which are commonly employed as proxy indicators and potential influencers of positive adaptation to stress,[1,8-11] were chosen because they represented related but distinct course-targeted skillsets. Students received small survey-completion gift card incentives.

Statistical Analysis

We analyzed changes at each timepoint (T1, T2, T3, T4) for the 3-year aggregate using a linear mixed effects model with subject-specific random effects and autoregressive correlation structure, using age, race, and study period (pre-COVID, early COVID) as covariates. Students who enrolled and completed T1 but did not ultimately attend the course were considered lost to follow-up and did not receive T2-T4 survey requests. All responses were analyzed.

We also analyzed percentage changes at each timepoint for the 3-year aggregate and within study periods using a linear mixed effects model with subject-specific random effects to account for repeated assessments. We used an autoregressive correlation structure of order one to account for correlations between repeated assessments, using age and race as covariates.

We examined normal probability and residual plots to verify model assumptions. We reported adjusted changes with corresponding 2-sided 95% confidence intervals and 2-sided *P* values. Statistical significance was defined as P<0.05. For all statistical analyses, SAS software (SAS Institute, Cary NC, version 9.4) was used.

RESULTS

Demographic Characteristics

Over 3 course-years, 40 students enrolled; 32 ultimately participated in the course. Participating students attended 6.82 (SD 1.31) sessions. All 40 enrollees completed T1; all 32 course participants completed all T1-T4 surveys.

Thirteen (40.6%) course participants indicated Asian or Asian American, Hispanic or Latino, and multiracial identities. Compared to our medical school student body representation (19.8%), these students were overrepresented. Cisgender women and gender-diverse students were also overrepresented (n = 26, 81.3%; n = 1, 2.5%; respectively) compared to student body representation (48.7%, <1%, respectively). See Table 1.

Table 1. Student Demographic Characteristics

Demographic Characteristics	Total Course Registrants, n=40 n (%)	Total Course Participants, n=32 n (%)
Age		
20-24 years	31 (77.5)	26 (81.2)
25-29 years	9 (22.5)	6 (18.8)
Training year		
First year	37 (92.5)	30 (93.7)
Fourth year	1 (2.5)	0 (0.0)
Other[a]	2 (5)	2 (6.3)
Residency status		
In-state	28 (70)	24 (75)
Out-of-state	12 (30)	8 (25)
Primary language[b]		
English	37 (92.5)	30 (93.8)
Vietnamese	1 (2.5)	1 (3.1)
Korean	1 (2.5)	1 (3.1)
Bengali	1 (2.5)	0 (0.0)
Race/ethnicity[c]		
Asian	11 (27.5)	8 (25)
Hispanic or Latino	4 (10)	2 (6.3)
White or Caucasian	21 (52.5)	19 (59.4)
Multiracial	4 (10)	3 (9.3)
Gender identity[d]		
Cisgender woman	33 (82.5)	26 (81.3)
Cisgender man	6 (15)	5 (15.6)
Nonbinary	1 (2.5)	1 (3.1)
Sexual orientation[e]		
Heterosexual	37 (92.5)	29 (90.6)
Bisexual	1 (2.5)	1 (3.1)
Queer	2 (5)	2 (6.3)

[a]Possibilities for "other" included gap year, MD-PhD student.
[b]No student identified Spanish, Chinese, Japanese, French, German, Portuguese, Russian, Arabic, Hindi as primary languages.
[c]No students selected Black or African American, Native Hawaiian, other Pacific Islander, American Indian, Alaska Native, or "self-describe" options.
[d]No student selected transgender or "self-describe" options.
[e]No student selected Gay, Lesbian, Questioning, "self-describe," or "choose not to disclose."

3-Year Aggregate

From the T1 to T2 assessments, resilience (0.4; CI, 0.2-0.5; $P < 0.01$), perspective-taking (0.3; CI, 0.2-0.4; $P < 0.01$), and self-compassion (0.5; CI, 0.4-0.6; $P < 0.01$) significantly improved; empathy did not change significantly ($P = 0.21$). From the T2 to T3 assessments, perspective-taking significantly worsened (-0.1; CI, -0.2 to 0.0, $P = 0.03$); no other outcomes changed statistically. From the T3 to T4 assessments, no outcomes changed significantly. Adjusted mean scores at all timepoints indicated moderate resilience and moderate self-compassion, based on published cut-off scores.[7,8] To our knowledge, no established perspective-taking or empathic concern (IRI-PT/EC) cutoffs exist.

Table 2. Evaluation of Overall Percentage Changes in Wellness Measures From Pre-course Baseline (T1) to 6 Months Post-Course Completion (T4)

Wellness Outcome	Period	Adjusted Means[a] (95% CI)	*P* Value	Percentage Change Interpretation	Adjusted Means for Change, Pre-COVID to Early COVID (95% CI)	*P* Value
Brief Resiliency Scale (BRS)[5]	Combined	8.8% (1.9-15.6%)	**0.014**[a]	**Improved**		
Scale range 1-5, higher score suggests	Pre-COVID	5.1% (-2.1 to 12.2%)	0.16	No change	**13.5% (1.9 to 25.0%)**	**0.024**[a]
greater resilience	Early-COVID	18.5% (8.0-29.1%)	**0.0012**[a]	**Improved**		
Interpersonal Reactivity Index-	Combined	5.5% (1.6-9.4%)	**0.0079**[a]	**Improved**		
Perspective Taking (IRI-PT)[6]	Pre-COVID	6.6% (2.2-11.0%)	**0.0046**[a]	**Improved**	-4.0% (-11.1 to 3.1%)	0.26
Scale range 1-5, higher score suggests	Early-COVID	2.6% (-3.9-9.1%)	0.42	No change		
better perspective-taking						
Interpersonal Reactivity Index-	Combined	2.2% (-1.7-6.0%)	0.26	No change		
Empathic Concern (IRI-EC)[6]	Pre-COVID	3.1% (-1.3-7.4%)	0.16	No change	-3.2% (-10.2 to 3.8%)	0.35
Scale range 1-5, higher score suggests	Early-COVID	-0.2% (-6.6-6.2%)	0.95	No change		
greater empathy						
Neff Self Compassion (NSC)[7]	Combined	16.7% (7.1-26.3%)	**0.0013**[a]	**Improved**		
Scale range 1-5, higher score suggests	Pre-COVID	17.7% (6.8-28.6%)	**0.0025**[a]	**Improved**	-3.7% (-21.3 to 13.9%)	0.67
greater self-compassion	Early-COVID	14.0% (-2.0 to 30.1%)	0.084	No change		

[a]Adjusted by age and race (non-White race and White race).

Assessing overall percentage changes between the T1 and T4 timepoints, resilience (8.8%; CI, 1.9%-15.6%; $P<0.01$), perspective-taking (5.5%; CI, 1.6%-9.4%; $P<0.01$), and self-compassion (16.7%; CI, 7.1%-26.3%; $P<0.01$) improved significantly; empathy did not change significantly ($P=0.26$). See Table 2.

Pre-COVID

Pre-COVID changes largely mirrored the aggregate. From T1 to T2, resilience (0.4; CI, 0.2-0.5; $P<0.01$), perspective-taking (0.3; CI, 0.2-0.5; $P<0.01$), and self-compassion (0.5; CI, 0.4-0.6; $P<0.01$) improved significantly; empathy did not change significantly ($P=0.07$). From T2 to T3, perspective-taking worsened significantly (-0.1; CI -0.3 to 0.0; $P=0.04$); no other outcomes changed statistically. From T3 to T4, no outcomes changed significantly. See Figure.

Assessing overall percentage changes from T1 to T4, perspective-taking (6.6%; CI, 2.2%-11.0%; $P<0.01$) and self-compassion (17.7%; CI, 6.8%-28.6%; $P<0.01$) improved significantly. Resilience and empathy did not change significantly ($P=0.16$, $P=0.16$, respectively). See Table 2.

Early-COVID

From T1 to T2, resilience (0.4; CI, 0.1-0.7; $P=0.01$), perspective-taking (0.2; CI, 0-0.3; $P=0.04$), and self-compassion (0.4; CI, 0.1-0.7; $P=0.01$) improved significantly; empathy did not change significantly. From T2 to T3 and T3 to T4, no outcomes changed significantly. See Figure.

Assessing overall percentage changes from T1 to T4, only resilience improved significantly (18.5%; CI, 8.0%-29.1%; $P<0.01$). Perspective-taking, self-compassion, and empathy did not change significantly ($P=0.42$; 0.08, 0.95, respectively). The resilience change pre-COVID versus early-COVID was significant (18.5% vs 5.1%; CI, 1.9%-25.0%; $P=0.02$). See Table 2.

DISCUSSION

This study demonstrated that following this novel medical student shared meal and resiliency skills course, several statistically significant well-being improvements were observed up to 6 months post-course. This included perspective-taking and self-compassion (pre-COVID) and resilience (early-COVID) but not empathy. This study also found that despite statistically significant improvements in self-compassion and resilience, clinical interpretations for these outcomes (eg, low, moderate, high) did not improve.

The first critical question is whether the statistically significant well-being improvements demonstrate meaningful psychological improvement. Finding no changes in resilience and self-compassion clinical interpretations, one possibility is that statistical outcome improvements do not reflect meaningful improvement in lived experiences. If this is true, then costs required to implement extracurricular resiliency courses (eg, monetary, time, effort) may exceed their expected benefits. Medical schools should carefully weigh decisions about well-being improvement resource allocation, accounting for this possibility. Many have conjectured that without interventions modifying stressors within the educational environment, resiliency courses will likely prove insufficient to address student well-being needs.[3]

Simultaneously, we understand that using standardized well-being questionnaires to capture changes in students' lived well-being experiences may be challenging and that qualitative work exploring course impact may help better elucidate the long-term effect of participating in resiliency courses. Dunn et al propose conceptualizing student well-being as mediated by a "coping reserve tank" that is fluid, depleting and replenishing depending on the student's perceived balance of emotional challenges and relational support.[12] Meal-sharing resiliency courses that offer

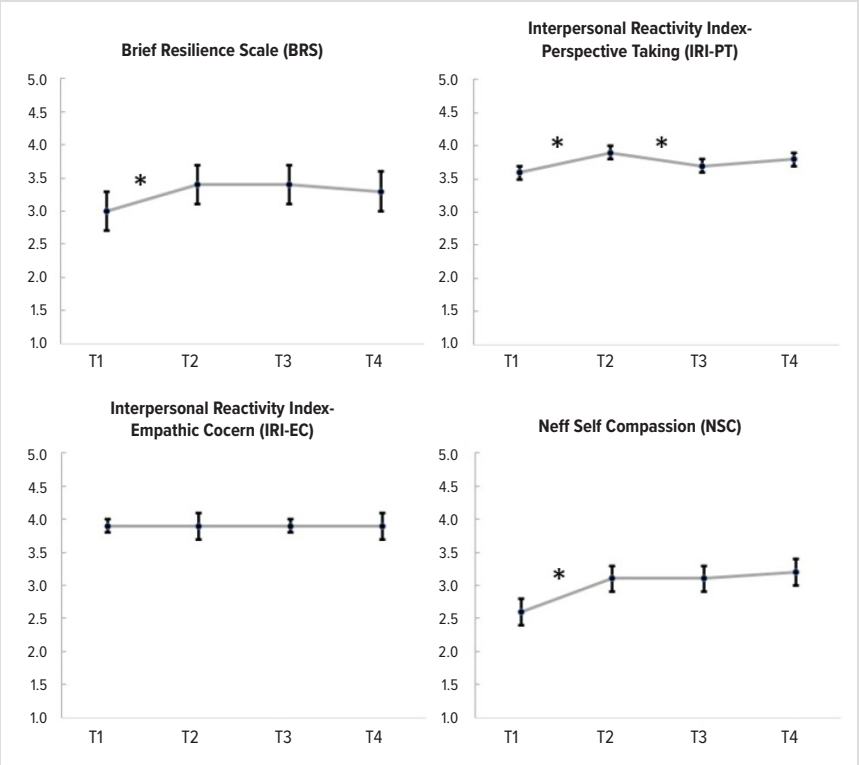
both emotional and relational support may help bolster a sense of well-being that is not easily quantified.

In this course, students adhered well to course attendance expectations despite no academic repercussions for deciding to discontinue or reduce course participation. We cautiously conjecture that the significant improvements in select well-being outcomes alongside excellent course attendance potentially signal meaningful perceived well-being benefits. Additionally, despite our small sample, we found statistically significant changes in certain measures, indicating that these findings would potentially hold in larger samples. Future studies should investigate the relationship between resiliency courses and empathy to understand why certain measures, but not empathy, statistically improved.

Our study also provides potential COVID-related insights. Our most notable COVID-related finding was that resilience improved significantly more during early-COVID than pre-COVID. Studies describing medical student resilience during the pandemic remain sparse, but literature describing community trauma responses following natural disasters is more robust.[13] Studies show that the "disaster environment provides an active and ongoing opportunity to reframe, reorganize, and construct new meaning in a compressed timeline," and communities commonly experience a sense of collective heroism.[13] Students who actively practiced resiliency skills or felt cared for in a resiliency-based community during the early-COVID period might have been particularly positioned to feel more resilient during post-course assessment, despite experiencing difficult pandemic-related emotions.[14] Meanwhile, the change to virtual sessions, which may have limited participants' abilities to portray body language, connect emotionally, or stay attentive, may have influenced other early-COVID outcomes.

Finally, we discovered that certain demographic characteristics aligned with course participation. Specifically, participants disproportionately identified as cisgender women, Asian descent, Hispanic/Latino descent, or multiracial; no participants identified as Black, African American, Native Hawaiian, Pacific Islander, American Indian, or Alaska Native. Studies have suggested that burnout is highest for cisgender women,[15] so overrepresentation of this group is not surprising. Additionally, structural inequities faced by students of color and students underrepresented in medicine (UIM) potentially may have augmented participants' needs to seek supportive connection and community via a resiliency course.[16] At the same time, some UIM students may have felt deterred from participating in the resiliency course, which was facilitated primarily by non-UIM physicians.

Figure. Model Adjusted Means and 95% Confidence Intervals for Wellness Outcomes at Each Time Point for the Combined Cohort



Indicates significant change between consecutive timepoints, $P < 0.05$

Limitations and Future Directions

The most important limitation is selection bias. Participants self-selected into the course, so this study offers insights about students seeking well-being support at a single institution. Additionally, the small pilot study sample limited our ability to develop and validate a comprehensive model capturing both the relational dependencies among outcomes and longitudinal changes within outcomes. Some studies have indicated that self-compassion may represent a key predictor of various well-being outcomes, including burnout and resilience; however, this must be explored further.[9,11] Additional large-scale studies would be valuable for exploring whether results vary by year in medical training and for examining medical student resilience during natural disasters (eg, pandemics/epidemics, hurricanes) to clarify COVID-related findings.

Finally, qualitative research may be important for elucidating perceptions of how resiliency courses influence well-being that quantitative studies may not effectively ascertain, as it may be difficult to interpret the impact of small but significant changes on surveys. Qualitative research also may support resiliency skills program development in generating best practices for responding to the well-being needs of UIM students and other students who experience structural inequities in medicine.

CONCLUSIONS

Whether shared meal resiliency courses meaningfully enhance well-being remains unclear. Multiple statistically improved well-being outcomes combined with excellent course attendance may suggest that the course offers benefits for self-selecting participants. Future studies should explore perspectives on resiliency course utility.

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Health at Every Size Principles: Clinician Perspectives To Limit Weight Stigma in Medical Care

Shelbey J. Hagen, BS, MSeC; Mary F. Henningfield, PhD

ABSTRACT

Objective: Health At Every Size is a paradigm that encourages body acceptance, intuitive eating, and other principles to increase healthy, peaceful living. The model is accepted by many in the mental health field, but in order for its principles to become standard in clinical (medical) care, clinician perspectives on Health at Every Size should be sought and understood.

Methods: Ten clinicians were interviewed (4 physicians, 2 nurse practitioners, and 4 physician assistants). Participants reviewed the HAES principles, and identified facilitators and barriers to respectful, weight-inclusive care.

Results: Most clinicians felt that body mass index is a useful, standard metric, but it is inadequate and can be a cause of distress. Providing non–weight-focused care was identified as the primary facilitator to respectful care.

Discussion: Participants viewed body mass index as useful in some scenarios but do not think it encompass a patient's well-being and has the potential to cause the patient distress (eg, perpetuating weight stigma). Barriers to using Health At Every Size in clinical practice included the need for clinician education, bias/stigma, and a focus on weight.

BACKGROUND

Weight stigma (or weight-based discrimination) is discrimination or stereotyping based on an individual's body weight, shape, or size.[1] Regardless of stigma being subconscious or overt, it has a negative effect on health and well-being. A 2018 systematic review revealed weight stigma to be positively associated with a variety of poor health outcomes, including obesity, diabetes risk, stress levels, depression, anxiety, and low self-esteem.[2] A plethora of research shows that elevated body weight is associated with myriad chronic health conditions, but the causality of the relationship between weight and health concerns is tenuous.[2]

The Health at Every Size (HAES) principles were developed in 2003 as a guide for a new organization called the Association for Size Diversity and Health, utilizing existing work by body size/weight researchers. HAES, a movement and approach to healthy living pioneered by several researchers, is a nontraditional approach to health and well-being that encourages people to honor their hunger and fullness cues (intuitive eating); eat a varied, unrestricted diet; and engage in joyful movement for health promotion instead of emphasizing weight loss. A HAES approach, implemented in small groups, has been shown to have long-term beneficial effects on eating behaviors (decreases in emotional eating, greater reliance on internal hunger cues), intuitive eating,[3-5] and body satisfaction.[4]

Several studies have investigated a HAES approach to health care and its effect on patients, but little research exists looking at clinicians' perceptions about the approach outside the mental health field. An important first step in shifting the paradigm from traditional medical advice of weight loss to a HAES approach is to understand the attitudes of health care professionals towards these principles.

METHODS

A 10-item semistructured interview guide (see Appendix) was developed. Each question was framed on the first three HAES principles: weight inclusivity, health enhancement, and respect ful care. Clinicians were recruited using two primary methods: social

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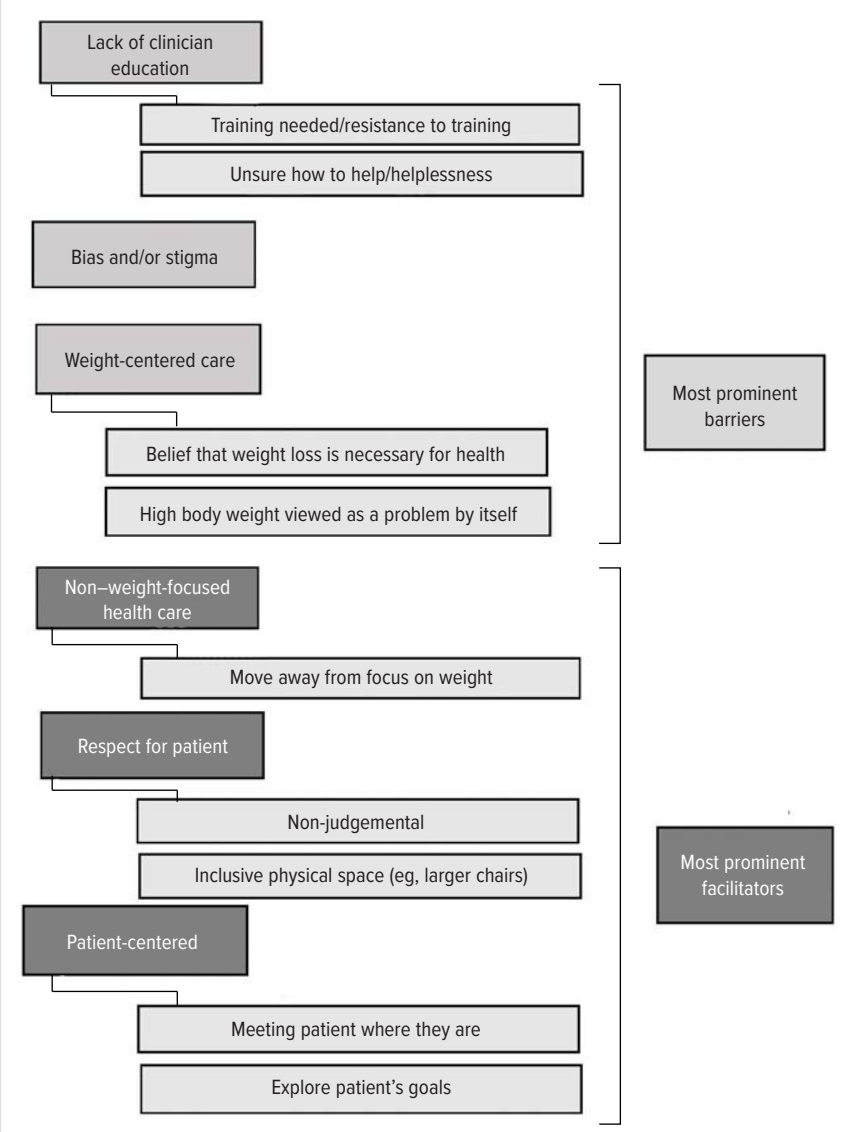
Table. Clinician Interview Responses

Quote	Theme
"I know some people, like, based on insurance…they don't go to the doctor because they're considered overweight."	BMI measure as a cause of patient distress Stops patients from visiting their doctor
"Especially since I have had patients that have gone through, like, anorexia nervosa and like diagnoses like that. And when I asked this specific patient, just like, when it all started and what she thought about that, she said that it was at her pediatrics office, when they were talking to her about her having a really high BMI."	BMI measure as a cause of patient distress Stops patients from visiting their doctor
"I wouldn't say that we would be weight blind, but I guess I'd say that we would be–you know, it's not like saying that we're going to be entirely color blind. It would be a move away from the focus on that."	Provide non–weight-focused care
"And kind of just knowing that that all bodies are different and genetics, and certain things all play a role."	Patient centered-care Respect for patient
"…I think again it's sort of an issue of education looking at the literature of what really improves life, not just improves BMI."	Clinician education needed
"…providers can have these notions that their weight is the only way to fix things when perhaps the patient is fine with their weight and fine with their body and how they feel."	Focus on weight-based care Weight is not a "problem to be solved"

Abbreviation: BMI, body mass index.

Figure. Barriers and Facilitators to Providing Respectful, Weight-Inclusive Care



media recruitment through a study poster (posted on Facebook) and an email blast to clinicians in the University of Wisconsin Family Medicine and UW Health clinician email list (convenience sample). The interviews took place using a secure, university-approved Webex virtual meeting room and were recorded for transcription purposes. Interviews typically took about 30 minutes. After the interview, the transcriptions were coded independently for categories and themes by two investigators using a content analysis strategy. Transcribed interviews were not returned to participants for notes/comments.

Three major findings from the interviews included clinician perspective on the body mass index (BMI) measure and both barriers and facilitators to respectful, weight-inclusive care.

RESULTS

Demographic information beyond job title was not collected for this pilot study. The sample of clinicians included 4 physicians, 4 physician assistants (including 1 student), and 2 nurse practitioners. Interviews were transcribed and coded by 2 independent researchers (SH, MH), who completed a qualitative thematic analysis. Analyses and study findings were derived after all data collection was completed, and participants were not invited to provide feedback on the findings.

BMI Measure

Because BMI is so frequently used in health care, clinicians were asked, "What are your thoughts on using BMI as a metric for measuring health and well-being?" A sample of their responses is included in the Table.

One of the most common themes that emerged in the qualitative analysis was that BMI was a useful but inadequate metric. Clinicians provided various reasons for inadequacy, including the following: BMI is not encompassing of well-being, BMI does not account for other health indicators, and BMI is a potential cause of patient harm (eg, stopping patients from seeing their doctors, triggering disordered eating habits or negative body image, or feeling stigmatized). Two of the 10 clinicians referenced BMI as a standard that has no alternative. Regarding BMI being a useful metric, many clinicians referenced it being a baseline tool for assessing health. Although clinicians cited BMI as a useful metric in some situations, they also mentioned that BMI is an inadequate measure of health and well-being.

Facilitators to Respectful, Weight-Inclusive Care

Clinicians were asked to identify qualities of care or describe what ideal care would look like (embodying the HAES principles of respectful, weight-inclusive care). The most poignant theme that emerged was providing non–weight-focused care. Subthemes mentioned within this overarching theme included a shift away from weight-focused care, an emphasis on respect for the patient and providing patient-centered care, and employing a multifactorial approach to care. Clinicians had varying ideas on how this could be incorporated in the current health care system.

Barriers to Respectful, Weight-Inclusive Care

Barriers to respectful, weight-inclusive care identified by clinicians in the interviews also provided a wealth of diverse answers. The most poignant barriers identified were the need for clinician education, bias, stigma, and employing weight-centered care (see Figure).

DISCUSSION

Conducting a small pilot study to gather initial insights from a small group of clinicians may lead to future research and greater adoptability of HAES principles in clinical care, resulting in better patient outcomes and reduced stigma. From the small sample of clinicians interviewed for this study, it is clear that while they viewed BMI as a helpful tool that is useful in some scenarios, it does not encompass a patient's well-being and has the potential to cause the patient distress (eg, perpetuating weight stigma). Participants shared a variety of ideas to improve weight-related health care, such as providing patient-centered care and shifting away from weight-focused care. They also identified shortcomings in the current system that serve as areas for improvement, including bias, stigma, and the need for clinician education.

While this pilot study provided insight into weight stigma and its role in health care from the clinician perspective, several limitations exist. The small sample size (n = 10) means that further research with larger, diverse samples are necessary. Clinicians interviewed were primarily from the Madison, Wisconsin area (n = 8) and worked within the same university health system; thus, views and perspectives may not reflect the opinions of clinicians who work in different settings and serve a different patient population. Additionally, knowing the interview was about weight stigma, clinicians may have been more inclined to discuss biases and shortcomings rather than successes regarding weight-inclusive care in the current health care system. Finally, selection bias is a limitation of this study, as clinicians who chose to participate had a prior opinion about or interest in the way weight is handled in medical care.

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Appendix: Available at wmjonline.org.

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Amiodarone Pharmacovigilance Through an Intelligent Electronic Health Record Application

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ABSTRACT

Background: Amiodarone is the most effective and commonly used antiarrhythmic medication. Given its risk of toxicity, routine monitoring is recommended but is challenging to ensure in clinical practice.

Methods: We created an intelligent application, built within our electronic health record, that identified every living patient with an active outpatient prescription by a clinician in our health system. The application was designed to identify patients with lapses in recommended monitoring and facilitate scheduling of overdue testing.

Results: The percentage of patients with overdue monitoring tests decreased with use of the application, with greatest improvement in pulmonary function testing.

Discussion: Implementing a program to monitor and mitigate adverse reactions to amiodarone by using programable features of an electronic health record is feasible.

BACKGROUND

Amiodarone is uniquely effective in treating ventricular and supraventricular cardiac arrhythmias and is the most widely used antiarrhythmic drug.[1] However, amiodarone also is associated with serious and potentially life-threatening adverse drug reactions, particularly with prolonged therapy.[1-6] To mitigate these risks, consensus guidelines recommend routine follow-up testing for liver-, thyroid-, and lung-related toxicities.[1-6] In clinical practice, it is often challenging to ensure that this testing is completed, and studies have shown that formal monitoring programs improve compliance with these guidelines.[1-6] Barriers to creating monitoring programs include the task's perceived complexity and additional costs.[6] The electronic health record (EHR) used by our institution (Epic; Epic Systems Corporation) has features that facilitate the creation of patient registries. The cardiology department at Mayo Clinic Health System in Northwest Wisconsin (MCHS NW WI) worked with our Cohort Knowledge Information Solution build team to design and implement an amiodarone monitoring application within our EHR. Here, we report our initial experience with the creation and implementation of this application.

METHODS

Project approval was secured in the fourth quarter of 2020. Programming of the application was completed by our institutional registry programmers during the first half of 2021, and pilot testing began in July 2021. Refinements and modifications were made throughout the rest of the year, and the product was fully functional in January 2022. Patient data were collected for this study from January 2022 through August 2022.

Every night, the application updated the list of living patients with an active outpatient prescription for amiodarone prescribed by a MCHS NW WI clinician. The application was populated with data of interest for each patient, according to the guidelines for recommended testing in patients treated with amiodarone (Table 1). Notable data incorporated were the most recent results

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of serum thyrotropin (TSH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) measurements, chest radiography, and pulmonary function testing (PFT). Other data fields were imported into the registry, such as primary care physician, date of most recent cardiology visit, and prescribing clinician.[1,3] Additional data columns in the application, when clicked on, could organize the list, bringing the patients most in need of intervention to the top. Tests that were more than 2 months beyond their due date were defined as overdue. Another column showed the total number of overdue results for a given patient; clicking on that column brought patients with the most overdue results to the top, which was an effective way for the amiodarone monitoring program coordinator (AMPC) to focus on those most in need of attention.

Because the application was integrated in the EHR, additional patient information was readily available to the AMPC by simply opening the patient record from within the application, which facilitated an individualized approach to addressing overdue testing. Notifications of overdue testing requests were sent as electronic messages if patients were active users of integrated patient portals or as telephone calls if they were not. Amiodarone-specific message templates were created to make this communication more efficient. Patients enrolled in hospice care were not directly contacted, although assistance with medication questions was offered to the patient's clinicians. After patients agreed to have amiodarone-specific monitoring testing, the AMPC marked the necessary orders as pending for the cardiologist to sign.

A new episode visit type entitled amiodarone monitoring was created, which enabled linking of all the AMPC's activity for a given patient to one location in the EHR. Programmers also created an Amiodarone Episode Smart Form that allowed for (1) manually enrolling or removing patients from the application; (2) documenting the reason for amiodarone discontinuation, such as therapy completed or adverse effect; (3) manually entering PFT results that predated our EHR (before 2017); and (4) manually assigning a patient's clinic region when it could not be autopopulated accurately. Patients were assigned to a region within our health system according to the practice location of the prescribing clinician. Importantly, the assigned region determined which workgroup would address a particular cohort of patients. At first, a considerable number of patients (nearly 1,000) could not be assigned a region because of a lack of specificity regarding the clinician's location in the EHR (eg, trainees). By interrogating additional data fields within the EHR, however, such as the primary hospital in which a clinician practiced, the number of patients with an unknown region in the health system was reduced to less than 80.

Programmers also facilitated several other application enhancements and process improvements. For instance, the AMPC found it helpful to write comments in a fixed column that documented previous work or information, such as "patient refused testing" or "[clinician] reports amiodarone will only be continued for 3 months." In addition, a process was developed for entering laboratory and chest radiography results from outside institutions.

Table 1. Guideline-Recommended Testing for Patients Using Amiodarone[1]

Organ System	Testing	Timing
Liver	ALT or AST	Baseline and every 6 months
Thyroid	TSH	Baseline and every 6 months
Lungs	Chest radiography Pulmonary function tests with DLCO	Baseline and every 12 months Baseline (repeat if clinical suspicion cion of pulmonary toxicity)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; DLCO, diffusing capacity of lung for carbon monoxide; TSH, thyrotropin.

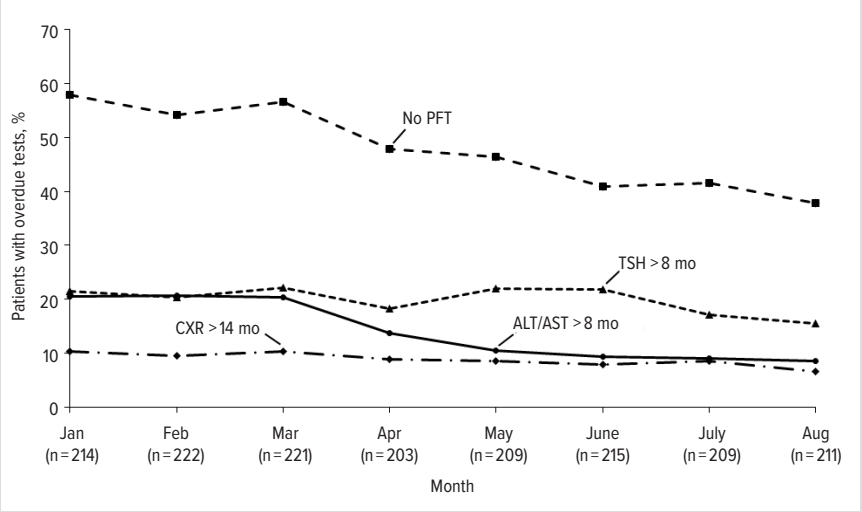
To determine whether time was significantly associated with a decrease in the number of overdue measures, a repeated measures logistic regression model was executed for each of the 4 outcomes. For all modeling, a significance level of .05 was used. Analysis was conducted in R version 4.1.2 (R Foundation for Statistical Computing).

RESULTS

Use of the application immediately identified 6 patients who had no testing for several years and were no longer followed up in the cardiology department. We contacted the primary care clinicians, and all were receptive to having the patient seen in the cardiology department to review testing and discuss whether continuing amiodarone had a favorable risk/benefit ratio. Next, the AMPC focused on patients with the most overdue tests. The number of patients overdue for all recommended testing decreased from 19 of 180 patients (10.6%) in July 2021 to 3 of 222 patients (1.4%) in February 2022. During the same time frame, the percentage of patients with 2 or more overdue tests decreased from 45.6% (82/180) to 34.7% (77/222).

The Figure shows the change in percentage of patients with overdue testing for several measures during the first 8 months of 2022. Efforts to address overdue tests often had a several-week time delay, and appreciable improvement in the measures was first noted after 4 months. The regression models confirmed that time was significantly associated with a decrease in overdue testing over the 8-month observation period for AST and ALT measurements, chest radiography, and PFT (all $P < .05$) but not for serum TSH measurement ($P = .12$). The greatest improvement was in PFT; the percentage of patients with overdue testing decreased by 20 points (57.9% to 37.9%) during the 8-month period. Indeed, at the end of 8 months' follow-up, patients had a 78% decrease in the odds of overdue status for PFT, compared with the start of 2022 (odds ratio, 0.22; 95% CI, 0.09-0.53; $P < .001$).

Figure. Patients Overdue for Recommended Testing



Graph shows the percentage of patients overdue for thyrotropin measurement by more than 8 months (TSH >8 mo) chest radiography by more than 14 months (CXR >14 mo), and alanine aminotransferase and aspartate aminotransferase measurement by more than 8 months (ALT/AST >8 mo) and patients having no pulmonary function testing (No PFT), per month. Data were collected from the application from January through August 2022. The number of patients per month is also shown.

Table 2. Summary of Full-time Equivalent Time Devoted to Creation of the Application in 2021

Task	Time spent, h
Programming	
Understanding needs of the practice	26
Developing the application in EHR	45
Demonstrating use to practice and functionalities of use	11
Total programming time	82
Amiodarone monitoring program coordinator time	65
Total FTE time programming and refining the application	147

Abbreviations: EHR, electronic health record; FTE, full-time equivalent.

Table 2 summarizes the time spent creating and refining the application throughout 2021—a total of 147 hours. Routine management of the patient cohort in 2022 occupied an average of 18.5 hours per month of AMPC time.

DISCUSSION

To our knowledge, this is the first description of the design and initial implementation of a medication-specific application in the Epic EHR to ensure monitoring of patients receiving antiarrhythmic drug therapy.[6] Our experience demonstrates that the implementation of such a program is feasible and is associated with clinically meaningful improvements in adherence to recommended guidelines. Improvements were apparent early in the project's implementation.

Baseline PFT showed the most opportunity for improvement and the greatest decrease in patients with overdue testing during the study period compared with other monitoring tests. We identified several reasons for such high percentages of patients without PFT during the beginning months. First, amiodarone is often started during acute illness when the performance of PFT will not result in accurate data; thus, the "baseline" function is more appropriately obtained after full recovery from the acute illness. In addition, PFT (as well as other follow-up and testing) often was delayed by logistics due to the COVID-19 pandemic. Because the pandemic peak was waning during the project in 2022, it most likely was easier for patients to successfully make appointments to complete their tests. Efforts are ongoing to further improve all metrics. The data from the application have provided useful feedback to clinicians regarding lapses in follow-up that must be addressed.

Barriers related to efficiently implementing applications of this type could be overcome with a focus on intelligent application development by EHR vendors and the incorporation of machine learning tools. The benefits for the development and automation of complex medication management monitoring systems include improved patient safety, improved medication management outcomes, and reduced administrative burden. Given that resources were scarce during this project, the application was designed to be as efficient as possible, without overburdening already strained clinicians with automatic (often erroneous) system-generated messages. The AMPC role proved invaluable for offloading clerical tasks, such as finding tests completed at outside facilities, determining which alerts truly required action, and marking appropriate orders as pending for overdue testing. Programming the registry to allow 2 months for routine testing to be completed in the course of routine care before triggering action by the AMPC saved considerable duplication of effort. Because this project had no outside funding, allocating resources such as AMPC time was a considerable challenge, and we anticipate this would also be a barrier for other institutions. The benefit to patient care, however, is also quite evident, and we believe that among the many initiatives that can be pursued with an EHR, pharmacovigilance programs of this sort will have an excellent return on investment. We anticipate that the programming and clerical burden will improve incrementally as the processes are standardized to incorporate other high-risk medications and as EHR vendors enhance registry capabilities.

Considering the success of this pilot project, we hope to expand use of this EHR intelligent application throughout the institution. Furthermore, the application was purposefully

designed so that other heart rhythm medications may be added, thereby allowing for efficient expansion of future pharmacovigilance efforts.

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Assessment of Uterine Fibroid Knowledge and Educational Interests Among Health Care Professionals

Morgan Briggs, MD; Benjamin Beran, MD

ABSTRACT

Background: Uterine fibroid diagnosis and management can be delayed by a lack of access to care. To combat this barrier, this study aimed to determine gaps in knowledge and investigate areas of education interest.

Methods: Obstetrics-gynecology, family medicine, and internal medicine resident and attending physicians received an electronic survey via RedCap. Descriptive statistics were performed in Mintab and Excel.

Results: Seventy of the 316 physicians (22%) who received the survey completed it. Most participants answered questions regarding diagnosis timing, instruments for validated reported outcomes, and risk factors incorrectly. Seventy-six percent of respondents desired more education about treatment options and guidelines.

Discussion: This study provides insight regarding current knowledge of uterine fibroids and areas of educational interest among different physicians.

BACKGROUND

Uterine fibroids are solid neoplasms of smooth muscle and fibroblast that can negatively impact an individual's health and well-being.[1,2] The prevalence of uterine fibroids among women documented in the literature ranges from 4.5% to 80% depending on study population and diagnostic methods utilized.[2,3] A single study also demonstrated that the cumulative incidence of uterine fibroids by age 50 years in the United States was nearly 70% in White women and 80% in Black women.[4]

Affected individuals can experience disruptive uterine bleeding, severe anemia, abdominal discomfort, pain, bowel and bladder dysfunction, and fertility issues due to uterine fibroids.[1,2] In addition to negative physical health outcomes, those individuals can experience significant emotional distress, fear, anxiety, anger, depression, and lower quality of life.[5,6]

Furthermore, in a study surveying 968 women aged 29 to 59, 28% reported missing work due to uterine fibroid symptoms.[7] A combination of this lost work, the direct health care costs of uterine fibroids, and attributable obstetrics health care outcomes results in an estimated cost in the United States of $5.9 billion to $34.3 billion annually.[8]

Although uterine fibroids result in significant negative health outcomes for individuals and high health care costs, many patients report a delay in diagnosis and establishing care.[9,10] Qualitative studies report that barriers to care include normalization of symptoms, low health literacy/knowledge, avoidance-based coping, dissociation from their uterine fibroids, and lack of an accessible and trusted health care professional.[9,10]

To combat the barrier of lack of access to a trusted health care professional, this study aimed to determine gaps in health care professionals' knowledge regarding uterine fibroids and then increase study participants' knowledge and awareness through targeted education programs. The study also aimed to expand on current literature as there are no studies to our knowledge investigating health care professionals' knowledge or education programs regarding uterine fibroids.

METHODS

Study Design and Setting

The project is a knowledge assessment conducted at a single academic medical center in Milwaukee, Wisconsin.

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Study Population

Obstetrician-gynecologist (OB-GYN), internal medicine, and family medicine physicians and residents working at Froedtert and the Medical College of Wisconsin in 2022 were included in the study. Internal medicine physicians surveyed were limited to the General Internal Medicine-Primary Care Department. The survey was provided to OB-GYN attending and resident physicians via current listservs. The research team worked with the internal medicine and family medicine department chairs and coordinators and residency program leadership to accurately provide the survey to current physicians. The survey was distributed to 316 physicians (89 OB-GYN, 144 internal medicine, and 83 family medicine).

Survey Development

The survey investigating health care professionals' knowledge was developed from information gained from research articles reporting on the epidemiology and symptoms of uterine fibroids, impact of obesity on gynecology and uterine fibroids, and new symptom and health-related quality-of-life questionnaires. Questions regarding peak time to diagnosis and questionnaires were included as these topics can be related to uterine fibroid diagnosis (Appendix). The team also utilized the American College of Obstetrics and Gynecology (ACOG) Practice Bulletin, which provides evidence-based recommendations for medical, procedural, and surgical management of symptomatic uterine fibroids.[1]

Table 1. Number (n) and Percentage of Total Participants (N) Who Answered Each Question Correctly

	All			OB-GYN			FM			IM		
Question	**n**	**%**	**(N)**	**n**	**%**	**(N)**	**n**	**%**	**(N)**	**n**	**%**	**(N)**
What is the most common symptom of UF?	53	82	(65)	23	92	(28)	15	79	(19)	15	83	(18)
Which are risk factors for UF?	16	25	(65)	4	14	(28)	6	32	(19)	6	33	(18)
At what age does the prevalence of UF diagnosis peak?	16	25	(65)	8	29	(28)	5	26	(19)	3	16	(19)
What race is most affected by UF?	59	91	(65)	26	93	(28)	15	79	(19)	13	72	(19)
According to the 2021 ACOG *Practice Bulletin on the Management of Symptomatic Uterine Leiomyomas*, which of the following are potential treatment options for patients with uterine fibroids?	50	79	(63)	25	93	(27)	13	68	(19)	12	71	(17)
The 2021 ACOG *Practice Bulletin on the Management of Symptomatic Uterine Leiomyomas* provides which of the following statements/recommendations?	25	40	(63)	8	30	(27)	10	53	(19)	7	41	(17)
Which of the following instruments are validated PRO tools specifically for UF?	14	22	(63)	7	26	(27)	4	21	(19)	3	18	(17)

Abbreviations: ACOG, American College of Obstetrics and Gynecology; FM, family medicine; IM, internal medicine; OB-GYN, obstetrics-gynecology; PRO, patient-reported outcomes; UF, uterine fibroids.

Table 2. Number of Participants (n) Who Reported Different Educational Interests Regarding Uterine Fibroids Among All Participants Who Answered the Question (N)

	All (N = 62)		OB-GYN (N = 26)		IM (N = 17)		FM (N = 19)	
Education Topic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Treatment options and guidelines	47	76	14	54	14	82	19	100
Patient-reported outcomes	28	45	13	50	7	41	10	53
Diagnostic options	23	37	4	15	9	53	10	53
General disease state education	20	32	3	12	7	41	10	53
Risk factors	19	31	4	15	6	35	8	42
Signs and symptoms	19	31	1	4	7	41	11	58
None	7	11	6	23	1	6	0	0

Abbreviations: FM, family medicine; IM, internal medicine; OB-GYN, obstetrics-gynecology.

Data Acquisition and Analysis

The knowledge survey link was provided to participants via email from August to October 2022. Data was stored in RedCap. Descriptive statistics were performed in Minitab and Excel.

RESULTS

Thirty-one OB-GYN (44%), 20 internal medicine (29%), and 19 family medicine (27%) physicians answered at least 1 question. Regarding years in practice, 37 (53%) reported 0 to 5 years, 15 (21%) reported 5 to 10 years, and 17 (24%) reported greater than 10 years. Less than 50% of participants correctly answered questions regarding peak time of uterine fibroid diagnosis, validated patient reported outcomes tools, risk factors, and ACOG's statement about uterine fibroid treatment data. Over 50% of participants correctly answered questions regarding treatment options, symptoms, and prevalence rates by race (Table 1). When comparing obstetrics-gynecology versus internal medicine versus family medicine, the specialty with the highest percentage of participants answering correctly varied by question (Table 1).

When asked what uterine fibroid education topics would be beneficial, 76% (n = 47) of physicians desired more education about treatment options and guidelines (Table 2). When comparing different specialties, greater than 50% of family medicine

Table 3. Number of Participants (n) Who Preferred Each Method of Additional Education Among All Participants Who Answered the Question (N)

Method	n	% (N = 63)
Live in-person	19	30
Live virtual	25	40
Virtual on-demand	35	56
None	5	8
Other	1	1

physicians desired more education on treatment options and guidelines, diagnostic options, patient-reported outcomes, general disease state education, and signs and symptoms of uterine fibroids, while internal medicine physicians desired more education on treatment options and guidelines and diagnostic options. A majority of OB-GYN physicians desired more education on treatment options and guidelines (Table 2).

Lastly, when asked what method of educational training is preferred, 56% (n = 35) of respondents reported a preference for a virtual, on-demand session versus 40% (n = 25) who reported a preference for a live, virtual session.

DISCUSSION

This study provides insight regarding current knowledge of uterine fibroids and areas of educational interest amongst OB-GYN, internal medicine, and family medicine physicians. These insights will inform the development of a targeted education session for physicians based on incorrectly answered questions. The session should include information about the diagnostic timing, risk factors, validated patient-reported outcome tools, and ACOG statements regarding uterine fibroids. In addition, the session should focus on treatment options guidelines and patient-reported outcomes, and it would most likely be best received via virtual live and on-demand platforms.

Our study was limited by a small sample size, which can be explained by the study being performed at a single location. Possible reasons for a small response rate could be survey fatigue, lack of interest, and lack of time. The sample size could be increased by expanding the study population to additional institutions, increasing the number of years of data, and providing incentives to complete the survey.

In addition to the low response rate, there is a risk of sampling bias. The individuals who responded may have a baseline interest in uterine fibroids. In addition, the data may be affected by response bias, such that physicians who have interest, experience, or knowledge may be more likely to respond to the survey. In this case, the results may have overestimated physician knowledge. Furthermore, the survey questions may have limited the evaluation of the physicians' knowledge. The survey contained 7 questions, which may not have been enough to adequately measure an individual's knowledge on this specific subject.

Although the data interpretation has limitations, the results provide educational targets with the goal of improving physicians' knowledge and confidence when caring for individuals with uterine fibroids.

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Appendix: Available at wmjonline.org.

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A Case That Will Take Your Breath Away: Acquired Methemoglobinemia Related to Trimethoprim-Sulfamethoxazole and Phenazopyridine Ingestion for Treatment of Urinary Tract Infection

Vinay Sharma, MD; Kevin Robertson, MD; Jason Domagalski, MD

ABSTRACT

Trimethoprim-sulfamethoxazole (TMP-SMX) and phenazopyridine are individually associated with methemoglobinemia through a series of altered reduction-oxidation reactions. We report a case of methemoglobinemia associated with concurrent use of TMP/SMX and phenazopyridine in a 70-year-old woman with recurrent urinary tract infections. She presented to the emergency department for worsening back pain in the setting of recurrent urinary tract infections, concerning for pyelonephritis. During her workup, she became acutely hypoxic. The emergency department provider suspected the presence of abnormal hemoglobin. An arterial blood gas showing elevated levels of methemoglobinemia confirmed the suspicion. The combined use of TMP/SMX and phenazopyridine was thought to be the likely etiology of hypoxia. This case highlights the importance of medication management in the geriatric population, as well as the judicious use of antibiotics for urinary tract infections--a common chief complaint in the primary care setting.

INTRODUCTION

Trimethoprim-sulfamethoxazole (TMP-SMX, brand name Bactrim) and phenazopyridine (brand name Pyridium) are individually associated with methemoglobinemia (MHb) through a series of altered reduction-oxidation reactions.[1-4] MHb occurs when the iron group located within hemoglobin oxidizes from the ferrous state ($Fe2^+$) to the ferric state ($Fe3^+$). MHb has an increased affinity for oxygen that results in decreased dissociation and availability at the tissue level. We report a case of methemoglobinemia associated with concurrent use of TMP/SMX and phenazopyridine in a 70-year-old woman with recurrent urinary tract infections.

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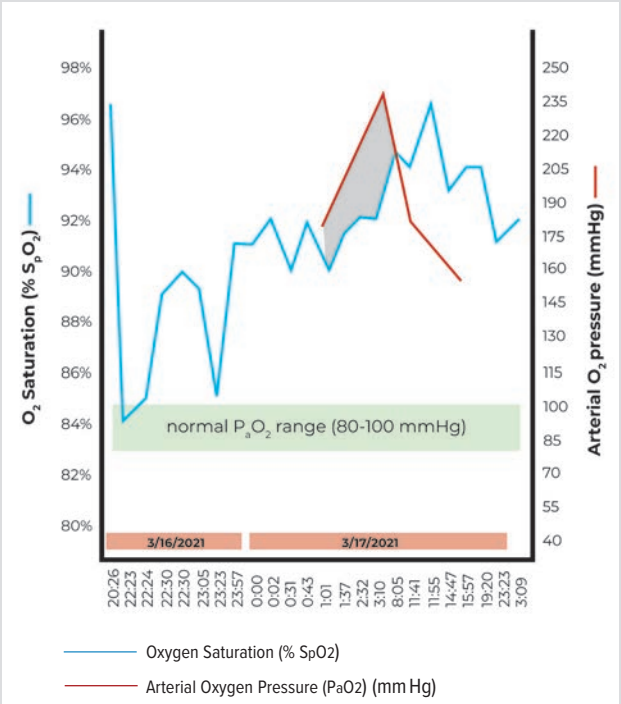
CASE PRESENTATION

A 70-year-old woman with a past medical history of hypertension, asthma, recurrent urinary tract infections (UTI), alcohol abuse, a remote history of morphine overdose, and active cannabis use presented to the emergency department (ED) for dysuria and back pain. She described a nonradiating, constant, 9/10 burning back pain with urination that improved with marijuana use. For her recurrent UTIs, she had been taking prophylactic Bactrim, half a tab every day, prescribed by her primary care provider for the previous 4 months. For pain control, she also was prescribed Pyridium (unknown dose) to use as needed for pain control. She had been intermittently using Pyridium for the past 3 to 4 months. The day prior to presenting to the ED, in addition to her prophylactic doses of TMP/SMX, she took 2 additional tablets (unknown dose) and another 2 tablets the day she presented to the ED. She obtained these medications from her sister, who had unused medication.

The patient's initial physical exam showed concerns for acute pyelonephritis/urosepsis. Her labs did not show leukocytosis, anemia, or electrolyte derangements. Computed tomography of the abdomen and pelvis was unremarkable. For pain, she received a single injection of 4 mg morphine.

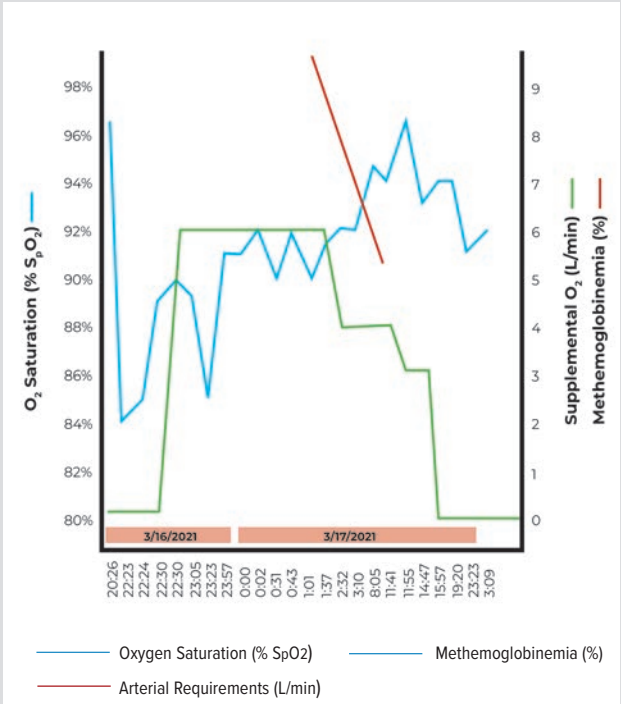
While in the ED, the patient suddenly became hypoxic, requiring 6 liters of oxygen delivered via OxyMask (Figure 1). A chest x-ray and computed tomography pulmonary angiogram protocol were negative for any acute process. She attempted multiple weaning trials with no improvement in hypoxia. An arterial blood gas (ABG) test showed a MHb level of 9.4% and a P_aO_2 of 176 mm Hg (normal MHb < 3%, P_aO_2 80-100 mm Hg). The ED provid-

Figure 1. Illustrating the Saturation Gap



Early in the patient's hospital course, she had very high levels of arterial oxygen pressures (red line) and persistently low oxygen saturations (blue line). The shaded region represents the "saturation gap," which can be an early sign of methemoglobinemia.

Figure 2. Oxygen Requirements Throughout Hospital Course



The patient's oxygen saturation (blue line) acutely dropped early in her emergency department course, requiring supplemental oxygen (green line). As methemoglobinemia levels decreased (red line), oxygen use decreased and saturations improved.

ers contacted poison control, which recommended admission with serial ABGs, complete blood cell counts, and vital signs until she could breathe on room air. The patient's breathing improved, and she weaned off oxygen to room air by time of discharge. Serial ABGs showed decreasing MHb levels (Figure 1). We attributed the cause of MHb to the concurrent use of phenazopyridine and TMP-SMX.

DISCUSSION

The mechanism underlying TMP/SMX and phenazopyridine-associated MHb is not well understood. It is hypothesized these medications interfere with the nicotinamide adenine dinucleotide (NAD) + hydrogen (H)/nicotinamide adenine dinucleotide phosphate (NADPH) reductase pathway, resulting in disrupted oxidation/reduction reactions.[3]

Symptoms of MHb are dependent on blood concentrations. Symptoms of patients with concentrations less than 10% range from asymptomatic to mild dyspnea. Some literature has shown patients are asymptomatic until levels are greater than 40%.[5] The most recognized symptom of MHb is cyanosis. Other symptoms include headaches, fatigue, worsening dyspnea, and chocolate brown blood. Seizure, coma, and death are all complications of MHb when concentrations are above 50%.[6] Treatment for MHb is methylene blue or ascorbic acid.[6]

A key diagnostic finding in the presentation of MHb is recognizing the "saturation gap" (Figure 2). The first indication of a saturation gap occurs when patients are placed on oxygen and saturations do not improve.[6-8] An ABG confirms the presence of a saturation gap, which shows high levels of P_aO_2 with consistently low hemoglobin saturations.

The patient presented in this report developed acute hypoxia in the setting of long-term TMP/SMX and phenazopyridine use for recurrent urinary tract infections. She did receive a dose of morphine in the ED, which could have contributed to her hypoxia; however, in the absence of other opioid-related symptoms, this is less likely. She also has asthma; however, her physical exam was not consistent with an exacerbation. She was negative for pulmonary embolism and SARS-CoV-2. Regarding her MHb percentage, symptoms are typically seen above 10%. Her asthma and marijuana and morphine use, while not actively contributing to her current clinical presentation, likely resulted in a form of chronic lung disease that predisposed her to symptoms of MHb at lower levels.[9] In the absence of other contributing medical history or a causative agent, the combined use of TMP/SMX and phenaozpyridine was the likely etiology of her acute hypoxia (Naranjo Adverse Drug Reaction Probability Scale[10] Score of 7 [probable]).[11]

While prolonged use of TMP/SMX and phenazopyridine is more likely to result in MHb, as we saw in this case, a slight increase in dose for a short period of time could be enough to result in symptoms.[11-13] This further highlights the need for primary care clinicians to be vigilant in medication management for patients, even for somewhat routine treatments or over-the-counter medications.

Of note, several geriatric patients have some extent of kidney disease, which can impact dosing of TMP/SMX and phenazopyridine. The Beer's List advises to use TMP/SMX with caution in patients taking angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or warfarin, common medications in the geriatric population.[14] This also highlights the need for patients to work with their provider for medication adjustments and to ensure they are safe.

CONCLUSIONS

UTIs are common occurrences in the general population and often are treated empirically with TMP/SMX, while phenazopyridine is available over the counter. With changing demographics in the American population and a growing geriatric percentage, recurrent UTIs may become a more common complaint and prophylaxis more widespread. While acute hypoxia due to MHb is rare, given the widespread use of these medications in the outpatient setting, it is important for providers to be aware of the association and educate patients about potential risk.

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An Unusual Presentation of Blastomycosis

Ryan Lokkesmoe, MD; Acacia Dishman, MD, PhD; John C. Feemster, MD; Daniel McKee, MD; Pinky Jha, MD

ABSTRACT

Introduction: Blastomycosis is a rare pyogranulomatous infection that most commonly involves the lungs and sometimes the skin. Other manifestations are much less common. Diagnosis relies on biopsy, histopathology, and culture of suspicious lesions.

Case Presentation: In this case, a healthy 42-year-old male from Wisconsin presented to the emergency department with a chief complaint of 2 weeks of knee pain without a clear mechanism of injury. Upon further examination, he was found to have lesions on his abdomen, which he had first noticed over 3 years prior and had been treated with antibiotics as cellulitis for nearly 18 months. Biopsy of these lesions was consistent with blastomycosis infection, and further work-up and examination was notable for brain and laryngeal lesions without any pulmonary involvement. Intense anti-fungal treatment was immediately initiated with dramatic improvement in his symptoms.

Discussion: This case highlights the importance of a thorough physical exam and consideration of rare infections in cases without clear answers. To our knowledge, this is the first published example of a blastomycosis infection involving brain, laryngeal, skin, and knee lesions without pulmonary infection.

INTRODUCTION

Blastomycosis is a pyogranulomatous infection caused by the organism *Blastomyces dermatitidis* that typically arises after inhalation of fungus conidia. It is endemic to the Ohio and Mississippi River valleys, the Great Lakes area, and the southeastern United States.[1] Even in the most commonly infected areas of Wisconsin, Arkansas, Mississippi, and Tennessee, incidence is less than 1 per 100,000 people.[1]

Up to 91% of cases of blastomycosis involve the lungs, with skin, bone, and other sites of infection being much less common.[2] In cases without pulmonary involvement, infection is likely a result of direct inoculation, and several case reports have been published with examples of skin or joint infection in isolation, usually following trauma. We have been unable to find any reported cases of multi-organ infection without pulmonary involvement. In Wisconsin, pulmonary infection is the sole manifestation in 77% of patients.[3] After *Blastomycosis dermatitidis* conidia are inhaled, they are susceptible to phagocytosis by pulmonary monocytes, typically resulting in an asymptomatic infection. However, if allowed to convert to the yeast form, *B dermatitidis* becomes more resistant to immune destruction and can proliferate.[4] Subcutaneous granulomatous nodules are possible following hematogenous spread from a primary lung infection; however, laryngeal and soft tissue involvement is rare. Skin involvement typically involves a verrucous lesion with irregular borders and colors ranging from gray to violet. Central nervous system (CNS) infection is present in 5% to 10% of cases and can include meningitis and intracranial or epidural abscesses.[4]

While many other deep fungal infections occur predominantly in immunocompromised patients, blastomycosis can occur in immunocompetent hosts.[5] Diagnosis relies primarily on histopathology and culture, although recently, antigen testing also has proven useful and expedient, despite exhibiting significant cross-reactivity between *B dermatitidis* and *Histoplasma capsulatum*.[6]

Samples for histopathology and culture can be obtained via sputum or, more reliably, bronchoalveolar lavage (BAL) for patients with lung involvement, skin biopsy for patients with skin involvement, cerebrospinal fluid (CSF) from patients with CNS

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involvement (although yield in this case is low), and even other sites of dissemination, including prostate and bone.[6] Samples for antigen testing can be obtained from urine, serum, CSF, or BAL.[6] At this time, the currently available standard immunodiffusion and complement fixation assays used for the diagnosis of other fungal infections are neither sensitive nor specific enough to diagnose blastomycosis.[6]

For most cases of disseminated blastomycosis, recommended treatment differs based on whether the disease is mild to moderate versus moderately severe to severe.[7] For mild to moderate disease, the recommended treatment is 200 mg oral itraconazole 3 times/day for 3 days, followed by 200 mg oral itraconazole 1 to 2 times/day for 6 to 12 months.[7] For moderately severe to severe disease, the recommended treatment is 3-5 mg/kg per day of lipid formulation amphotericin B, or 0.7-1 mg/kg per day of amphotericin B deoxycholate, for 1 to 2 weeks or until the patient improves clinically, followed by 200 mg oral itraconazole 3 times/day for 3 days and then 200 mg oral itraconazole 2 times/day for at least 12 months total.[7] In all cases, serum itraconazole levels should be monitored after at least 2 weeks of treatment to ensure adequate dosage.[7] For patients with blastomycosis that has disseminated to the CNS, the recommended treatment is 5 mg/kg per day of lipid formulation amphotericin B for 4 to 6 weeks followed by an oral azole for at least 12 months and until resolution of CSF abnormalities.[7] The oral azole can be 800 mg/day of fluconazole, 200 mg 2 to 3 times/day of itraconazole, or 200-400 mg 2 times/day of voriconazole.[7]

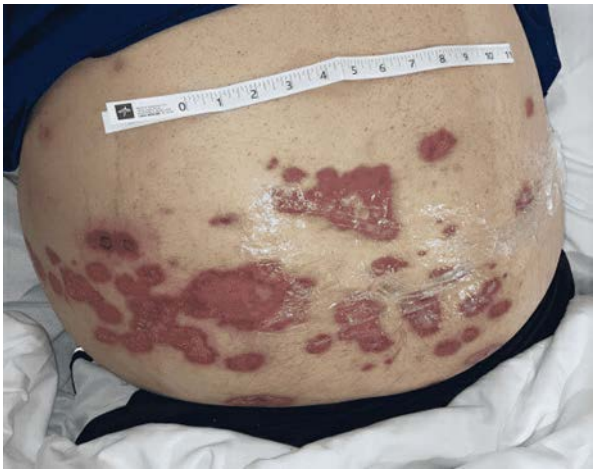
CASE PRESENTATION

A 42-year-old immunocompetent male from northern Wisconsin with a history of hypertension and obesity presented to our hospital with a chief complaint of right knee and thigh pain and abdominal rash.

His clinical course began about 3 years prior. He initially noted a nonpainful, approximate 2-cm lump beneath the skin of his abdomen. The lump persisted for 2 years before becoming tender and inflamed in 2020. In October 2020, he was seen by an outpatient gastroenterology advanced practice nurse prescriber (APNP), who diagnosed him with cellulitis and prescribed cephalexin. At a follow-up visit 2 weeks later, the lump had ruptured, draining blood and pus. Antibiotic coverage was thus changed to trimethoprim sulfamethoxazole (TMP-SMX). Symptoms did not improve following a 10-day course of TMP-SMX, so his course of treatment was extended for 5 days.

Although his symptoms did not resolve and he continued to experience abdominal lesions that grew beneath the skin before rupturing and draining, the patient did not follow up with a clinician until May 2021, at which time he presented with left lower extremity pain. He also continued to have an abdominal rash. He was diagnosed with cellulitis of the left lower extremity and prescribed a 14-day course of TMP-SMX. At this visit, he also was told that his body mass index was likely the predisposing factor to his repeated infections and counseled to lose weight.

Figure 1. Cutaneous Findings on Patient



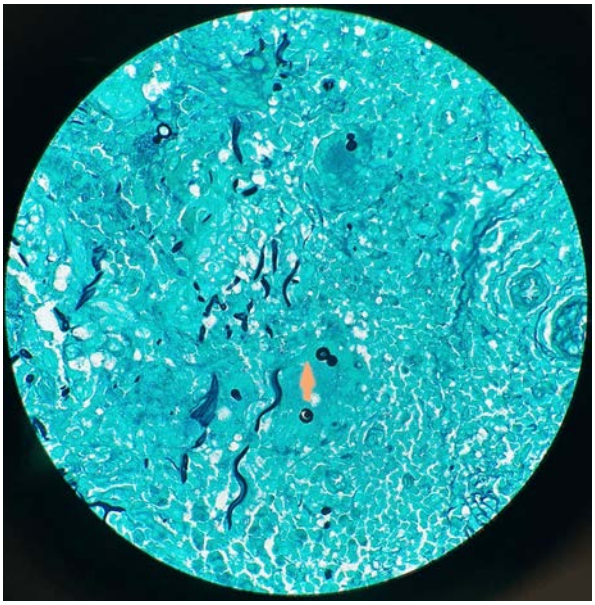
Lesions were present for years prior to diagnosis.

Several months later in 2021 at his annual physical exam, his persistent abdominal lesions were noted, and he was diagnosed with abdominal cellulitis. He was prescribed a 14-day course of doxycycline and counseled to lose weight.

In March 2022, he began to experience right lower extremity pain, contralateral to his previously treated left lower extremity pain. He first noticed this pain as a slight limp before palpating a small lump under the skin on his right thigh. Two days after he noticed these symptoms, he awoke with a very tender, swollen, warm knee that was exquisitely painful to movement and palpation. He described the pain as sharp, stabbing, "like a muscle constantly contracting," nonradiating, and 10/10 in severity. His abdominal symptoms persisted as well, although on presentation his knee pain was his primary concern. He presented to an outside emergency department on April 6, 2022, where he was admitted for extensive workup. Magnetic resonance imaging (MRI) demonstrated signal concerning for myositis and knee effusion. Further workup, including creatine kinase, arthrocentesis, antinuclear antibodies, myeloperoxidase, proteinase 3, anti-neutrophil cytoplasmic antibodies, and inflammatory bowel disease differentiation, was ultimately negative.

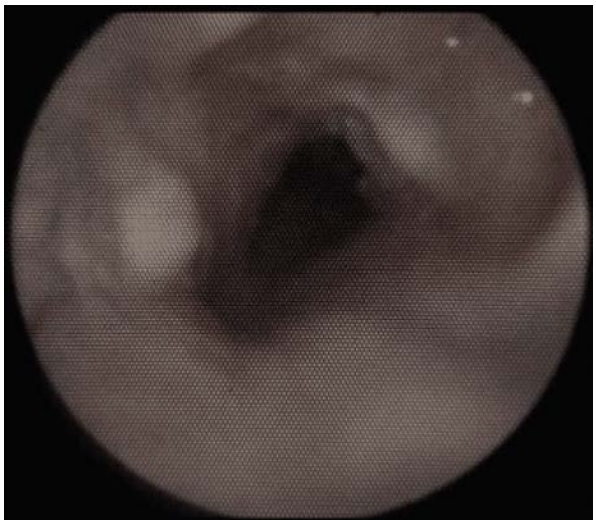
The patient was discharged with supportive measures and referred to our hospital. On admission, in addition to his lower extremity symptoms, he also complained of an abdominal rash that involved 30-40 mm, nonpainful lesions that grew beneath the skin of the abdomen and would eventually rupture and release pus and fluid. After rupturing, these lesions would slowly heal and crust over. Exam was notable for numerous red, ovoid, confluent lesions of varying sizes and stages of healing spread diffusely across the abdomen (Figure 1). Several had crusting around the edges.

Figure 2. Skin Punch Biopsy Sample



Gomori's methenamine silver stain x 400 showing broad-based budding yeast (yellow arrow) consistent with blastomycosis.

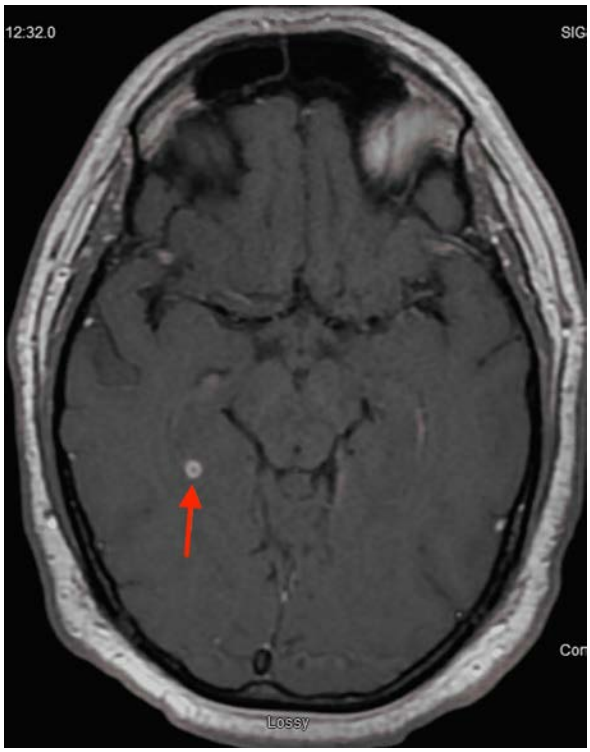
Figure 3. Transnasal Laryngoscopy Findings



Two 1x1-cm punched-out lesions appeared to be in an earlier stage of healing.

After extensive workup demonstrated mild leukocytosis, thrombocytosis, elevated erythrocyte sedimentation rate and C-reactive protein, and unremarkable chest x-ray, a skin biopsy revealed broad-based yeast forms (Figure 2) with surrounding inflammation and pseudoepitheliomatous hyperplasia consistent with blastomycosis infection. Urine blastomycosis antigen was positive as well. Computed tomography (CT) of the chest was remarkable for

Figure 4. Magnetic Resonance Imaging Brain From Patient With an Example of One of the Small Ring-Enhancing Lesions (red arrow)



no pulmonary consolidation or nodule. Head/neck CT was concerning for tracheal narrowing, and transnasal laryngoscopy was notable for vocal cord lesions consistent with disseminated blastomycosis (Figure 3). MRI brain demonstrated 3 small ring-enhancing lesions also consistent with disseminated blastomycosis (Figure 4). Interestingly, the patient denied any neurological symptoms throughout his clinical course, and exams were consistently negative for any abnormal neurological findings.

He was started on intravenous amphotericin B, with progressive symptomatic improvement of his knee pain reported as early as the following morning. His rash remained stable, and repeated laryngoscopy after 10 days showed complete resolution of vocal cord lesions and healthy-appearing mucosa. He was discharged after an 11-day hospital course with plans to take voriconazole 400mg twice daily for 1 year with close follow-up with infectious disease specialists. At his 1-month follow-up, he reported "substantial improvement in energy level, thigh pain, and skin lesions."

DISCUSSION

We report a case of disseminated blastomycosis with atypical presentation in a patient without evidence of pulmonary involvement but with widespread CNS, skin, and soft tissue pathology. Blastomycosis is endemic to the Great Lakes area, the Ohio and

Mississippi River valleys, and the southeastern United States. The patient described resides in Green Bay, Wisconsin, and presented to us in Milwaukee, Wis.

This case highlights several important points. First, it demonstrates the importance of a thorough physical exam on all patients. Knee pain and inconclusive MRI findings in isolation would never have been sufficient to lead to a diagnosis of blastomycosis. Despite a 3-year gap between the onset of this patient's abdominal rash and knee pain, the two were ultimately linked to the same underlying pathology.

Second, this case highlights an important bias often seen in medicine: anchoring on a common or initial diagnosis. When this patient was first evaluated, a diagnosis of cellulitis was not unreasonable; however, when repeated courses of antibiotics failed to resolve his symptoms, an alternative diagnosis should have been considered. By the time of admission, he had been evaluated by at least 4 clinicians, among whom only one broadened their differential beyond cellulitis in their assessment. Each of these clinicians prescribed antibiotics, despite historical inefficacy. In April 2022, a full 18 months and 6 office visits after his first evaluation, the patient was referred to a dermatologist for further examination and workup. Several factors, including clinician time constraints, easy and convenient alternative diagnosis, and multiple previous visits documenting cellulitis, likely played a role in this failure of the medical system.

Finally, this case records a highly unusual manifestation of blastomycosis with CNS, cutaneous, laryngeal, and muscular involvement completely free of respiratory symptoms and without pulmonary abnormality on chest CT. Most instances of a fungal infection of this etiology will involve the lungs exclusively; however, this case demonstrates an example of widespread infection that seemingly spares the lungs. Blastomycosis is typically transmitted through inhalation of spores leading to pulmonary disease and possible subsequent hematogenous dissemination,[8] but direct cutaneous inoculation is also possible. Several published cases report widespread cutaneous lesions without pulmonary involvement, including a case in 2022 describing a similar patient with knee pain who was diagnosed with cutaneous blastomycosis and treated successfully with itraconazole.[9] However, this patient did not have evidence of infection in any other organ system.

To our knowledge, we provide the first reported case of nonpulmonary multiorgan blastomycosis. This case highlights the fact that even if a patient does not have pulmonary blastomycosis, they may still have widely disseminated blastomycosis with involvement of multiple organ systems. A lack of pulmonary infection does not rule out disseminated blastomycosis infection altogether. This case also highlights the importance of expansion of a differential when a patient presents with persistent, atypical, or repeated cutaneous infection unresponsive to antibiotics, particularly in an area where blastomycosis is endemic.

CONCLUSIONS

In this case, we highlight an unusual presentation of disseminated blastomycosis in an immunocompetent host to increase awareness among clinicians. This case also highlights the importance of considering the diagnosis of blastomycosis in patients who are not responding to therapy like antibiotics. This case demonstrates the importance of involving specialists early on in cases where patients present with unexplained refractory signs and symptoms of disease after treatment, as specialists can aid in the identification of more rare diseases, such as blastomycosis. Early detection and treatment can prevent morbidity and mortality.

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Maintenance of Ionized Calcium During Prolonged Extreme Massive Transfusion During Liver Transplantation

Ricardo P. Dorantes, BS; Stylianos Voulgarelis, MD; Harvey J. Woehlck, MD

ABSTRACT

Introduction: Massive transfusion may cause ionized hypocalcemia, a complication that, when severe, causes hemodynamic instability. Extant literature fails to provide effective guidance on replacement strategies to avoid severe ionized hypocalcemia in the most extreme situations.

Case Presentation: We discuss a liver transplant in which our empiric calcium replacement strategy resulted in no critically low ionized calcium values during the pre-reperfusion phase of a liver transplant with over 140 000 mL of bank blood transfusion, with an average of 10 000 mL per hour for 14 hours.

Discussion: Few comparable reports exist. Most rely upon monitoring with subsequent replacement, but these have not been effective at avoiding severely low ionized calcium values.

Conclusions: Our empiric calcium replacement strategy of 1 gram of calcium chloride per liter of citrated bank blood transfused, in 200 mg/200 mL increments, resulted in successful maintenance of ionized calcium during the anhepatic phase of liver transplantation while on continuous veno-venous hemofiltration.

INTRODUCTION

Massive transfusion is associated with ionized hypocalcemia due to citrate intoxication, a complication in which the anticoagulant citrate, added to banked blood products, chelates ionized calcium in the circulation with hemodynamic and potentially coagulopathic consequences. Citrate intoxication can be severe during liver transplantation because citrate metabolism is impaired by liver failure and is potentially nonexistent during the anhepatic phase of liver transplantation in patients with renal failure. Extant studies, opinions, and case reports suggest calcium administration paradigms that vary widely, with no effective guidance on replacement strategies.[1] As a result, a combination of empiric calcium salt administration plus reactive correction in response to measured ionized calcium values has been reported with variable success. Critically low ionized calcium values are associated with severe and life-threatening cardiovascular complications during massive transfusions.

In liver transplantation, our institution has published data on supplemental calcium requirements and resultant ionized calcium values during massive transfusion. Although no mandatory protocol exists at our institution, the results of our study[2] have become a de facto calcium replacement paradigm in the pre-reperfusion time frame amongst our small team of liver transplant anesthesiologists. Although QT interval has been shown to correlate with ionized calcium in massive transfusion,[3] this parameter would be difficult to monitor continuously with the necessary precision at our institution with our equipment.

We report the efficacy of a nominal 1 gram calcium chloride per liter of citrated blood, when given in 200 mg $CaCl_2$/200 mL citrated blood boluses, in a single patient who received the largest transfusion during liver transplantation performed to date at our institution. This was also the largest transfusion in a patient who survived that is available for comparison in peer-reviewed medical literature.[3] This transfusion consisted of approximately 140 liters of blood products, with 50 liters of transfusion during the anhepatic/pre-reperfusion phase of the operation when citrate metabolism was minimal.

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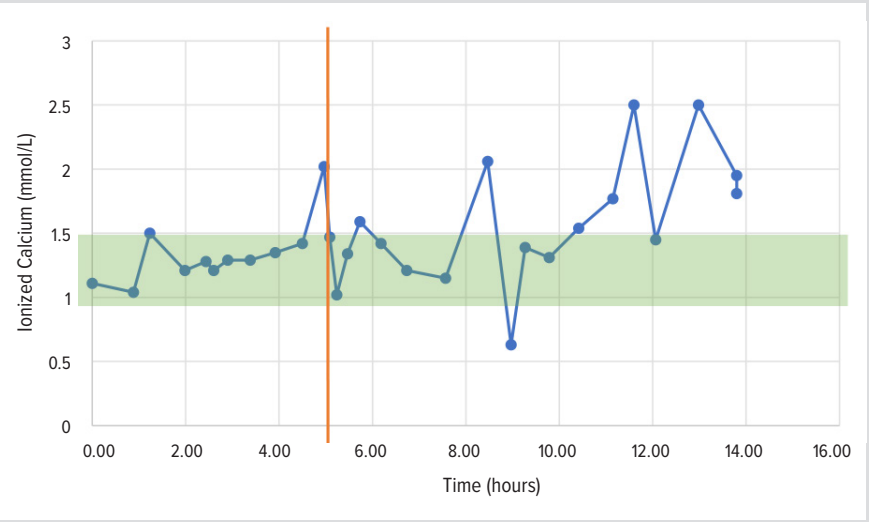
CASE PRESENTATION

The patient is an approximate 40-year-old 75 kg male with a history of sclerosing cholangitis receiving his third liver transplant for cirrhosis and end-stage liver failure, with a total bilirubin of 27 mg/dL and a direct bilirubin of 19 mg/dL at the time of transplant. Each of his prior transplants lasted approximately 10 to 15 years with good function before the recurrence of cirrhosis and liver failure. He has no significant history of alcohol or illicit drug use. He was transferred to our center because of anticipated difficulty with transplantation, substantial abdominal scarring, portal vein thrombosis, and adhesions. These predisposing factors, the projected inability to decompress the portal venous system during transplantation, and technical issues related to vascular anastomoses suggested massive blood loss would ensue during transplantation.

Figure. Ionized Calcium Values Versus Time



The shaded region represents values near the normal range (1.18 to 1.34 mmol/L at the authors's institution) and above those identified as critically low in the literature. The vertical line at 5 hours represents the time of reperfusion of the liver.

The operation proceeded conventionally using femoral to subclavian venous bypass with a heat exchanger to maintain body temperature in the normal range. Because the patient had renal failure secondary to hepatic failure with a creatinine of about 4 mg/dL, continuous veno-venous hemofiltration (CVVH) was instituted primarily for management of transfusion-associated hyperkalemia and acidosis, although CVVH also has the potential benefits of reducing hyperphosphatemia as well as calcium-citrate complexes from bank blood. CVVH blood flow was at 250 mL/min and dialysate with a 0K+ electrolyte solution (NxStage RFP-402) was run at 4 L/min. It was not possible after several attempts to decompress the portal venous system with venous bypass due to thrombosis of major vessels. A venous conduit was created to supply portal blood flow to the transplanted liver and decompress the portal venous system but was not available for venous bypass, as reperfusion was performed as soon as the conduit was completed. Massive blood loss was encountered on entry to the abdomen as all peritoneal surfaces were involved with engorged collateral vessels. The rate and volume of blood transfused was quantitatively measured via the Belmont Rapid Infuser (Belmont Medical Technologies, Billerica, Massachusetts), which was used solely for packed red cell, fresh frozen plasma, and crystalloid products. End of case totals were obtained from summation of measurements indicated by our blood center on individual units of blood products.

Of the 142 558 mL total volume of blood transfused, approximately 50 000 mL was given in the pre-reperfusion period. The transfusion prior to reperfusion was managed by a single anesthesiologist (corresponding author) and was performed by giving a 200 mL bolus of a 1:1 ratio of packed cells and fresh frozen plasma at up to 500 mL/min through a Belmont rapid infusion device. Although the nominal flow rate of 500 mL/min could be achieved with crystalloid solution, the actual blood product flow achieved was typically around 300 mL/min due to pressure limiting at 300 mmHg because of the higher viscosity of blood products compared to crystalloid solutions. The individual initiating the bolus of bank blood products gave a simultaneous bolus of 200 mg $CaCl_2$ intravenously through a different port of a central line. Platelets and cryoprecipitate were administered through a separate intravenous (IV) infusion set, and the patient received a proportional amount of $CaCl_2$. When cell saver blood was available, fresh frozen plasma and a proportional dose of $CaCl_2$ was administered in approximate equal volumes. Therefore, 50 grams of $CaCl_2$ were administered for these 50 liters of citrated bank blood.

On average, the ionized calcium level was recorded every 26 minutes after the initial reading at the start of the surgical intervention, resulting in a total of 13 measurements during the pre-reperfusion period of the operation (lasting 5 hours, 16 minutes). The mean and standard deviation for ionized calcium values during this time frame was 1.32 mmol/L ± 0.26 mmol/L. Of note is that there were no ionized calcium values below 1.0 mmol/L during this phase of the operation, suggesting that no critically low values resulted from this infusion paradigm.

Post-reperfusion, patient care was managed by a different anesthesiologist (second author). Clinical signs indicated that hepatic function and, therefore, citrate metabolism was reestablished. For the next approximately 93,000 mL of blood transfu-

sion over the following 8.5 hours, approximately 38 grams of calcium chloride were administered. A more "reactive" paradigm of calcium administration was performed, giving less calcium when blood was administered slowly and more calcium when blood was administered more rapidly up to the ratio used pre-reperfusion. The actual amount of calcium replacement was based on the intuition of the anesthesiologist, with corrections based on measured ionized calcium values. Measurements of ionized calcium were performed on average every 32 minutes during the post-reperfusion phase, and only one critically low measurement of ionized calcium was recorded. From the standpoint of citrate metabolism, in both phases of the operation, an average of over 10 000 mL of citrated blood was given per hour until hemostasis was obtained at the end of the case.

The Figure graphically shows ionized calcium versus time, with the shaded region representing values close to the normal range (1.18-1.34 mmol/L) at our institution. The vertical line at 5 hours represents the time of reperfusion of the liver. Prior literature suggests that critically low ionized calcium values that impact hemodynamic function and outcome begin at a lower limit around 1.0 - 0.9 mmol/L;[2] hence, the shaded region representing optimal values has a lower limit in the Figure of 1.0 mmol/L. The upper limit of the shaded region represents the mid normal range ± 1 SD of the pre-reperfusion values (1.24 mmol/L ± 0.26 mmol/L), giving 1-1.5 mmol/L as optimal ionized calcium values. There were no critically low values pre-reperfusion and only one post-reperfusion. Although several high values existed, the value immediately pre-reperfusion was an intentional prophylactic $CaCl_2$ bolus for hyperkalemia on reperfusion. Elevated ionized calcium values post reperfusion are common during liver transplantation. At the end of surgery, the ionized calcium was approximately 1.8 mEq/L, although the total calcium was 19.8 mg/dL (normal range 8.5-10.2 mg/dL). Most blood gas electrolyte values were in the normal range intraoperatively, with potassium values of 4.5-5.5 mEq/L, and only a few intraoperative potassium values were elevated by blood gas.

DISCUSSION

The ability to perform massive transfusion has evolved to extreme levels for prolonged durations, and for those managing the transfusions and metabolic consequences, this creates the emerging problem of proper calcium management to avoid citrate toxicity. Critically low ionized calcium concentrations are associated with worse outcomes during massive transfusion, although the literature involves diverse surgical populations of trauma, transplant, and vascular surgery. In trauma patients, critically low ionized calcium concentrations are associated with larger transfusions and also with more severe injuries; therefore, multiple confounders exist in this relationship, making the study of individual factors more difficult. However, in the liver transplant population, very large transfusions are possible, and proper management of ionized calcium concentrations can be more readily associated with protocols of transfusion management without concurrent pathology as a confounding factor in the size of the transfusion. In liver transplantation, it is common to progress from low citrate metabolism compared to normal, to no citrate metabolism in the anhepatic phase, to normal or high citrate metabolism post-reperfusion in a functioning hepatic graft. This gives distinct phases to this operation in terms of how calcium replacement is managed for citrated blood products.

The size of the bolus delivered through the rapid infusion device is partially based on the practical consideration of 200 mL representing approximately 2-3 mL citrated blood/kg for a 70-100 kg adult. Similarly, we chose a 200 mg bolus of calcium chloride to match calcium to citrate using our previously published data prior to reperfusion of the liver. Because we routinely place central lines in liver transplant recipients, the calcium chloride is given through the central line to reduce the risk of peripheral vein sclerosis. Adverse events occasionally have been observed or reported with larger boluses of calcium chloride through central lines or when calcium administration causes transient extreme hypercalcemia. Cardiovascular collapse has been described with excessive calcium administration, possibly related to hypercalcemia-mediated mast cell degranulation.[4] Acute hypercalcemia also has been associated with tachyarrhythmias[5] and bradyarrhythmias.[6,7] The package insert for calcium chloride[8] recommends a maximum rate of 100 mg $CaCl_2$ per minute through a central vein, although the clinical scenario of massive transfusion and citrate intoxication is not mentioned in this recommendation. Clearly, the rate we required in this transfusion of 10 000 mL/hour would require a continuous infusion rate of 167 mg/min if the transfusion had been uniform and continuous; but in reality, the transfusion was neither continuous nor uniform. Rates of 300 mL/min blood with calcium chloride replacement at 300 mg/minute were required at times, as that was the maximal achievable blood flow rate with our equipment and extant vascular access.

CVVH undoubtedly helped with some electrolyte abnormalities during this massive transfusion. Our prior study indicated that ionized calcium was kept in a narrower range closer to normal when CVVH was used.[2] The solution used during most of the procedure, which incorporated all of the massive transfusion, was NxStage RFP-402, with 140mEq/L Na^+, 0 mEq/L K+, 1.35 mEq/L Ca^{++}, 109 mEq/L Cl-, 1 mEq/L Mg^{++}, 100 mg/dL glucose, and 35 mEq/L bicarbonate. This may explain why we were able to use less calcium than the prior study[2] indicated in the average of patients who had lower usage of CVVH. Only 850 mEq of bicarbonate were used during this 14-hour operation, so the bicarbonate content of CVVH may have reduced the propensity to develop a metabolic acidosis, as blood products have substantial loads of lactic acid from the anaerobic metabolism of red cells in storage.[9]

CONCLUSIONS

This case demonstrates that in the absence of citrate metabolism, matching 200 mg of calcium chloride with each 200 ml of citrated bank blood bolus provides good results in massive transfusions prior to reperfusion by keeping ionized calcium levels near the normal range and preventing critically low values. After reperfusion, an average of 40% of this ratio of $CaCl_2$ to banked blood was required due to metabolism of citrate.

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Neck Pain Secondary to Post Radiation Fibrosis Managed With Ultrasound-Guided Adhesiolysis

Mackenzie McGrath, MD; Hariharan Shankar, MBBS

ABSTRACT

Background: Radiation therapy may result in complications, including fibrosis, which can result in pain and difficulty with movement – especially in the neck.

Case Presentation: A 52-year-old man with right-sided vague neck pain unresponsive to conservative management had a computed tomography scan that showed a vagal paraganglioma in the carotid sheath surrounding the right carotid arteries and internal jugular vein. Following radiation therapy, he noticed a new pain in his right jaw and neck worse with certain movements of the neck. Nonsurgical conservative measures including physical therapy and pharmacological management were unsuccessful. An ultrasound evaluation demonstrated fibrosis beneath the sternocleidomastoid muscle and in proximity to the carotid sheath. After careful trajectory planning using ultrasound imaging, a 25 G needle was introduced real time in proximity to the fibrosis. Using a dexamethasone/saline mixture under real-time ultrasound guidance, adhesions were released. After 3 injections, the patient reported greater than 90% pain relief, which lasted 4 months. Subsequently, he required similar injections approximately every 3 months to achieve greater than 75% pain relief.

Conclusions: This is a successful demonstration of the utility of ultrasound evaluation and guidance for adhesiolysis following radiation therapy.

INTRODUCTION

Paragangliomas are rare, highly vascular, benign neuroendocrine tumors arising within the paraganglia system located all over the body. Ninety percent of tumors are in the adrenal paraganglia, which are called pheochromocytomas, while only 3% of extra-adrenal tumors occur in the head and neck.[1] The most common head and neck paraganglioma is the carotid body paraganglioma. Vagal paragangliomas make up 5% of head and neck paragangliomas, are located at 1 of 3 ganglia, have a female predominance, and are more common on the right side.[1] They commonly present as a neck mass and are located within the carotid sheath, which includes the carotid artery and internal jugular vein.

Treatment options for head and neck paraganglioma traditionally have included surgery and/or radiation therapy (XRT). Because of speech (vocal cord paralysis secondary to vagus nerve resection) and/or swallowing difficulties post-surgery, surgery often is not considered as the first management option. While surgical intervention, including preoperative embolization, often has been the approach, recent improvements in diagnostic imaging and XRT have paved the way for cautious observation and nonsurgical intervention, including stereotactic radiation therapy.[1] The aim of surgical intervention is to achieve complete remission. XRT hopes to prevent disease progression, with local control achieved greater than 90% of the time after 5 years. Both surgical and XRT modalities may result in significant morbidity.[2] With the "wait and watch" approach, 40% of these tumors have remained stable.[1] According to Consensus Guidelines for Surveillance and Management of Metastatic and/or Unresectable Pheochromocytoma and Paraganglioma from the North American Neuroendocrine Tumor Society, XRT is the best studied option for patients with unresectable paraganglioma.[3]

Unfortunately, XRT is associated with multiple well-documented side effects that contribute to morbidity and decreased quality of life. In a study by the Rare Cancer Network that included

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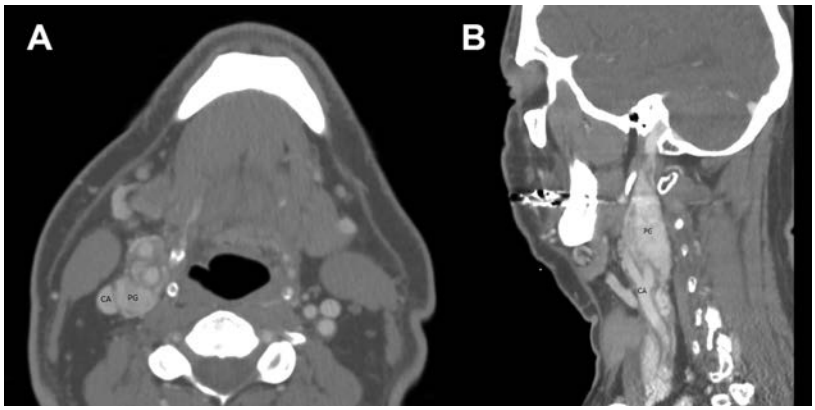
76 patients with head and neck paragangliomas who underwent XRT, the median age at diagnosis was 50 years, and local control was achieved in 90% of patients.[2] In our selected review of the literature, currently there is no documentation of any management options for the pain and secondary effects of radiation-induced fibrotic adhesions.

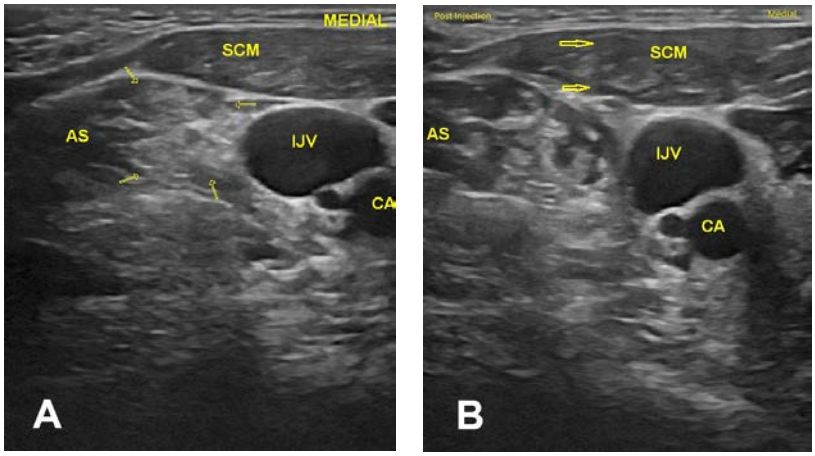
We report the case of a patient with significant neck pain following XRT for an unresectable head and neck paraganglioma, which was controlled following a series of ultrasound-guided release of adhesions.

Figure 1. Computed Tomography Scan of the Patient's Neck



A. Axial image showing the right carotid artery and paraganglioma.
B. Sagittal image showing the carotid artery and paraganglioma encircling the right carotid artery.

Figure 2. Ultrasound Images of the Right Side of Patient's Neck (A) Before and (B) After First Injection



Abbreviations: SCM, sternocleidomastoid; CA, carotid artery; IJV, internal jugular vein; AS, anterior scalene.
Thin arrows = post radiation fibrosis; thick arrows = out-of-plane needle.

CASE REPORT

A 52-year-old man presented to his primary care clinician for right-sided neck and right upper extremity radicular pain. His medical history was significant for Lewy body dementia, depression, posttraumatic stress disorder, type 2 diabetes, and hypertension. His symptoms were initially thought to be secondary to tensing his neck and arm muscles to control his tremor; therefore, he was started on cyclobenzaprine and referred to physical therapy.

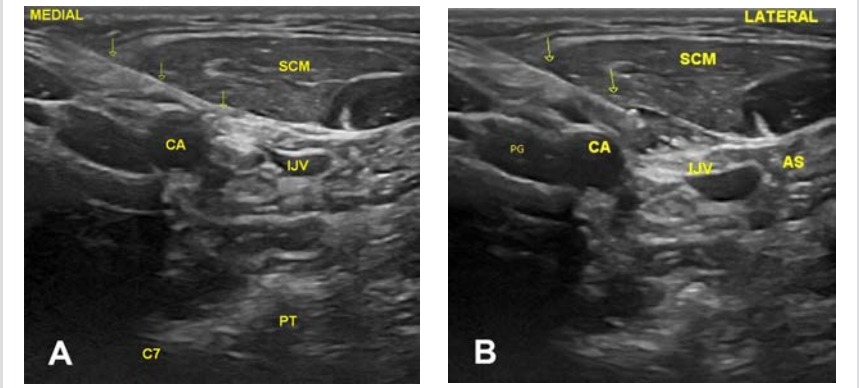
However, as his symptoms did not improve after 6 weeks, magnetic resonance imaging (MRI) of his cervical spine was performed, demonstrating a disc extrusion at C6-C7, small disc protrusions at C4-C5 and C5-C6, and a partially visualized right carotid mass. The mass prompted computed tomography (CT) imaging, which showed a mass in the cervical region compressing the right internal jugular vein and surrounding the right carotid arteries (Figure 1). Biochemical screening with 24-hour urine testing for catecholamines and metanephrines was positive for dopamine. Based on imaging and biochemical testing, a presumptive diagnosis of paraganglioma was made.

The tumor board recommended a "watch and wait" approach with repeat imaging in 3 to 6 months because of the morbidity associated with surgical and XRT interventions. A year later, the patient underwent a C6-C7 hemilaminectomy and discectomy, with relief of only his arm symptoms. Positron emission tomography (PET) scan performed 18 months after the start of his symptoms showed avid fluorodeoxyglucose uptake in the right-sided glomus vagale paraganglioma with no evidence of metastasis. Surgery was deferred as the tumor was within the carotid sheath with the potential for injury/damage to major vascular structures.

The patient underwent XRT. Immediately after its completion, he noticed a new constant pain in his right jaw and neck, a "pinching/choking" sensation in the midline neck, headache, xerostomia, and taste changes. Certain movements (turning to the opposite side) and positions of the neck made the pain much worse, including an inability to lay on either side affecting his sleep. Nonsurgical conservative measures, including physical therapy, stretching, and ice, as well as nonsteroidal anti-inflammatory drugs, did not significantly improve his pain.

He was then referred to the pain clinic for right-sided neck pain and headaches. On examination, he had exquisite tenderness to palpation over the sternocleidomastoid muscle (SCM). To ascertain the location of the pain in relation to the SCM muscle, in a

Figure 3. Ultrasound Images of the Right Side of Patient's Neck (A) Before and (B) After Second Injection



Abbreviations: SCM, sternocleidomastoid; CA, carotid artery; IJV, internal jugular vein; AS, anterior scalene; C7, cervical vertebra 7; PT, posterior tubercle of C7; PG, paraganglioma.

Arrows point to the in-plane needle.

Box. Complications Associated With Head and Neck Radiation Therapy

Xerostomia	Auricular problems/vertigo
Mucositis	Hearing loss
Trismus	Recurrent ear infections
Osteoradionecrosis	Dysarthria
Dysphagia ± feeding tube	Decreased vocal quality
Aspiration	Radiation induced fibrosis
Ageusia	Pain

maneuver like Carnett's sign, his head was turned to the opposite side, and he was asked to actively resist against pressure applied to his jaw, preventing him from turning his head This causes the SCM to be tensed, allowing for identification of the pain at or below the SCM (Shankar's maneuver). The pain was found to be deeper than the SCM, as he did not have any pain on palpation over the SCM when it was tensed. An ultrasound examination using a linear array transducer revealed significant hyperechoic areas between the SCM and anterior scalene muscles and in proximity to the carotid artery and internal jugular vein, suggestive of scarring or fibrous tissue at multiple locations.

The decision was made to release the adhesions using a large volume of steroid in saline mixture under ultrasound guidance. After informed consent, standard ASA monitors were applied, and an intravenous line was started. Using a linear array transducer, the area was scanned in both sagittal and axial views including color flow Doppler to plan a trajectory (Figure 2). Subsequently, a 25G hypodermic needle was advanced in an out-of-plane approach, and hydrolocalization using normal saline was used to locate the needle tip. Once appropriate fibrotic areas were accessed, 2 mL of solution was injected under real-time ultrasound guidance at 2 locations between the SCM and anterior scalene muscles in proximity to the carotid artery. The injectate contained 10 mg dexamethasone, 3 mL of normal saline, and 1 mL of 1% lidocaine. About a month later, the patient had a follow-up evaluation and reported that he had approximately 50% pain reduction that lasted about 5 days. He also endorsed ongoing improvement in baseline pain and noted that pain was rarely greater than 5/10. A similar injection was performed again under ultrasound guidance at other painful fibrotic areas, as we could not identify any fibrosis at the previous locations. This time the locations were accessible using an in-plane approach based on trajectory planning with color flow Doppler. He then followed up approximately 2 weeks later (Figure 3) and reported 90% pain reduction that was ongoing. He noted that pain was 2/10 that day, and the procedure was repeated this time closer to the paraganglioma to alleviate more of his pain.

At approximately 4.5 months, he started having neck pain again, and the procedure was repeated. He had 2 other episodes after that with good pain relief for approximately 10 weeks. He could not perform any physical therapy of his muscles due to his tremors, which may have prolonged the benefit. He insisted that we publish this report so that patients with similar complaints in his paraganglioma support group would also benefit. We obtained patient consent to publish this report.

DISCUSSION

A long-term side effect of XRT is radiation-induced fibrosis (RIF), which can result in functional impairment.[4] The most significant risk factors for RIF are treatment related, including both the total dose and dose per fraction of XRT, volume of tissue irradiated, and time course of treatment.[4] Other complications specific to head and neck XRT are listed in the Box.

As fibrosis progresses, pain and limited range of motion can develop, as seen in our patient. Our understanding of skeletal muscle injury following XRT is not very clear. Muscles with high glycolytic capacity have been shown to be most vulnerable for XRT-induced damage. Imatinib, simvastatin, enalapril, and dexamethasone are some medications that have demonstrated the ability to mitigate RIF pathology.[4] Fibrosis-causing adhesions has been a major cause for dysphagia following XRT, with almost 22% self-reporting swallowing difficulties.[5]

Adhesiolysis has been attempted and proved effective at multiple locations, including epidural and around peripheral nerves, scar tissues, and intraabdominal adhesions.[6] Surgical release has also proven successful for intrabdominal adhesions. Agents used for adhesiolysis include steroids, hypertonic saline, and hyaluronidase. Hypertonic saline injection can be painful; hence, local

anesthetics are added. Additionally, hypertonic saline can cause arrhythmias, pulmonary edema, ear pain, and hemiplegia. Besides being painful, hyaluronidase can cause anaphylactic shock.[6] Dexamethasone is a nonparticulate steroid safe for injection in highly vascular areas, as in our patient. If injected into carotid or, more importantly, vertebral artery, particulate steroids can cause major neurovascular injury, including paralysis. The 10 mg dose of dexamethasone is equivalent to 40 mg of depot methylprednisolone, which is commonly used for various injections including joints. The small amount of steroid added to the injectate potentially decreases inflammation and decreases further formation of fibrosis. However, steroids can cause various side effects, including bone demineralization, effects on glucose metabolism, and suppression of adrenocortical axis and, if given in large doses, may result in Cushingoid features.

In the few decades, the utilization of ultrasound imaging for needle guidance and bedside evaluation has increased tremendously. Ultrasound has multiple advantages, including lack of radiation, ability to visualize vascular structures and nerves, and portability. In addition, ultrasound guidance facilitates targeting in real time, helping to avoid critical structures in the vicinity. Although ultrasound imaging guidance has been utilized for release of scar tissue around peripheral nerves and intraoperative assessment during hysteroscopic adhesiolysis, challenging intermuscular adhesion release close to major vascular structures, as in our patient, has not been documented.[7] There is only 1 report of ultrasound-guided pressure injection of a large volume of steroid and local anesthetic anterior to the hip joint for release of scar tissue following arthroscopic repair of acetabular labrum.[8]

CONCLUSIONS

This report documents successful management of pain secondary to intermuscular adhesions secondary to fibrosis following XRT. Ultrasound imaging facilitated safe needle guidance and injection in an area surrounded by major vascular structures. Larger study of demonstration of ultrasound-guided injections is needed as RIF is widespread among those treated with XRT and can have a significant impact on quality of life.

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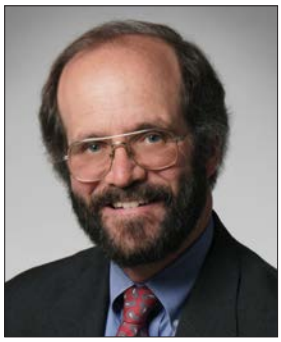

Robert N. Golden, MD

Stem Cell Science and Regenerative Biology: Tools for Building New Treatments

Deneen M. Wellik, PhD; Robert N. Golden, MD

Advances in medicine are dramatically improving patient outcomes. Solid tumors can be removed, the progression of heart disease can be slowed, and the ability to more effectively treat diabetes continues to advance, yet progress in regenerating diseased, damaged, or resected tissue has been limited. Advanced lung, heart, kidney, and liver disease too often lead to end-of-life care. There are no effective treatments to repair tissue damage following myocardial infarction or stroke. Muscular dystrophies remain progressive, debilitating diseases.

Stem cell and regenerative biology research drives the mission of the Stem Cell and Regenerative Medicine Center at University of Wisconsin–Madison and the Department of Cell and Regenerative Biology at the UW School of Medicine and Public Health (SMPH). Our vision includes gaining knowledge about how stem cells behave and translating those insights into new treatments. Current efforts focus on coaxing existing stem and progenitor cells to respond to catastrophic tissue damage, loss, or disease. Progress on this research frontier offers great potential for advancing clinical care.

• • •

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STEM CELL AND REGENERATIVE BIOLOGY RESEARCH IN WISCONSIN

UW–Madison has a storied history in stem cell research. One game-changing breakthrough was the 2007 demonstration that isolated human skin cells could be reprogrammed to return to a "stem cell-like" state. These "induced pluripotent stem cells" (iPSCs) can differentiate into the major cell types required to form a new organ. This discovery was immediately recognized for its potential to harness these cells to generate replacement tissue.

Labs at UW–Madison and around the world have found ways to coax iPSCs into hundreds of specific cell types. Breakthroughs were made possible following decades of basic developmental biology research that defined the signaling factors required for cell differentiation. Generating specific cell types from iPSCs relies on recapitulating these signals, including strict requirements for the order, concentration, and timing of treatment with these factors. The most notable successes in this approach include stem cell-based islet replacement therapy for Type 1 diabetes, a field that has advanced into clinical trials. This disease is caused primarily by the loss of a single cell type, pancreatic beta cells. Many research groups have focused on how iPSCs can be differentiated into beta cells, or at least into pancreatic progenitor cells that can mature further after transplantation. The latter process utilizes the body's ability to develop a new blood supply to the transplant and direct continued differentiation to functional beta cells. Clinical trials have reported encouraging results, allowing some patients to discontinue insulin treatment. More work is needed to decrease the risk of rejection of transplanted cells.

Replacing damaged or diseased organs requires the generation of complex structures that incorporate different cell types into functional tissue. One approach involves creating "organoids"—small, three-dimensional versions of organs that contain several differentiated cell types relevant for organ function. Organoids have been successfully generated for many tissue and organ types, including brain, kidney, and heart. While current organoids are not yet advanced enough for transplantation, they are already valuable for modeling for diseases, screening for drugs, and understanding the cell-to-cell interactions that are required for organ function. Colleagues at the SMPH are modeling brain organoids generated from human cells with Down syndrome and comparing neural development of these organoids to those generated from human cells without the trisomy abnormality of Down syndrome. Because patients with Down syndrome also have a greater risk for diabetes, iPSCs also may be used to create pancreatic organoids that could increase our understanding of the differentiation processes in pancreatic tis-

sues. In other labs, retinal organoids are being utilized for reproducing several key retina cell types. Recent work suggests that retina neural and ganglion cells generated by these methods can reestablish functional connectivity after transplantation.

Numerous challenges remain in the development of iPSC-based therapies. Producing the countless kinds of cells that make up a functional, complex organ requires a large, sustained effort. Successful generation and transplantation of a fully functional organ from an iPSC line theoretically would require generating iPSCs from each patient. Generating new iPSC lines from every human patient and completing the laborious and complicated process of new organ generation are daunting tasks. Researchers are actively exploring other means of avoiding rejection following transplantation by using human leukocyte antigen matches or iPSCs from compatible "super donors."

WHAT ARE THE "HOTTEST" NEW AREAS IN STEM CELL AND REGENERATIVE BIOLOGY?

Discoveries from the earliest era of regenerative biology research are opening doors to future advancements. In the 1950s, scientists found that salamanders can regenerate an entire limb after surgical removal; and in the 1990s, several groups reported that fish are capable of regenerating fins and hearts. In recent decades, advanced microscopy and molecular approaches led to the identification of progenitor cells in non-mammalian organisms that permit such regeneration. Surprisingly, these cells are not as special as this remarkable regenerative ability suggests. In the case of the regenerating limb or fin, existing reserve connective tissue of the injured limb is recruited via regenerative signaling to form a new "blastema," stem/progenitor cells that grow and undergo redifferentiation to replace the missing limb. Thus the "stem cells" are the normal stromal cells found in all limb tissues that can be reactivated for regeneration. In the fish heart, cardiomyocytes that undergo de-differentiation begin proliferating and subsequently replace the damaged heart tissue.

Parallel research in humans and other mammalian species has shown that most of our organs maintain similar reserves of organ-specific stem/progenitor cells. These cells can be induced to proliferate and give rise to the different cell types required for rebuilding an organ. Unfortunately, the potential for this restorative process in mammals is much lower than for other organisms. Scientists have learned much about the identity of reserve bone cells that are capable of extensive proliferation and regeneration of skeletal tissue; these are the cells we rely on for healing a fractured bone. Muscle stem cells also are capable of repairing moderately damaged muscle. However, if a limb is amputated or severely damaged, these reserve bone and muscle progenitors are incapable of mounting the level of repair and regeneration required for full replacement. Recent observations suggest this limitation is not due to a lack of regenerative capacity. Rather, there are two main roadblocks to human regeneration: our immune system and our metabolism. Humans have developed complex immune systems compared to other non-mammalian species. This highly evolved immune system serves us well in combatting viral or bacterial infections, but the strong inflammatory response triggered by severe injury or disease appears to block robust regenerative responses. Recent data also suggest that metabolic state has a tremendous influence on regenerative responses. Many regenerative systems across species rely on glycolysis, a relatively inefficient metabolic state that produces energy in cells quickly without requiring oxygen. Adult mammals, however, largely switch their metabolic profile to fatty acid oxidation, a slower but more efficient means of producing energy. While this metabolic change is ideal for overall health, it is incompatible with the cellular demands of regeneration. Developing ways to overcome this inhibitory effect of metabolism on regenerative capacity is one of the most exciting new areas of research.

The overall research trajectory in regenerative biology is extremely impressive. We are learning more each day about the control switches that regulate inflammatory responses and metabolism. And we continue to develop basic knowledge regarding how tissues and organs develop and regenerate normally. Ten years ago, available information suggested that regenerative organisms retained different kinds of cells compared to mammals, a limitation that would be difficult to address. Current research supports the idea that cells capable of mounting a full regenerative response exist in almost all human organs, including the brain. Researchers are focusing on understanding how these reserve stem/progenitor cells can be activated, and how we can block the inflammatory and metabolic responses that mute regeneration. These are not easy problems to solve, but the exceedingly rapid emergence of new findings provides great hope for the future.

We are learning more each day about the control switches that regulate inflammatory responses and metabolism. And we continue to develop basic knowledge regarding how tissues and organs develop and regenerate normally.

CONCLUSION

Regenerative biology does not have a dedicated institute at the National Institutes of Health (NIH), and federal funding in this area is insufficient to support all the promising avenues. While the NIH supports important work in this area, there is no centralized, coordinated approach. Expanded investment in stem cell research and regenerative biology will accelerate our progress in developing new healing modalities across the broad spectrum of human illness.

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