

# COVID-19 on mental health

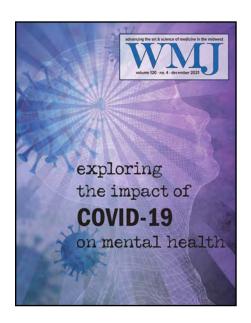




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#### **COVER THEME**

# Exploring the Impact of COVID-19 on Mental Health

The COVID-19 pandemic has shaken the health care environment to its core, heightening mental health issues in the general population and among clinicians. In this issue of WMJ, authors explore several issues related to COVID-19, clinician burnout, mental health interventions, and more.

Cover design by Kendi Neff-Parvin

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### The Impact of COVID-19 on Mental Health

Sarina Schrager, MD, MS, WMJ Editor-in-Chief

the quadruple aim, described in a seminal article in 2014 by Bodenheimer and Sinsky, establishes clinician health as a key metric for measurement of quality of care.1 And as Fojtik articulates in his commentary in this issue,2 the previously well-defined triple aim (enhancing patient experience, optimizing population health, and reducing health care related costs) is not attainable unless the health care team is healthy. Burnout, or the feeling of emotional exhaustion and inability to feel effective in daily practice, is rampant and is correlated with decreased quality of care.3 High electronic medical record responsibilities, patient volumes, and heightened acuity have all contributed to the high levels of burnout among clinicians. And when clinicians are unhappy and feel ineffective, patients are less healthy. Thus, health systems around the world are working to find ways to support clinicians and mitigate the ever-increasing pressures of patient care.

Meanwhile, the COVID-19 pandemic has further stressed health care providers. From the vast unknown about a brand-new virus, to shortages of personal protective equipment at the beginning of the pandemic, to frustration with unvaccinated patients now, clinicians have been continually challenged over the last 2 years. New clinical processes and personal safety issues have pushed many clinicians out of the field. Since February 2020, almost 18% of all health care workers have left their jobs.<sup>4</sup> Some data suggests that of those who remain, about a third have considered leaving. <sup>4</sup> Unfortunately,

as more clinical staff leave, the pressure on everyone else intensifies. Clinicians have demonstrated higher levels of anxiety and depression as well as posttraumatic stress disorder.<sup>5,6</sup>

out rate of 62% among the 43 respondents to the survey. Burnout rates were higher among women (78%) and were related to high patient volumes and unrealistic workload, which also

From the vast unknown about a brand new virus, to shortages of personal protective equipment at the beginning of the pandemic, to frustration with unvaccinated patients now, clinicians have been continually challenged over the last 2 years.

A paper in this issue by Jewell et al looks at coping strategies by emergency department (ED) providers during two waves of the COVID-19 pandemic.7 Data suggests that burnout is very high among ED providers at a baseline.8 In the Jewell study, around 70% of people noted increased stress due to the pandemic. The researchers categorized coping strategies as being positive ("approach") or negative ("avoidant"). The respondents described more approach coping than avoidant coping with some interesting distinctions. Women tended to use more approach coping strategies than did men, and residents tended to use more avoidant coping strategies than faculty.7 The physician assistants who responded to the survey described more excess stress than any of the other groups.

Another paper in this issue by Glisch et al looks at burnout rates among a group of academic hospitalists at the Medical College of Wisconsin.<sup>9</sup> This study found an overall burn-

interfered with the clinicians' ability to teach medical students. And there's little doubt hospitalists have been increasingly stressed due to the high COVID patient volumes that continue in Wisconsin.

Multiple programs to address clinician well-being have included enhancing team-based care, improving communication, and prioritizing wellness—as well as specific process issues that overburden clinicians. 10 Health care systems need to focus on these measures to successfully recruit and retain an excellent workforce.

The pandemic also has heightened mental health issues in the general population,<sup>11</sup> a topic addressed by authors of two papers also in this issue – one on the therapeutic effects of yoga<sup>12</sup> and another about the efficacy of a culturally adapted intervention for depression in African American adults.<sup>13</sup> Hampton and Bartz reviewed the literature, looking for evidence

that supports the use of yoga to treat certain medical and psychological conditions. They found that yoga improved both depression and back pain and served to promote overall health and improve mental health.<sup>12</sup> Ward et al found that a structured, culturally adapted class improved depression in a group of African American adults.<sup>13</sup> This study challenges the health care profession to adapt interventions for diverse populations of people.

Finally, as the COVID-19 pandemic has shaken the health care environment to its core, the *WMJ* continues to publish content on clinical and system issues related to this virus, including a papers in this issue regarding COVID management and cultural practices in the Hmong community<sup>14</sup> and more. To access a curated collection of all the papers *WMJ* has published regarding myriad aspects of COVID-19 in Wisconsin, visit our website.

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# The Three Confounding Elements of the Triple Aim

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### Health Equity Tourism: The *WMJ* Editorial Board Responds

C. Greer Jordan, PhD; Sherry-Ann Brown, MD, PhD; Sarina Schrager, MD, MS

AMA published a theme issue on August 17, 2021, focused on "racial and ethnic disparities and inequities in medicine and health care." A subsequently published commentary revealed that four of five of the lead authors of the original research papers in the JAMA issue were White.1 The concept of "health equity tourism" was coined. This concept captures how increasing attention and availability of funding for health equity research has attracted White researchers, some with little or no track record of research or scholarship in health equity, sometimes pushing out researchers of color. They use their established research networks, resources, and reputations to enter the field.

Health equity tourism presents two significant challenges to academic journals and trustworthy, quality science. First, a system that fosters the appropriation of the work of researchers and scholars who have devoted their careers to community-based and rigorous health equity research perpetuates inequity in

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science. Such inequity prevents the recognition and advancement of the work of the best scientists and scholars. Many career health equity researchers and scholars have lacked the resources, reputation, and knowledge-

Traditionally, journals do not request information about the race or ethnicity of authors or reviewers. Two surveys published in 2021<sup>3,4</sup> looked at the race/ethnicity of editors and editorial boards and found very low rates of

## The Editorial Board of the WMJ is committed to taking steps to ensure an anti-racist publication.

able peer reviewers to publish their work in high-status journals like *JAMA*. Second, health equity tourism may produce lower quality science or even incorrect science, which, in the case of racial health disparities, can severely impact Black, Indigenous, and People of Color (BIPOC) who already have poorer health and a lower life expectancy. Similar lack of access to prestigious publications has been demonstrated between male and female researchers as well.<sup>2</sup>

In early 2021, the *WMJ* published a special issue about the impact of race and racism on health in Wisconsin (wmjonline.org). There were a total of 20 articles published in this issue. Out of the 20 articles, seven first authors were BIPOC. The breakdown was as follows:

	lo. of BIPOC 1st Authors
Editorial/narrative/commentary (na	=8) 4
Original research (n=5)	2
Brief reports (n=6)	0
Review articles (n=1)	1

BIPOC members. Some of the criticism of racism in publishing identifies the fact that editors, editorial boards, and reviewers are overwhelmingly White. In the *JAMA* special issue, members of the editorial board provided some suggestions to improve accountability and transparency in medical publishing.<sup>5</sup> They suggest that journals measure outcomes by collecting information on the diversity of the editors and editorial boards, as well as reviewers and authors. The information to be collected includes:

- Effectiveness of processes developed to assure appropriate editorial review of all submissions.
- Diversity of the editorial staff.
- Number of publications about structural racism and health inequity.
- Diversity of reviewers.<sup>5</sup>

A blog published in July 2020 in *Health Affairs* provides a structured list of suggestions for journals to use in order to increase their inclusivity and focus on health equity by describing standards for publishing about

health equity and including guidelines for researchers, reviewers, and journal staff.<sup>6</sup>

The Editorial Board of the *WMJ* is committed to taking steps to ensure an anti-racist publication and to highlight the diversity and richness of our community. As such, we will work toward collecting data from all authors and reviewers to ensure diversity and transparency. Some future directions of the journal include:

- Explore ways to document race/ethnicity of authors and peer reviewers.
- Use the AAMC Health Equity Guide language to standardize the language used in the journal.<sup>7</sup>
- Find or create a repository of health equity researchers, in medicine in general and for subspecialties.
- Keep a list of health equity journals and peruse their authorship.
- Highlight community-based participatory research or action research in published papers.
- Browse Twitter lists to find health equity experts.

- Recruit health equity experts to the WMJ Editorial Board and as peer reviewers.
- Invite health equity experts to write invited commentaries or editorials.
- Encourage researchers to include community members as co-authors or collaborators
- Partner with the National Medical Association or statewide organizations for diverse clinicians on the above initiatives.

As we work to implement these steps, we invite your feedback.

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# The Three Confounding Elements of the Triple Aim

Joseph Edward Fojtik, MD, MPH

he United States health care system has been described as inefficient, delivering inconsistent levels of care and inordinately expensive; the question is not if it needs transformation but how to do so. In 2008, Donald Berwick and associates described the Triple Aim, in which improving the patient's experience of care, improving the health of populations of patients, and reducing the per capita cost of care may lead to a high-quality health care system, facilitating this transformation.<sup>1</sup>

Several issues have since evolved, impeding the Triple Aim from attaining its goals. Although several could be cited, three are of primacy: the decline of primary care, physician burnout, and the accumulating amount of unmeaningful work for practicing physicians. These three confound the Triple Aim, act as barriers to any meaningful transformation, and need mitigation to move forward; they also may be interrelated and irreducible to the extent correcting one requires correcting all.

Primary care continues to decline.<sup>2</sup> Despite several studies showing a strong primary care presence improves a community's health care

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outcomes,<sup>3</sup> it continues to be underfunded, challenged in recruiting medical students, and increasingly fragmented.<sup>4-6</sup>

Primary care spending, an index for primary care funding, has remained historically low in

care outside their generalist's purview, circumventing and minimalizing the patient-physician relationship.<sup>10</sup>

Team-based care and patient-centered medical home initiatives, among other devel-

# Of the three confounding issues to the Triple Aim, unmeaningful work may be the least understood and its adverse effects on primary care and physician burnout most underappreciated

the United States at 5.5% to 7.1% and compares unfavorably with other countries.7 This may partially explain the comparatively low income of generalist specialists and why medical students choose primary care in anemic numbers.8 Medical student recruitment also is challenged by primary care's demising prestige, which has been exacerbated by the recent political demands to expand scope of practice laws by other health care professions. Medical students may pause and consider that their education is now societally perceived to be not necessary in order to deliver presumptively equitable primary care. Primary care also has become more fragmented and difficult to manage. Generalists, increasingly electronically isolated and unaware of their patient's location in the medical neighborhood, may believe the "chart on the rake" is quiescent when, in fact, the patient is in a nearby intensive care unit (ICU).9 Patients, encouraged to be health care consumers, seek alternative modes of

opments, may reverse some of these trends. More innovated interventions are needed, as the decline of primary care adversely affects the Triple Aim by limiting access to the high level of quality care it implicitly requires.

The effects of physician burnout on physicians have been described for over 2 decades,<sup>11</sup> but only recently has its indirect sequalae on patients, populations of patients, and the cost of care been appreciated.

Patient care is directly affected by burnout. Medical errors, ICU mortality rates, and longer discharge recovery times are positively correlated with burnout and decrease the patient's experience of care. 12-14 Populations of patients are also indirectly affected. Increased physician turnover, decreased physician work effort, and productivity are positively correlated with burnout, 15-17 which impedes access to care, strains local health care resources, and destabilizes remaining physicians' patient panel sizes. 18 The cost of care is also affected. Increased medical

orders and referral rates<sup>19</sup> and increased physician turnover are all positively correlated with burnout, which increases health care costs. The decreased physician work effort and productivity, equivalent to the lost productivity of 7 graduating medical school classes,<sup>20</sup> may also transform simple, inexpensive care into delayed, expensive care.

Recent initiatives addressing burnout have been promising. Medical schools now incorporate physician burnout in their curricula, national organizations have wellness initiatives, and medical groups have initiated wellness committees with chief wellness officer positions. Although the prevalence of physician burnout has improved,<sup>21</sup> it remains significantly entrenched in the profession. More innovations are critically needed, as physician burnout affects the Triple Aim specifically at the 3 areas it endeavors to improve.

Of the 3 confounding issues to the Triple Aim, unmeaningful work may be the least understood and its adverse effects on primary care and physician burnout most underappreciated. Any work associated with direct patient care may be meaningful. However, work not licenselevel appropriate nor clinically relevant to the work at hand may be perceived as unmeaningful. Unmeaningful work could be further defined as cognitive work demanded upon a physician that is not license-level appropriate, adds no value to a clinical encounter, and typically must be completed to finalize that encounter. Further work is needed to refine unmeaningful work's definition and develop its taxonomy. Preliminary subgroups could include miscellaneous unmeaningful work units, electronic frustrations, and redundant layers of complexity.

Several examples of these subgroups could be given, but only a few will suffice to underscore unmeaningful work's subtle pervasiveness in medicine. Unmeaningful work units include the requirement of computerized physician order entries to be completed only by physicians due to the persistent misinterpretation of regulatory statutes associated with them.<sup>22</sup> Electronic frustrations, widespread within the now widely perceived dysfunctional electronic health record (EHR) ecosystem, include the seemingly endless EHR pop-ups intruding into a clinical encounter.<sup>23</sup> Redundant layers of com-

plexity are the added, unnecessary requirements health care entities compel physicians to complete to order to practice medicine within those entities and that supersede a Medical Practice Act's requirements and include discordant continuing medical education and maintenance of certification activities.<sup>24</sup>

Unmeaningful work intrudes upon the cognitive work needed in a clinical encounter, acts as a disrupter to care, and invades the cognitive workspace needed by a physician in that encounter. Recent work evaluating cognitive load in clinical settings has been promising,25 but further work on how unmeaningful work negatively affects physician well-being is needed. A principle or overarching ethic is also wanting-one that describes the physician's cognitive workspace utilized in a clinical setting and endeavors to safely protect it. Further studies also are needed to evaluate if protecting a physician's cognitive workspace decreases unmeaningful work, decreases physician burnout, and affects the ongoing demise of primary care.

The dysfunctional status of the US health care system persists. Meaningful transformation remains elusive. Several factors confound the Triple Aim, and unmeaningful work is the least understood. Its presence underscores that an ethic is needed to protect physicians and their cognitive workspace within a clinical setting.

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# Coping Strategies Utilized by Emergency Department Providers During the COVID-19 Pandemic

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#### **ABSTRACT**

**Introduction:** COVID-19 has exposed health care workers to new stressors; emergency department providers are at risk of increased stress. It is unknown how coping strategies are utilized by this group during a pandemic.

**Methods:** A cross-sectional survey incorporating the Brief COPE inventory was deployed to residents, fellows, faculty, and physician assistants at a single US academic emergency department in the spring (April 2020 - May 2020) and winter (December 2020 - January 2021). Scores for 14 individual coping strategies, as well as approach (positive) and avoidant (negative) coping categories, were measured, and utilization of these coping strategies was compared with respect to the provider's role, sex, number of people living at home, presence of pets and/or children at home, and stress level.

Results: The response rate was 58/103 (56.3%) and 50/109 (45.9%) for the spring and winter distributions, respectively. In the spring, 70.6% of responders reported increased stress vs 66% in the winter. Overall utilization of coping strategies increased slightly between spring and winter for approach coping (32.22 to 32.64) and avoidant coping (20.95 to 21.73). Resident physicians utilized less approach coping and more avoidant coping when compared to faculty/fellows. Substance use overall had a relatively low score, which increased slightly between spring and winter distributions (2.93 to 3.04).

**Conclusions:** Approach coping was frequently utilized among ED providers during the COVID-19 pandemic study period. Resident physicians had higher utilization of avoidant coping strategies compared to faculty/fellows and could benefit from targeted wellness interventions during times of increased stress.

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#### **INTRODUCTION**

The SARS-CoV-2 virus that caused the COVID-19 pandemic has brought massive changes to emergency departments (ED) around the world, as new policies and protocols were implemented in response to new data. Increased stress, anxiety, depression, and burnout in health care workers is widespread as hospitals struggle to continue to provide care during one of the most severe global health crises in history. 1,2 As the pandemic has continued, ED providers have dealt with unprecedented work-related stressors, including fluctuating ED volumes and hospital overcrowding.3 Emotional exhaustion and burnout among ED physicians, as well as increased stress both at home and at work, have significantly increased since the pandemic began in early 2020.4 In addition, many aspects of daily life have yet to return to normal, severely decreasing the availability of protective factors against burnout over a prolonged period, including access to ED providers' extended family and friends,

participation in hobbies or interests, and opportunities for community engagement.<sup>4</sup> Finally, though the vast majority of US physicians have now been able to receive COVID-19 vaccines,<sup>5</sup> they must still deal with whether their families (some of whom may not be vaccinated) will contract the virus, the uncertainty of when their previous work routines can return, and the potential for decreased job security that has come from reduced utilization of emergency departments.<sup>3,6</sup>

In times of stress, individuals will respond differently by employing coping strategies to overcome stressors. Positive coping

strategies (also known as approach coping) help individuals experiencing stress deal with it in a productive manner; these include acceptance, reframing, and planning (Table 1).7 However, physicians are known to be an at-risk group for negative coping mechanisms (also known as avoidant coping) that may exacerbate stress, such as substance use, venting, and denial.8 An understanding of provider coping strategies—especially during times of increased departmental stress (eg, fluctuating volumes, staffing changes) is essential in order to develop appropriate infrastructure to support providers during these difficult times. While there are multiple measures of coping strategies, there is validity evidence for the Brief COPE inventory in multiple populations—including patients and medical professionals—as an efficient and effective means of measuring both approach and avoidant coping strategies.9-11 More recently, the Brief COPE has been utilized in the general population living in lockdown, as well as with those struggling with chronic comorbidities during the COVID-19 pandemic. These studies have revealed an association between use of negative coping strategies (eg, denial, substance use, and venting) during the pandemic and increased stress and rates of mental illness (eg, anxiety and depression).12,13

The utilization of coping strategies in emergency physicians in areas outside the US has been described in prior research. These studies utilized different scales of coping—including the Ways of Coping Questionnaire and the Jalowiec Coping Scale Part A (JCS-A)—and revealed an overall high use of positive adaptive strategies, particularly planning and eliciting emotional support from others. 14-16 Additional work has revealed increased distress of the ED workforce in the context of the severe acute respiratory syndrome (SARS). 17 However, these studies are dated, and coping strategy utilization may be significantly altered in the setting of the global pandemic.

The experience of the state of Wisconsin with the COVID-19 pandemic paralleled the experience of much of the US: while spring 2020 brought the most rapid and acute changes in the form of lockdowns and school closures, fall and winter brought the largest surge of cases after months of pandemic fatigue. This study aimed to investigate the degree of coping strategy utilization among ED providers during the SARS-CoV-2 pandemic, as well as any differences that arose at different phases of the pandemic.

#### **METHODS**

#### Study Design, Setting, and Population

A cross-sectional survey was administered to all residents, fellows, faculty, and physician assistants (PA) who worked at least part time in a single academic emergency department in the Midwest during April 2020–May 2020 of the COVID-19 pandemic ("spring") and December 2020–January 2021 ("winter"). All providers in this group were eligible for participation. In our ED, fellows treat patients independently of staff residents and PAs. Participants were contacted via email using departmental listservs. There were 103

Coping Strategy	Description
Approach	
Acceptance	Learning to accept that the problem exists
Active coping	Taking actions to correct the problem
Positive reframing	Attempting to reassess the problem in a positive light
Use of emotional support	Seeking empathy from others
Planning	Devising a plan to overcome the problem
Use of instrumental support	Seeking advice on correcting the problem from other sources
Avoidant	
Self-distraction	Focusing on other activities to take one's thoughts off the problem
Venting	Expressing negative emotions concerning the problem
Self-blame	Blaming or criticizing one's self for the problen
Substance use	Using alcohol or other drugs as a means of dealing with the problem
Behavioral disengagement	Giving up taking actions to solve the problem
Denial	Refusing to accept the problem exists
Jncharacterized	
Humor	Making fun of the situation
Religion	Turning to religious beliefs (new or old) as a means of support

eligible providers during the first survey distribution and 109 in the second distribution due to changes in active staff roster. The study institution is associated with a 3-year emergency medicine (EM) program that has 12 residents per class. The authors were excluded from participation as they were involved with study design.

#### **Study Protocol**

The survey was deployed to all participants on April 30, 2020 and December 31, 2020. Three preplanned reminder emails were sent out at approximately 1-week intervals to enhance the response rate. Both surveys were closed 4 weeks after they were deployed. In-person reminders also were presented to participants at weekly departmental didactic conferences and the monthly departmental faculty meeting. The survey was administered anonymously online using Qualtrics (Provo, Utah). Overall response rate was calculated using the second definition of response rate as defined by the American Association for Public Opinion Research (AAPOR).<sup>18</sup> The authors had no means of determining the identity of who had filled out the survey, and responding was explicitly stated to be voluntary in the recruitment emails. No inducements for survey completion were implied or offered, and no compensation was provided to respondents. The data were compared between survey distributions to determine if the utilization of coping strategies by ED physicians changed between the spring and winter phases of the pandemic. The study design was submitted to the study site's institutional review board and was determined to be exempt from formal review.

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Demographics	Spring Responders (%)	Winter Responders (%)
Staff role		
Residents	19 (32.7)	17 (34.0)
Faculty/Fellows	29 (50.0)	27 (54.0)
Advance Practice Providers	10 (17.2)	6 (12.0)
Sex		
Male	33 (56.9)	30 (60.0)
Female	24 (41.4)	20 (40.0)
No. other people living in home		
0	7 (12.1)	11 (22.0)
1+	51 (87.9)	39 (78.0)
Children living at home (at least part-	time)	
Yes	30 (51.7)	21 (42.0)
No	28 (48.3)	29 (58.0)
Pets living in the home		
Yes	40 (69.0)	35 (70.0)
No	18 (31.0)	15 (30.0)
Average stress level over last 2 mont	hs	
Above average	41 (70.7)	33 (66.0)
Average/below average	17 (29.3)	17 (34.0)

Coping Strategy	Spring Mean Score (95% CI)	Winter Mean Score (95% CI)
Approach	32.22 (30.76-33.67)	32.64 (31.06-34.22
Acceptance	6.55 (6.23-6.86)	6.70 (6.33-7.08)
Use of emotional support	5.38 (4.95-5.80)	5.55 (5.09-6.00)
Active coping	5.36 (4.98-5.75)	5.21 (4.73-5.69)
Positive reframing	5.29 (4.90-5.69)	5.34 (4.89-5.79)
Planning	5.20 (4.85-5.55)	5.05 (4.63-5.47)
Use of instrumental support	4.42 (4.06-4.78)	4.75 (4.37-5.13)
Avoidant	20.95 (19.90-21.99)	21.73 (20.38-23.08
Self-distraction	5.36 (4.97-5.75)	5.14 (4.68-5.59)
Venting	4.47 (4.07-4.87)	4.64 (4.26-5.01)
Self-blame	3.29 (2.93-3.65)	3.75 (3.32-4.18)
Substance use	2.93 (2.57-3.29)	3.04 (2.61-3.48)
Behavioral disengagement	2.54 (2.30-2.77)	2.68 (2.41-2.95)
Denial	2.38 (2.19-2.57)	2.47 (2.19-2.75)
Uncharacterized		
Humor	5.00 (4.56-5.44)	5.57 (5.09-6.05)
Religion	3.13 (2.69-3.56)	3.18 (2.72-3.64)

#### **Survey Development**

The survey instrument consisted of multiple demographic questions as well as the Brief COPE inventory (Appendix). The Brief COPE inventory consists of 28 total questions, with 2 questions corresponding to each of 14 coping strategies. These coping strategies are listed in Table 1. The frequency of an individual's use of these strategies results in the summation of two 4-point scales (with 1 corresponding to "I have not been doing this at all" and 4 corresponding to "I have been doing this a lot"), creating an overall score of 2 to 8. Though not recommended as a part of the original Inventory by its creator, prior work has found validity

evidence that these 14 coping strategies can be further grouped into 2 larger subscales of 6 known as "approach" (positive) and "avoidant" (negative) coping. (The remaining 2 strategies, humor and religion, are not easily characterized by either the approach or avoidant category.)<sup>10,20</sup> Scores for these 2 subscales were calculated as the sum of each of the 12 questions corresponding to the 6 included coping strategies, resulting in an overall score of 12 to 48, with higher scores indicating higher utilization of these coping strategies. The survey was reviewed and edited with input from the Emergency Medicine Research Committee at the study site prior to deployment.

#### **Statistical Analysis**

Descriptive statistics were calculated for the approach and avoidant categories for the overall study population. Subgroups were generated based on role (residents, faculty/fellows, PAs), sex (male or female), whether the responder lived alone or with others, whether or not children lived in the home (yes or no), whether or not pets lived in the home (yes or no), and self-reported average stress level over the past 2 months (below average/average or above average). The average scores on the approach and avoidant categories were calculated, along with 95% confidence intervals. If a respondent did not answer one or both questions referring to a particular coping strategy, their score for that coping strategy was excluded from final analysis. Respondents who did not answer enough questions from the Brief COPE to meet at least the minimum score for approach or avoidant coping (12/48) were excluded from the final analysis to avoid negatively skewing the results. The subgroups were compared using 2-sample Wilcoxon rank sum tests. Results from the survey were analyzed in the same manner for both the spring and winter data. Overall sample scores also were compared between the current sample and the data collected from spring using Wilcoxon rank-sum tests. The authors utilized an alpha-level of 0.05 to determine whether differences were statistically significant. A wave analysis was conducted to assess for nonresponse bias using the data from responders within the last week of the survey as a proxy for those who did not respond based on the average scores on the approach and avoidant categories of the Brief COPE. This was calculated separately for the spring and winter data. Statistical calculations were made using STATA v 15 (College Station, Texas), except for the wave analysis, which used Microsoft Excel (Redmond, WA).

#### **RESULTS**

The overall response rate of those who responded at least partially was 58/103 (56.3%) and 50/109 (45.9%) for the spring and winter distributions, respectively. Three respondents with partial filled-out surveys were excluded (5.17%) from the spring distribution and 6 were excluded from the winter distribution (12%). The baseline characteristics of responders are shown in Table 2.

ED staff utilized all 14 coping strategies to varying degrees.

Overall, responders tended to use approach coping rather than avoidant coping. The mean score for approach coping was 32.22 (95% CI, 30.8-33.7) in the spring and 32.64 (95% CI, 31.1-34.2) in the winter. For avoidant coping, the mean score was 21.0 (95% CI, 19.9-22.0) in the spring and 21.7 (95% CI, 20.4-23.1) in winter. The most frequently employed overall coping strategy was "acceptance;" the least likely coping strategy to be employed was "denial." Table 3 shows the mean scores of all responders for each of the 14 individual coping strategies.

In the spring, females utilized significantly more approach coping strategies when compared to male responders (average 32.55 vs 30.24; P = 0.037). Those living alone utilized significantly more avoidant coping versus those living with at least 1 other person (23.64 vs 21.34; P=0.0408). Additionally, residents also utilized significantly more avoidant coping than faculty or fellows (22.47 vs 19.48; P = 0.0117). Those reporting above average stress utilized significantly less avoidant coping than those reporting average or below average stress levels during the pandemic (20.00 vs 22.13; P=0.0201). Table 4 shows approach and avoidant coping across various subgroups during the spring and winter distributions.

During the winter, there were no significant differences between male and female respondents in approach or avoidant coping strategies used. Resident physicians utilized significantly less approach coping than faculty or fellows (29.25 vs 34.35; P<0.05), a change from the spring. Resident physicians continued to utilize more avoidant coping than faculty or fellows in the winter, but this was not significant (23.67 vs 20.77; P=0.057). Finally, those without children showed significantly more avoidant coping than those with children (23.46 vs 19.65; *P*<0.05).

There were no significant differences in approach or avoidant coping between spring and winter distributions (Table 4).

ED providers largely self-reported they were experiencing above average stress during the pandemic, with the proportion decreasing slightly in the winter of the pandemic (70.7% to 60.0%). PAs reported the highest rates of above average stress in both survey distributions (100% and 83.3% for early and late pandemic, respectively).

The wave analysis did not show a significant degree of nonresponse bias for the analyzed variables. Test statistics for the wave analysis can be seen in Table 5.

#### **DISCUSSION**

Our study assessed coping strategies utilized by physicians and PAs during a pandemic in an academic emergency medicine department with a yearly volume of approximately 60,000 patients. As a whole, department staff demonstrated a tendency towards approach versus avoidant coping.

Resident physicians engaged in a higher proportion of avoidant coping strategies when compared to faculty or fellows in the spring of the pandemic. However, as the pandemic went on, it seems that this difference did not persist; instead, residents were noted to use

	Subgroup/ Category	Mean (95% CI)	P value
Spring			
Sex	Male	Female	
Approach	30.24 (28.61 - 31.87)	32.55 (30.93 - 34.17)	0.0370
Avoidant	20.60 (19.32 - 21.87)	22.23 (21.04 - 23.43)	0.1163
Role	Resident	Faculty/Fellows	
Approach	31.10 (28.60 - 33.61)	32.70 (30.54 - 34.87)	0.2449
Avoidant	22.47 (20.59 - 24.36)	19.48 (18.04 - 20.92)	0.0117
Lives alone	Yes	No	
Approach	33.00 (30.16 - 35.84)	31.32 (30.01 - 32.63)	0.4165
Avoidant	23.64 (21.49 - 25.80)	21.34 (20.39 - 22.28)	0.0408
Children	Yes	No	
Approach	30.87 (29.14 - 32.61)	32.11 (30.41 - 33.82)	0.2975
Avoidant	20.78 (19.53 - 22.04)	22.06 (20.95 - 23.18)	0.0909
Pets	Yes	No	
Approach	31.30 (29.84 - 32.77)	32.00 (29.86 - 34.14)	0.6735
Avoidant	21.77 (20.63 - 22.91)	21.25 (19.96 - 22.54)	0.7096
Stress level	Above average	Average/below average	
Approach	30.03 (27.50 - 32.57)	32.00 (30.64 - 33.36)	0.2733
Avoidant	20.00 (17.95 - 22.05)	22.13 (21.19 - 23.08)	0.0201
Winter			
Sex	Male	Female	
Approach	33.36 (31.27 - 35.45)	31.68 (29.10 - 34.27)	0.1577
Avoidant	21.32 (19.53 - 23.11)	22.26 (20.03 - 24.50)	0.5121
Role	Resident	Faculty/Fellows	
Approach	29.25 (26.78 - 31.72)	34.35 (32.15 - 36.55)	0.0078
Avoidant	23.67 (20.62 - 26.71)	20.77 (18.97 - 22.57)	0.0579
Lives alone	Yes	No	
Approach	30.50 (27.11 - 33.89)	33.18 (31.31 - 35.05)	0.2375
Avoidant	22.3 (20.42 - 24.18)	21.45 (19.71 - 23.19)	0.3185
Children	Yes	No	
Approach	33.70 (31.22 - 36.18)	31.75 (29.62 - 33.88)	0.2149
Avoidant	19.65 (17.85 - 21.45)	23.46 (21.68 - 25.24)	0.0018
Pets	Yes	No	0.0010
Approach	32.90 (31.06 - 34.74)	3207 (28.67 - 35.47)	0.6586
Avoidant	21.63 (19.91 - 23.36)	21.93 (19.51 - 24.35)	0.7999
Stress level	Above average	Average/below average	0.7555
Approach	31.27 (28.14 - 34.40)	33.34 (31.48 - 35.21)	0.1270
Avoidant	20.60 (18.65 - 22.55)	22.31 (20.48 - 24.14)	0.3130
Timing of survey	Spring	Winter	0.0100
Approach	32.22 (30.76-33.67)	32.64 (31.06-34.22)	0.7887
Avoidant	20.95 (19.90-21.99)	21.73 (20.38-23.08)	0.5018

significantly less approach coping when compared to fellows or faculty. This is concordant with prior data that indicate residency as a time of greater mental health risk and potentially use of less constructive coping strategies, such as self-blame.<sup>18</sup> Because of this, EM resident physicians previously have been targeted for wellness interventions, including targeting adaptive coping skills such as use of emotional support.<sup>21</sup> The results from this study suggest that these efforts may need to be redoubled during times of stress.

The lack of significant differences between faculty, residents, and PAs in their utilization of approach and avoidant coping suggests

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	Proportion of NR	Mean Early Responders	Mean Late Responders	Mean Early- Mean Late	Nonresponse Bias (Max)
arly					
Approach	0.436893	32.878	35.000	2.122	0.927 (48)
Avoidant	0.436893	22.780	23.500	0.72	0.315 (48)
Humor	0.436893	5.073	6.500	1.427	0.623 (8)
Religion	0.436893	3.098	3.750	0.652	0.285 (8)
.ate					
Approach	0.541284	33.000	28.800	4.190	2.27 (48)
Avoidant	0.541284	21.500	21.476	0.0238	0.0129 (48)
Humor	0.541284	5.170	5.670	0.500	0.271 (8)
Religion	0.541284	3.060	3.330	0.278	0.150 (8)

that ED providers tend to employ similar types of coping strategies whether they operate in a learner or supervisory role. Previous work has found that ED staff tend to employ coping strategies similarly regardless of department size, 15 although a study examining distress levels and coping strategies during the 2002-2003 Severe Acute Respiratory Syndrome (SARS) pandemic in China found that employees with different departmental roles experienced varying levels of distress, though this study also included other ED staff such as nursing and nursing assistants not captured in the current study. 17 Our study suggests coping strategy-based wellness interventions can be targeted at all providers and do not need to be broken up by departmental role.

The most heavily used coping strategy overall was "acceptance" during both spring and winter. The approach coping strategies of "active coping" and "use of emotional support" were also employed as often or more frequently than any avoidant strategies. This is consistent with prior research done in China during the initial SARS pandemic in which these coping strategies were also noted to be used heavily, as well as other studies specifically looking at the coping strategies used by ED physicians. 14-17 It is unclear whether or not an inherent characteristic of the pandemic lends itself more towards "acceptance" or "active coping" as compared to other stressors placed on health care providers. For example, it has been popularly noted that the pandemic caused a beneficial increase in family time and a decrease in in-person work meeting obligations for some. 22

There was an increase in the number of providers who utilized "substance use" heavily (score > 6) as the pandemic went on (5% in the early pandemic to 12% in the late pandemic). This is consistent with prior research indicating ED physicians have relatively high rates of substance use.<sup>8,23</sup> Importantly, rates of substance use reported here initially were lower than what has been reported elsewhere, but, as the pandemic went on, increased to previously reported levels for physician substance use.<sup>24</sup> However, the previous baseline within our study population is unknown, and whether this represents a sampling issue or a behavior change

early in the pandemic is unclear. Those most likely to report substance use as a coping strategy were those who reported increased stress versus those who did not. This fits with prior literature indicating a relationship between acute stress and alcohol intake, although the directionality of this relationship in our study is unclear.<sup>25</sup> Future research may be directed towards identifying and supporting this subgroup.

Participants who reported living alone did not differ significantly from those living with others in their utilization of approach coping at either time point. However, these participants were noted to be more likely

to engage in avoidant strategies in the spring, suggesting that living alone may be associated with important differences in one's coping strategies. Social isolation previously has been identified as a risk factor for an impaired response to stress and an independent risk factor for mortality.<sup>26,27</sup> While professional social isolation has been described n the literature,<sup>28</sup> to our knowledge, this is the first study to look at providers from the perspective of their home lives and deserves future study. However, by winter, this effect was no longer seen, perhaps suggesting that those who live alone were able to identify more productive coping mechanisms on their own. Given the possible detrimental health effects of social isolation, individuals reporting high levels of avoidant coping may benefit substantially from targeted interventions creating increased opportunity for social interaction.

Taken in aggregate, there were no overall differences in approach and avoidant coping as the pandemic continued. However, resident physicians were found to have increased avoidant and decreased approach coping. Additionally, those without children and those living alone were found to have increased utilization of avoidant coping. Therefore, these groups may be the highest yield for departmental support initiatives.

#### Limitations

The survey was only deployed to a single academic hospital emergency department. Therefore, the results may not be generalizable to other regions or other ED environments. Our response rate for both surveys was relatively low, which could have led to potential nonresponse bias. However, this is a common problem with survey studies, especially those assessing health care populations.<sup>29</sup> Our response rates were similar to what has been reported previously in this population, and the wave analysis did not show a considerable amount of calculated nonresponse bias in the selected questions (indicating that nonresponders likely did not differ significantly from responders to the survey). In addition, it is possible that differences between our sample and the previously collected data are due to differences in sampling given the response rate in both

survey distributions. Given that the survey was distributed using departmental listservs and answers were anonymous, the survey did not exclude any providers who began or ended employment at our institution during the time between survey distributions. This likely led to the discrepancy in the sample sizes between the 2 survey distributions.

Because the surveys dealt with sensitive topics like substance use and maladaptive coping, it is possible that social desirability bias may have affected participants' willingness to honestly report problematic behaviors. Furthermore, it is possible that the high frequency use of negative coping strategies reported by residents may be due to inherent stress experienced during the demands of residency training and unrelated to the current pandemic. This latter possibility represents a potential avenue for future research.

#### **CONCLUSIONS**

Positive approach coping strategies continue to be widely used by ED providers, suggesting that most have developed a variety of successful strategies for dealing with the stress of being on the front lines of the current pandemic. While there were no overall differences in coping utilization as the pandemic continued, several groups appeared to be at higher risk for less adaptive avoidant coping strategies. These groups included resident physicians, staff who live alone, and those who do not have children. Therefore, these groups may gain the most benefit from future targeted interventions during times of crisis.

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### Perceptions of Burnout Among Academic Hospitalists

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#### **ABSTRACT**

Introduction: There is a paucity of data on burnout among academic hospitalists in Wisconsin.

**Objective/Methods:** To evaluate perceptions on burnout among academic hospitalists at an academic center in Wisconsin, a survey was distributed to academic hospitalists at the Medical College of Wisconsin. Questions addressed job satisfaction, factors contributing to burnout and its consequences, and various preventive steps. A section was included for respondents to provide any additional comments.

**Results:** Out of 52 academic hospitalists surveyed, 43 (83%) responded. Sixty-two percent of participants reported feeling burnout. Burnout rates did not differ by gender (males vs females, 58% vs 73%, respectively; P=0.65), career length as a hospitalist (P=0.28), or satisfaction as a hospitalist (P=0.11). High patient census (94%) and unrealistic workload (83%) were the most commonly cited factors for burnout. Possible consequences of burnout included lack of enthusiasm (95%) and mental exhaustion (93%). A majority of respondents (81%) indicated that high clinical demands interfered with their ability to teach medical students. Improving the structure of work (88%) and incorporating respect, care, and compassion as a group culture (88%) were the most common themes reported to prevent burnout.

**Conclusion:** This study shows a high prevalence of burnout among academic hospitalists and highlights various opportunities to reduce burnout risk.

#### INTRODUCTION

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The term burnout was first coined by psychologist Herbert Freudenberger and recently has been recognized as an occupational phenomenon in the World Health Organization's (WHO) 11th revision of the International Classification of Disease (ICD-

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11).<sup>1,2</sup> Dr Freudenberger ran a practice on New York City's Upper East Side and also started a free clinic on the Bowery, where he cared for young clients who abused drugs.<sup>3</sup> He observed that many of his clients held cigarettes, watching as they burned out – thus the inspiration for the term "burnout."

In recent years, burnout has been a topic of big concern among physicians. Burnout is a work-related syndrome involving 3 chief dimensions: emotional exhaustion (losing enthusiasm for work), depersonalization (treating people as if they were objects), and a sense of low personal accomplishment (having a sense that work is no longer meaningful).<sup>4</sup> Numerous studies involving nearly every medical and surgical specialty indicate that approximately 1 out of 3 physicians is experiencing burnout at any given time.<sup>5,6</sup> Physician

burnout may affect core domains of health care delivery, including patient safety, quality of care, and patient satisfaction. However, this evidence has not been systematically quantified. Salyers et al conducted a meta-analysis of 82 studies on 210,669 health care providers that showed consistent relationships with perceived poorer quality health care, reduced patient satisfaction, and lowered safety for patients. Further investigation of burnout is critical given its association with increased physician turnover, poor quality of care, and adverse personal consequences for physicians and their families. 8.9

Physican burnout has been increasingly studied and recongized over the past several decades; however, few studies have specifically examined how burnout affects academic hospitalists. 10,11

Variables	n (%)
Sex (N=43)	
Male	26 (61%)
Female	16 (37%)
Prefer not to respond	1 (2%)
Time as hospitalist (N=43)	
0-3 years	18 (42%)
4-6 years	11 (26%)
7-9 years	9 (21%)
≥10 years	5 (12%)
Are you satisfied with working as a hospitalist? (N=42) <sup>a</sup>	
Extremely dissatisfied	2 (5%)
Somewhat dissatisfied	3 (7%)
Neither satisfied nor dissatisfied	6 (14%)
Somewhat satisfied	28 (67%)
Extremely satisfied	3 (7%)
Have you experienced burnout as a hospitalist? (N=42)a	
Yes	26 (62%)
No	7 (17%)
Not sure	9 (21%)

Hospital medicine is a relatively new specialty with a unique aspect of work-life balance. It includes various clinical and non-clinical responsibilities like medical education and research, which possibly can place hospitalist physicians at high risk of burnout. We conducted a survey-based project with academic hospitalists at the Medical College of Wisconsin regarding job satisfaction, perceptions on burnout and its consequences, and approaches to improve burnout.

#### **METHODS**

#### **Study Design and Survey Elements**

Froedtert Hospital and the Medical College of Wisconsin (MCW) is an academic tertiary care center based in Milwaukee, Wisconsin, with 607 beds and over 31,000 inpatient admissions annually. A web-based Qualtrics survey (www.qualtrics.com) was emailed to all 52 academic hospitalists based at Froedtert Hospital and MCW. All responses were anonymous. In addition to collecting demographic information and general perceptions of burnout, the survey also aimed to capture information regarding several elements related to burnout, including job satisfaction, factors leading to burnout, the effects of burnout, and preventive steps. The responses were obtained either on a dichotomous (yes/no) or a 5-point Likert scale (strongly disagree, disagree, neutral, agree, strongly agree). A section to solicit anonymous, open-ended comments also was included. The study was approved by the MCW institutional board review.

#### **Statistical Analysis**

Data were analyzed as respective frequencies and percentages. Association between the variables, which were essentially categori-

Possible Factors Leading to Burnout	Agree/ Strongly Agree n (%)
High patient load/census (N=42)	39 (93%)
Unrealistic work load/feeling over worked (N=42)	35 (83%)
Caring for complex and demanding patients (N=42)	34 (81%)
Feeling pressured by higher expectations (teaching, providing excellent patient care, meeting provider performance metrics, administrative duties, scholarly projects, etc) (N=42)	33 (79%)
Unpredictability in the work structure and patient volume (N = 4.	2) 33 (79%)
Lack of transparency/communication between leadership and hospitalists (N=42)	31 (74%)
Pushback from the consult services on the requested consults: hesitation or refusing to see patients (N = 42)	31 (74%)
Not feeling valued as a hospitalist by the residents and other subspecialty peers (N=42)	29 (69%)
Lack of recognition/reward/incentive for your performance (N = 42	2) 27 (64%)
Dissatisfaction with compensation/incentives despite increased clinical duties (N = 42)	26 (62%)
Feel unsupported by leadership (N=42)	24 (57%)
Lack of flexibility/work life balance/amount of control over work schedule (N = 42)	23 (55%)
Do not feel as a part of a group/poor group dynamics (N = 42)	21 (50%)
Lack of protected time for scholarly projects (N=42)	19 (45%)
Lack of structured mentorship for career guidance/professional development/scholarship (N=42)	18 (43%)
Uncertainty about your career as a hospitalist (N=42)	18 (43%)

cal, was analyzed using the chi-square test. All tests were 2-sided and *P* values < 0.05 were considered statistically significant. All analyses were performed using SAS 9.4.

#### **RESULTS**

Forty-three Medical College of Wisconsin hospitalists (83%) responded, although some did not complete all questions. Twenty-six (61%) were male and 18 (42%) had been working as a hospitalist for  $\leq 3$  years (Table 1). Only 3 (7%) said they were extremely satisfied working as a hospitalist, whereas 28 (67%) said they were somewhat satisfied. Twenty-six (62%) reported experiencing burnout, while 7 (17%) did not, and 9 (21%) were unsure. Factors that respondents said most contributed to burnout were high patient census (n = 39, 93%), unrealistic workload or feeling overworked (n = 35, 83%), caring for complex and demanding patients (n = 34, 81%), feeling pressured by higher expectations (n = 33, 79%), unpredictability in work structure and patient volume (n = 33, 79%), and lack of transparency or communication between leadership and hospitalists (n = 31, 74%) (Table 2).

Hospitalists reported the most common consequences of burnout were lack of enthusiasm and energy to work (n = 39, 95%), followed by mental exhaustion (n = 38, 93%), doubt that their work made a difference (n = 33, 83%), physical exhaustion (n = 33, 81%), feeling their personal life has been affected negatively

**Table 3.** Perceptions of Hospitalists Regarding Possible Consequences of Rumout

Possible Consequences of Burnout	Agree/ Strongly Agree n (%)
Lack of enthusiasm and energy to work (N = 41)	39 (95%)
Mental exhaustion (N = 41)	38 (93%)
Doubt that your work really makes any difference or question the quality of your work (N=40)	33 (83%)
Physical exhaustion (N=41)	33 (81%)
Feeling that your personal life has also been affected negatively $(N=40)$	31 (78%)
Feeling that the quality of your life has been compromised (N=4	0) 31 (78%)
Feeling detached/depersonalization/cynicism (losing your ability to interact, empathize, and connect with your patients and coworkers) ( $N=41$ )	31 (76%)

**Table 4.** Perceptions of Hospitalists Regarding Various Possible Steps That Can Prevent Burnout

Possible Steps to Prevent Burnout	Agree/ Strongly Agree n (%)
Improving the structure of the work/manageable workload (N=41 Incorporating respect, care and compassion among the hospitalist as a group culture (N=41)	36 (88%) 36 (88%)
Improving coordination/support from other sub specialists and consult services (N = 41)	34 (83%)
Increased or more competitive compensation, incentives, acknowledgments, rewards, or awards (N=41)	34 (83%)
Protected time for scholarly pursuits (N = 41)	34 (83%)
Transparency in policy and communication within the group ( $N=4$ )	31 (76%)
A strong mentorship program to support personal and professional development (support to achieve goals including promotion, leadership, scholarship and overall career development) (N = 41)	ıl 28 (68%)
Increased leadership role in monitoring and preventing burnout issues (N = 41) $$	27 (66%)
A wellness program or faculty resilience training to support the hospitalists (N = 41) $$	24 (59%)

(n=31, 78%), and feeling that the quality of their life has been compromised (n=31, 78%) (Table 3).

Among proposed means to prevent burnout and increase wellness, hospitalists cited improving the workload (n = 36, 88%); incorporating respect, care, and compassion among the hospitalists as a group culture (n = 36, 88%); improving support from subspecialists and consult services (n = 34, 83%); introducing increased or more competitive compensation, incentives, acknowledgements, rewards, or awards (n = 34, 83%); and ensuring protected time for scholarly pursuits (n = 34, 83%) (Table 4). The burnout rates experienced between males and females were not statistically significant (58% vs 73%, respectively; P = 0.65). Burnout rates were 50%, 55%, 88%, and 80% in hospitalists with career length 0-3 years, 4-6 years, 7-9 years, and 10 or more years, respectively

(P=0.28). Burnout was not associated with job satisfaction as a hospitalist (P=0.11). In total, 34 (81%) hospitalists surveyed felt that the high demands of clinical work interfered with their time and interest to teach medical students.

Of the 42 hospitalists who completed the survey, 11 (26%) provided open-ended comments about burnout. Common themes on possible reasons for burnout included increased workload and lower financial compensation. Perceived consequences included interference in the hospitalists' teaching ability and work-life balance issues, whereas suggested prevention strategies included the leadership's willingness to commit to address burnout. Multiple respondents mentioned workload, with some citing "uncertainty in the amount of work" and also "absence of NP (nurse practitioner)/PA (physician assistant)." Several respondents commented on teaching in the clinical setting, including one who said, "I find it almost impossible to provide good teaching to medical students rotating with me on the hospitalist service." Another said, "Service is busy, and it is hard to be a consistent good teacher." Some comments suggested capping a non-house staff team at 15 patients a day when working with a student or having students work only with the house staff teams. Several respondents expressed their desire to be valued and not considered "just as workforce." Respondents also expressed concerns about the effect of work on their physical health and interpersonal relationships, and multiple respondents proposed that leadership should address burnout and well-being in the hospitalist group.

#### **DISCUSSION**

In this study of academic hospitalists at a single tertiary care center, more than half of the respondents reported experiencing burnout. Academic hospitalists are a unique group of physicians with many responsibilities; thus, there are many triggers for burnout. Increasing numbers of non-house staff clinical services and high patient census were cited as the most common contributors to burnout. These escalating clinical demands discouraged hospitalists' interest and effectiveness in teaching medical students and residents.

Two studies examining burnout among academic hospitalist medicine showed burnout rates of 23% and 30%, respectively. 10,11 Our study demonstrates a higher burnout rate of 62%. Based on the survey results, the strongest contributors to this higher burnout rate were higher volume of clinical work and higher expectations (teaching, provider performance metrics, administrative duties, scholarly activities). Challenges unique to academic medicine also were identified, such as pushback from consult services and a lack of protected time for scholarly projects. This is consistent with a prior study by Glasheen et al, which found that academic hospitalists had inadequate amounts of protected scholarly time due to high demands for non-house staff clinical work. 10

In our study, the rate of burnout increased with the duration

of practice as a hospitalist. Hospitalists who had worked in the group 3 years or less composed 42% of the study group, while 33% of respondents had served in the hospital for 7 years or more.

With a high burnout rate observed in the hospitalist group, these findings possibly suggest a high likelihood of hospitalists leaving the job as a consequence of burnout, among other reasons. Rapid workforce turnover has important implications on the health care organization's finances.<sup>12</sup>

In the open-ended comments section, several respondents expressed that the high volume of nonteaching clinical work made them feel as if they were working in a community hospitalist (nonacademic) group. Since the Accreditation Council for Graduate Medical Education initiated resident duty hour restrictions in 2003, there has been a growth in non-house staff services required to care for hospitalized patients at most academic medical centers. Unless solutions are proposed, the expansion of these non-house staff teams will continue to pose logistical challenges and contribute to burnout. Additionally, a heavier clinical burden leads to a lack of protected nonclinical time, hindering early career hospitalists from developing academic interests, such as teaching or research. Protected nonclinical time may be a vital step to improving burnout rates in academic hospitalist medicine while cultivating scholarly activity.

There is a need for both individual-focused and organizational solutions to address burnout among academic hospitalists. Physician-centered approaches include mindfulness, stress reduction, resilience training, and communication skills training. Organization-level changes are typically much harder to implement and sustain.<sup>4,15,16</sup>

Several studies with interventions to mitigate burnout have been published; the results are best summarized by a systematic review and meta-analysis that showed both individual and organizational-focused strategies may be able to reduce burnout among physicians.<sup>17</sup> Based on our survey data, high patient volume is perceived as the strongest contributor to burnout and, thus, requires serious attention. Strategies that can be effective include increasing the number of hospitalist teams available, capping the number of patients per hospitalist, arranging coverage for predictable life events, and giving hospitalists more control of their schedule. In addition to addressing work conditions, other steps to improve or prevent academic hospitalist burnout include incorporation of mindfulness and teamwork practices, decreasing the burden of the electronic health record, providing protected time for scholarly activities and teaching, making self-care a larger part of medical professional culture, improving mentoring systems, advocating for academic promotion, scribes, and wellness programs.<sup>3,18,19</sup>

Academic hospitalists play an important role in educating medical students and residents. In this study, 81% of hospitalists indicated that high demands of nonteaching clinical work interfered with their time and interest to teach medical students. This finding strongly suggests that rigorous clinical demands negatively affect

the academic hospitalist's role as a teacher. This is consistent with a prior study that found lower teaching scores for academic hospitalists associated with higher amounts of clinical work.<sup>20</sup> Perceived consequences of burnout on the teaching role are perhaps best captured by the study respondent who said, "Some days I resent having them [medical students], and I didn't go into academics to feel that way." Respondents proposed several solutions to improve teaching, including a 15-patient cap for hospitalists working with a student or moving all students to the resident teaching teams. These comments and proposals reflect the frustration of hospitalists who want to teach but are also extremely busy on non-house staff services. These findings add to prior research that described benefits and barriers to learning experienced by medical students during the hospital rotation,<sup>21</sup> including being on a busy service, limited interaction with the attending physician, and variability in rounding methods.

One strength of this study was the high percentage of survey participation (83%). Because the survey was anonymous, another strength was the transparency of comments by hospitalists about how burnout affects medical education. The study was limited in that it was a single-center design, and there may be factors related to burnout that are specific to our institution. Further, this study did not use the most widely accepted burnout scale—the Maslach Burnout Inventory (MBI)—but relied upon hospitalists to define their own burnout.<sup>15</sup> Previous studies have shown that the singleitem measure of burnout served as a reliable substitute to MBI across occupations. Such measure also assisted in abbreviating survey material and potentially increasing response rates.<sup>22-24</sup> Our study used dichotomous responses incorporating hospitalists' perceptions of burnout rather than using various levels of burnout, so it is possible that the burnout rates observed in our study could represent overestimation or underestimation.8,9

As newer studies consolidate our awareness and advance our understanding of the causes and consequences of burnout and its solutions, the current era demands more rigorous investigation of contributing factors and delineation of strategies more specific to the local practicing environment, which our study has attempted to accomplish at an academic medical center in Wisconsin. While a recent study reported a burnout rate of 46% among Wisconsin physicians, our study is the first to describe burnout among academic hospitalists in Wisconsin.<sup>25</sup>

#### CONCLUSIONS

Our survey-based study on academic hospitalists showed that more than half of the group experienced burnout. Academic hospitalists are uniquely positioned to serve in a heavy clinical workload environment and fulfill several responsibilities including educator and researcher, in addition to the clinical care of patients. While it is generally accepted that both individual-focused and organizational solutions can help prevent and mitigate burnout, further studies are needed to determine which combinations of interventions are

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effective for the hospitalist population. Burnout research on academic hospitalists remains meager; therefore, longitudinal studies exploring the contributing factors and interacting variables need to be conducted to further refine our understanding of the causes and consequences of burnout in this group.

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# A Culturally Adapted Depression Intervention for African American Adults: An Efficacy Trial

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#### **ABSTRACT**

**Background:** Major depressive disorder (MDD) is one of the most common, costly, and debilitating psychiatric disorders in the United States, and the World Health Organization has identified MDD as a leading cause of disability. Although the rates of MDD among African American and White populations in the US are comparable, African Americans in the US tend to experience higher rates of disability associated with MDD compared to White people. Despite the high burden of MDD among African Americans, their use of mental health services is low, in part due to suboptimal care.

**Objectives:** This study evaluated the efficacy of a culturally adapted depression intervention (Oh Happy Day Class [OHDC]) compared to an active control, the Coping with Depression (CWD) course.

**Methods:** A clustered randomized controlled trial was conducted with a sample of 132 patients with mild to moderate depressive symptoms. They were randomly assigned in a 2-armed randomized controlled trial. They received 1 of 2 (OHDC or CWD) 12-week interventions in weekly inperson group sessions. The primary outcome was a change in depressive symptoms during and post-intervention, measured with the Center for Epidemiologic Studies Depression Scale (CES-D) and the Quick Inventory of Depression Symptoms (QIDS). Analyses included log-rank test and mixed effects linear regression models.

**Results:** Both interventions were efficacious in reducing symptoms of depression. However, a greater dose of the culturally adapted intervention, Oh Happy Day Class, showed a greater reduction in depression symptoms.

**Conclusion:** This study represents the first randomized controlled trial evaluating the culturally adapted treatment depression intervention, Oh Happy Day Class. These findings provide evidence for and the need for culturally adapted treatments. Future research with larger samples of African Americans from different regions across the US could examine effectiveness and generalizability of the Oh Happy Day Class depression treatment.

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#### **BACKGROUND**

Major depressive disorder (MDD) is one of the most common, costly, and debilitating psychiatric disorders in the United States, and the World Health Organization has identified MDD as a leading cause of disability.<sup>1,2</sup> Additionally, MDD is associated with higher rates of chronic diseases and impaired functioning.1 The societal costs of MDD include lower educational attainment and low probability of marrying with early onset MDD; increased rates of teen pregnancy with early onset MDD; negative impact on work performance, which then negatively affects financial success; and high comorbidity with a wide variety of chronic physical disorders, including arthritis, asthma, cancer, cardiovascular disease, and diabetes.3 Despite the debilitating burden of depression, treatment use is low among individuals with depression, and treatment is often inadequate or of low quality.1,4,5

#### African American Adults, Major Depressive Disorder, and Care

African Americans across the US experience significant disparities in mental health care.<sup>6-9</sup> According to the US Department of Health and Human Services seminal

2001 publication, *Mental Health: Culture, Race and Ethnicity*, <sup>10</sup> African Americans have less access to mental health care and tend to receive poorer quality mental health services. <sup>4,10</sup> Additionally, these disparities are associated with poor mental health outcomes. The 12-month prevalence of MDD among African American and

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White populations is relatively similar (7.9% and 5.4%, respectively); however, African American adults report more chronic MDD and higher rates of disability associated with MDD than do White adults (56.5% vs 38.6%, respectively).<sup>1,6</sup>

Although African Americans are burdened by depression, they report less adequate mental health care. A national psychiatric epidemiology survey that examined access and quality of depression care in the US showed that African Americans received adequate mental health care only 14% of the time.<sup>2</sup> Another study showed even lower rates of outpatient service use among African Americans—only 5.6% reported having 4 or more visits within 12 months, compared to 81.6% of White individuals reporting having 4 or more visits within 12 months.<sup>6</sup> Additionally, African Americans showed higher rates of attrition from psychotherapy and pharmacotherapy than White patients.<sup>1,3</sup> Despite their low use of outpatient mental health services, African Americans are overrepresented among inpatient psychiatric care patients. In particular, their use of emergency departments for mental health problems—including MDD—far exceeds other groups.<sup>8-10</sup>

Poor quality depression care for African Americans might partially explain the lower rates of service use, the high attrition, and the high rates of inpatient psychiatric care. One study that examined the quality of depression care among a representative sample of African Americans in the National Survey of American Life (N=3,673) found optimal depression care among African Americans is low.<sup>2</sup> This finding is consistent with earlier research, suggesting that African Americans are often underdiagnosed and undertreated for depression.<sup>6,7,9,11,12</sup> In sum, the literature suggests that depression care remains suboptimal for African Americans who suffer from major depressive disorder.<sup>2,13,14</sup>

#### **Culturally Adapted Treatments**

The term culturally adapted treatments (CAT) refers to any modification to evidence-based mental health treatments that involves either changes to the approach to service delivery, the nature of the therapeutic relationship, or the components of the treatment itself to accommodate the cultural beliefs, attitudes, and behaviors of the target population.<sup>7,15</sup> Research indicates culturally adapted interventions are effective in treating mental disorders among racial and ethnic minorities.<sup>7,11</sup> However, there is a need for more research on culturally adapted interventions designed specifically for African American adults with depression.<sup>7,15,16</sup>

#### **Purpose of Study**

We examined the efficacy of a culturally adapted depression intervention (Oh Happy Day Class [OHDC]) compared to a standardized active control (Coping With Depression Course [CWD]) among African American adults with depression. Both the OHDC and CDW are 12-week behavioral group interventions. Although our earlier work showed efficacy of the OHDC among African American adults with depression in the short term (3 months pos-

tintervention),<sup>17</sup> we did not compare OHDC with an unadapted intervention. Currently, best practices call for comparing the culturally adapted with the unadapted intervention to increase the rigor of CATs research. In addition, a meta-analysis of 78 studies of CATs identified only 9 studies that use the culturally adapted vs unadapted forms of the same intervention design.<sup>16</sup> We examined the efficacy of the OHDC compared to the unadapted CWD in reducing symptoms of depression among African American adults at 6 and 12 weeks, and 3 and 6 months postintervention. We hypothesized that the OHDC compared to the CWD would result in fewer depressive symptoms. Because of the high rates of disability associated with depression among African Americans, we predicted the OHDC would increase self-reports of improved mental and physical health.

#### Interventions

#### Oh Happy Day Class

OHDC is a culturally adapted depression intervention adapted from CWD, an intervention originally designed for White adults experiencing MDD. Details about adapting the CWD to develop the OHDC have been reported elsewhere. <sup>17</sup> A brief description of OHDC and preliminary data supporting effectiveness of the OHDC are summarized below.

OHDC is 12-module group therapy intervention that uses cognitive behavioral therapy and a support group format, combined with a strong psycho-education focus.<sup>17</sup> The weekly sessions are called classes. Classes are 2.5 hours long, and the content is focused on increasing participants' knowledge of depression and treatment options, developing healthy coping behaviors, and shifting negative perceptions of health and disability status to more positive attitudes. The clinical sessions were delivered by 2 African American counselors, each with a masters' degrees in counseling psychology. See Table 1 for OHDC modules.

OHDC effectiveness was examined in 2 pilot studies. Results for pilot 1 indicated that 73% of subjects completed the full OHDC—with a 0.38 effect size—and showed a statistically significant decline in depression symptoms from preintervention to postintervention. Results for pilot 2 indicated that 66% of subjects completed the full OHDC—with a 1.01 effect size for men and a 0.41 effect size for women—and showed a statistically significant decline in depression symptoms from preintervention to postintervention.<sup>17</sup> These promising findings provided pilot data to support the National Institutes of Health-funded randomized controlled trial reported in this paper.

#### Coping with Depression Course

The CWD is a multimodal psychoeducational group treatment for depression. It is referred to as a course because of the prioritization of an explicit educational experience for patients, whereby patients are taught techniques and strategies for coping with problems related to depression. <sup>18</sup> CWD is grounded in social learning theory and cognitive behavior theory and uses a psychoeducation

format in which participants learn skills to help them cope with their depression. 18-20 CWD focuses on several target behaviors (social skills, thinking, pleasant activities, relaxations), in addition to other behaviors aligned with cognitive behavior therapy. 19-20 CWD has 12 modules and is delivered as a course offered weekly, with 2-hour sessions in a clinical setting. The clinical sessions were delivered by 2 White psychologists, each with a PhD in clinical psychology. See Table 1 for the CWD course modules.

CWD is the most studied depression intervention. <sup>17,18</sup> A meta-analysis of 25 studies examining the effectiveness of CWD found it to be effective in the treatment of MDD, which influenced our decision to culturally adapt the CWD in developing the OHDC (discussed elsewhere <sup>17</sup>).

In their meta-analysis, Cuijpers and colleagues<sup>20</sup> found that CWD reduced symptoms of depression compared to controls (effect size 0.28, 95% CI, 0.18-0.39 with 18 trials).

#### **METHODS**

#### **Design and Sample**

A clustered randomized controlled trial<sup>21,22</sup> was conducted to examine the efficacy of the culturally adapted depression intervention (OHDC) compared to the unadapted intervention (CWD) in reducing symptoms of depression among African American adults. Participants were randomly assigned to OHDC or CWD. After randomization, participants in the OHDC and CWD arms were grouped into class groups of 7 participants each.

Although the groups were configured by gender, no specific gender stratification was used in configuring the groups. The study was reviewed and approved by the institutional review board of the University of Wisconsin-Madison. All participants provided written informed consent for screening and separate consent for random assignment to the depression interventions.

We powered the trial based on measures of change in our aims, specifically in the level of depression (Center for Epidemiologic Studies Depression Scale [CES-D] and Quick Inventory of Depression Symptoms [QIDS]), and change in mental health status (Short Form Survey [SF-12 mental]) and physical health status (SF-12 physical). The sampling for the trial was based on detecting effect sizes in average CES-D reduction from .62 $\sigma$  and a 20% increase in SF-12 mental and SF-12 physical (effect sizes of .58 $\sigma$  and .68 $\sigma$ , respectively). Using the smallest detectable effect size (.58 $\sigma$ ), we project that an optimal grouping of 13 groups of 7 patients, or a total of 26 groups and 182 participants, are required to achieve power at .80 and detect the proposed effect at  $\alpha$  = .05

Week	Oh Happy Day Class (OHDC)	Coping With Depression (CWD)
1	Introduction, overview of group counseling and Nguzo Saba principles	Depression and social learning
2	Depression etiology, risk factors, symptoms and treatment options	How to design a self-learning plan
3	Men/women and depression	Learning to relax
4	Depression and chronic physical illness	Relaxation in everyday situation
5	Community resources	Pleasant activities and depression
6	Anger management	Formulating a pleasant activities plan
7	Stress management and learning to relax	Two approaches to constructive thinking
8	Constructive thinking	Formulating a plan for constructive thinking

Table 1. Modules for the Oh Happy Day Class and Modules for the Coping with Depression Course

Pleasant activities and depression

Maintaining gains and developing a life plan using
Nguzo Saba

Review and graduation celebration

Using your social skills

Maintaining your gains

Developing a life plan

Forgiveness

Booster session and reunion (3 months postintervention) postintervention)

(1-tailed test), assuming a substantial design effect >  $2.0.^{21-23}$ 

Social skills: the ability to be assertive

Inclusion criteria were self-identified African American men and women, between the ages of 30 and 65, with symptoms of depression as evidenced by data from CES-D, a 20-item self-report inventory. Although the age of inclusion was broad, our earlier studies have shown positive outcomes with mixed aged groups. 17 The exclusion criteria included individuals who self-reported alcohol or other drug abuse/dependence; major psychotic illnesses, such as schizophrenia; self-reported changes in antidepressants (dosage or type) less than 6 weeks prior to participating in the study; self-report of current psychotherapy treatment; and self-report of current suicidal ideations. To be eligible for the study, participants needed to have current MDD and to be negative for mania, psychosis, or alcohol or drug abuse or dependence in the past 3 months. The demographic characteristics of the sample are presented in Table 2.

#### **MEASURES**

#### **Screening Measures and Outcome Measures**

The CES-D was used both as a screening measure and an outcome measure. The CES-D is a 20-item self-report inventory developed by the National Institute of Mental Health to assess the frequency and severity of depression symptoms in the past week.<sup>24,25</sup> Respondents indicated how often each symptom was experienced during the past week on a 4-point scale from "rarely or none of the time (0)," "some or a little of the time (1)," "occasionally or a moderate amount of the time (2)," or "most or all of the time (3)." The item scores have been summed for analyses, with a possible range of 0 to 60. A standard cutoff score of 16 indicates depressive symptoms.<sup>24,25</sup> The CES-D has good reliability and is sensitive to changes in patients' depression status after treatment.<sup>24,25</sup> In our study, we have had Cronbach's alpha of 0.87 at baseline.

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	C	CWD		OHDC	
	Mean	SD	Mean	SD	
Age	52.17	6.5	51.08	8.4	
Number of Children	3.4	2.2	3.3	2.1	
	Freq	%	Freq	%	
Gender					
Female	42	77.78	25	67.5	
Male	12	22.22	12	32.4	
Income					
\$0–10,000	44	83.02	24	68.5	
\$10,001–\$20,000	2	3.77	5	14.2	
\$20,001–\$30,000	5	9.43	1	2.8	
\$30,001–\$40,000	2	3.77	4	11.43	
Employment status					
Employed full-time	5	9.26	4	11.4	
Employed part-time	6	11.11	5	14.2	
Retired	2	3.7	1	2.8	
Disability	18	33.33	7	20	
Other	23	42.59	18	51.4	
Socioeconomic status					
Working class	31	65.96	22	70.9	
Middle class	9	19.15	5	16.1	
Upper middle class	0	0	2	6.4	
Retired	7	14.89	2	6.4	
Insurance					
No	13	26	10	27.0	
Yes	37	74	27	72.9	
Marital status					
Married	4	7.27	6	16.6	
Living with partner	7	12.73	2	5.50	
Separated Separated	5	9.09	2	5.5	
Divorced	10	18.18	5	13.8	
Widowed	0	0	1	2.78	
Never married	26	47.27	20	55.5	
Married—separated	1	1.82	0	0	
Living with—never married	2	3.64	0	0	
	2	3.04	U	U	
Do you have children	12	24.02	_	10.0	
No	12	21.82	6	16.2	
Yes	43	78.18	31	83.7	
Educational level	,	4.05	•	^	
Elementary	1	1.85	0	0	
8th grade	6	11.11	4	10.8	
High school degree or GED	23	42.59	16	43.2	
2-year college or technical college	12	22.22	12	32.4	
Bachelor's degree	4	7.41	1	2.7	
Master's degree	1	1.85	1	2.7	
Other	7	12.96	3	8.11	

#### **Outcome Measures**

#### Primary Aim 1: Decreased Depression Symptoms

Decreased depression symptoms were measured with the CES-D described above and the 16-item QIDS. The QIDS uses DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) criteria to assess depressive symptom severity and symptom change. Scores range from 0 to 27 and higher scores suggest higher severity.<sup>26</sup>

We used the clinician-rated QIDS-CR. Studies show high internal consistency for the QIDS-CR (0.85),<sup>26</sup> which was consistent with our QIDS-CR of 0.79.

### Secondary Aim 2. Change in Physical and Mental Health Functioning

Physical and mental health was measured by the Short Form Survey (SF-12), a self-report scale of physical and mental health status. The SF-12 was developed to measure physical health (role limitations resulting from physical health problems, bodily pain, general health, energy, and fatigue) and mental health (social functioning, role limitations resulting from emotional problems, psychological distress, and psychological well-being).<sup>27</sup> Published procedures for scoring were used to create 2 set of scores: the physical component summary and the mental health component summary. Scores range from 0 to 100 (mean = 50, SD = 10); scores greater than 50 suggest above average health. The SF-12 demonstrates good internal consistency and reliability among African Americans.<sup>27</sup> In our work, we had Cronbach's alpha = 0.89 for the physical health status and 0.76 for mental health status.

#### **Descriptive Measure/Covariates**

A demographic questionnaire was used to obtain year of birth, city of residence, education, income, marital status, number of children, health insurance status, employment status, and socio-economic status.

#### **Procedures**

The sample for this study was drawn from an urban city in the Midwest. We worked with community health clinics and community agencies to recruit participants. Local health clinics serving African American patients were informed of the study and agreed to refer patients/clients. Information sessions were held at local clinics to inform both clinical staff and receptionists about the study and to facilitate appropriate identification and referrals. Study flyers were posted in the waiting areas of clinic lobbies. Community agencies with existing relationships and partnerships with our study team readily endorsed the study and publicized it in the African American community. For example, the Urban League and local urban housing complexes offered to post flyers in their common office areas and lobby bulletin boards. All eligible individuals age 30 years and older who expressed interest in the study were screened using the CES-D after providing written informed consent. Upon meeting the inclusion criteria, participants were enrolled in the study and, based on randomization, attended the 12-week OHDC or 12-week CWD. Data were collected from participants at baseline, 6 and 12 weeks, and 3 and 6 months postintervention.

#### **Statistical Analysis**

Hypothesis Testing and Data Analysis

Primary Aim 1: Examine efficacy of the OHDC in reducing

symptoms of depression at the middle (week 6) and immediate end (week 12) of the intervention and 3 and 6 months postintervention. We hypothesized that among African Americans adults with depression, the OHDC would result in a greater reduction in depressive symptoms compared to the CWD at weeks 6 and 12 and 3 and 6 months postintervention.

Primary Aim 2: Examine the efficacy of the OHDC in improving self-report of mental and physical health status. We hypothesized the OHDC compared to the CWD would result in greater self-report of improved mental and physical health status at the immediate end of the intervention (week 12) and 3 and 6 months postintervention.

#### Data Analysis

Hypotheses for primary aims 1 and 2 were assessed using 2-level mixed effects linear regression models with repeated measures.<sup>28,29</sup> A secondary analysis of treatment fidelity was also conducted using the mixed effects model.<sup>29</sup> All analyses were conducted using Stata Version 16. See Table 3.

#### **RESULTS**

Demographics and clinical characteristics for our participants are summarized below and in Table 2. Demographic data showed that over 50% of the participants were working class and had a disability. Thirty-two percent had some college education (2-year college or 4-year college graduate). Thirty-five percent were unemployed, and slightly over 60% reported income of \$0 to \$10,000 per year. African American women made up 74% of the sample. Marital status included married, divorced, and living with partner, while 51% of the sample reported never having married. Regarding mental health status,

42% reported history of depression. At the time of enrollment in the trial, 100% participants tested positive for diagnosis of major depressive disorder.

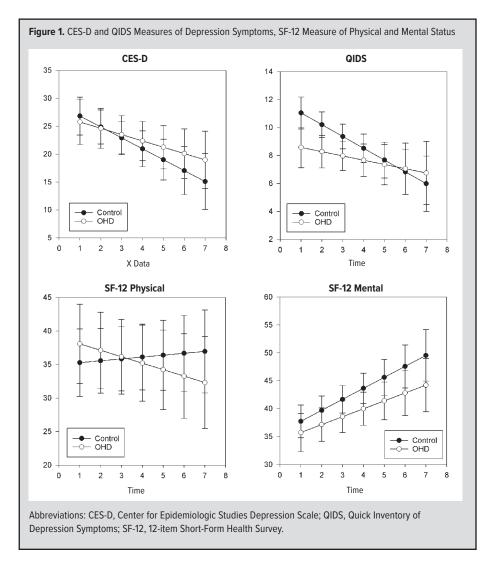
#### **Depression Symptoms**

In both OHDC and CWD groups, symptoms of depression were compared over time. We hypothesized that among African

Table 3. Fidelity Ana		oidemiologic Studi	es Denressia	n Scale //	^FS-D\
Fixed Effects	Coefficient	Standard Error	z z	P> z	95% CI
Low	-2.359226	5.519476	-0.43	0.669	-13.1772 to 8.458749
High	-5.533661	4.579595	-1.21	0.227	-14.5095 to 3.44218
Time	-2.99722	0.990718	-3.03	0.002	-4.938992 to -1.055448
Low X time	3.382752	3.212242	1.05	0.292	-2.913128 to 9.678631
High X time	2.384056	1.66014	1.44	0.151	-0.8697591 to 5.63787
Constant	30.51467	2.56805	11.88	0.000	25.48138 to 35.54795
Random Effects	Coefficient	Standard Error	R-square		95% CI
Group level	12.96208	8.652741	0.210		3.503173 to 47.96098
Patient level	122.0059	12.80601	0.038		99.32 to 149.8734
	Quick I	nventory of Depres	ssion Sympto	oms (QIDS	;)
Fixed Effects	Coefficient	Standard Error	z	<i>P</i> > z	95% CI
Low	-0.0131513	1.545606	-0.01	0.993	-3.04248 to 3.016181
High	-1.453977	1.032525	-1.41	0.159	-3.47768 to 0.569735
Time	-0.0807986	0.0952018	-0.85	0.396	-0.267390 to 0.1057935
Low X time	0.4513376	0.5121654	0.88	0.378	-0.552488 to 1.455163
High X time	0.081918	0.149985	0.55	0.585	-0.212047 to 0.3758832
Constant	9.2581	0.6568294	14.10	0.000	7.97073 to 10.54546
Random Effects	Coefficient	Standard Error	R-square		95% CI
Group level	1.898688	.8912951	0.082		.7566181 to 4.764644
Patient level	19.83757	.9134547	0.017		18.12565 to 21.71119
		SF-12 Physi	cal Score		
Fixed Effects	Coefficient	Standard Error	z	<i>P</i> > z	95% CI
Low	3.644762	4.89808	0.74	0.457	-5.955299 to 13.24482
High	-0.7342404	4.397788	-0.17	0.867	-9.353747 to 7.885267
Time	-0.14106	0.2146898	-0.66	0.511	-0.5618442 to 0.2797242
Low X time	0.1703807	0.8405784	0.20	0.839	-1.477123 to 1.817884
High X time	0.0059132	0.3215571	0.02	0.985	-0.6243271 to 0.6361534
Constant	35.43684	2.85533	12.41	0.000	29.8405 to 41.03319
Random Effects	Coefficient	Standard Error	R-square		95% CI
Group level	50.94499	21.8001	0.005		22.02217 to 117.8536
Patient level	107.9199	4.554611	0.007		99.35223 to 117.2263
		SF-12 Ment	tal Score		
Fixed Effects	Coefficient	Standard Error	z	<i>P&gt;</i>  z	95% CI
Low	-10.90048	3.274445	-3.33	0.001	-17.31828 to -4.482687
High	-3.188375	2.526148	-1.26	0.207	-8.139534 to 1.762785
Time	0.2065984	0.2074916	1.00	0.319	-0.2000776 to 0.6132744
Low X time	0.4036951	0.8127201	0.50	0.619	-1.189207 to 1.996597
High X time	-0.0781648	0.3108164	-0.25	0.801	-0.6873537 to 0.5310241
Constant	42.42334	1.650104	25.71	0.000	39.1892 to 45.65749
Random Effects	Coefficient	Standard Error	R-square		95% CI
Group level	13.63171	6.057935	0.141		5.705271 to 32.57051
Patient level	101.0428	4.262453	0.038		93.02463 to 109.7522

American adults, the OHDC would result in greater reduction in depressive symptoms (CES-D and QIDS) compared to the CWD at 6 and 12 weeks during the intervention and at 3 and 6 months postintervention. Depression scores on the CES-D and the QIDS are provided in Figure 1. Both CES-D and QIDS measures declined for both groups over time. Early measures of the QIDS

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indicated that the OHDC group was significantly lower than the CWD group but converged later on.

#### **Mental and Physical Health Status**

Mental and physical health status at 6 and 12 weeks during the intervention and at 3 and 6 months postintervention showed both groups increasing in parallel for SF-12 mental scores. Interestingly, the SF-12 physical indicated a general decline for the OHDC group while the CWD was stable (Figure 1).

#### **Fidelity Analysis**

Fidelity or dose of treatment was explored by splitting the OHDC group into subjects who attended less than 4 sessions as low dose and those who attended 4 or more as high dose. Those high-dose subjects exhibited a steady decline in CES-D measures compared to the lower-dose and CWD subjects (control). Measures of depression using the observable QIDS indicated high-dose subjects were lower overall in depression symptoms than the low-dose and controls but were stable across time. Measures of SF-12 physical showed little difference in dose but, in general, were lower

than the controls. Both dose groups were also higher than controls for SF-12 mental measures. Marginal means for low dose at 6 months (time period 5) could not be estimated due to zero cases. See Figure 2.

#### **DISCUSSION**

We examined the efficacy of the OHDC compared to the control CWD in reducing symptoms of depression among African American adults at 6 and 12 weeks and at both 3 and 6 months postintervention. We hypothesized the OHDC versus the CWD would result in fewer depressive symptoms. Given the high prevalence of depression and the high rates of in-patient psychiatric admissions among African American adults in Wisconsin, the decline in depression symptoms we observed was impressive. CES-D and QIDS measures declined for both groups over time, suggesting that both interventions were efficacious in helping participants move from moderate to mild symptoms of depression.

Interestingly, the results from fidelity analysis of treatment dose among the OHDC group showed those subjects who had high dose (4 or more sessions) showed a steady decline in depression as measured in CES-D versus the lower dose of OHDC and also CWD subjects. In addition, find-

ings of depression as observed in the clinician-administered QIDS indicated the high-dose subjects in OHDC were lower overall in depression compared to the low-dose and CWD subjects. These findings suggest a positive dose response relationship, indicating that a higher dose of OHDC treatment is associated with decline in depression symptoms.

Our study and results represent the first fidelity dose response among African Americans. Although dose response to treatment is consistently examined in biomedical research, we found no studies that addressed dose response to behavioral treatment among African Americans adults with depression. These concerns are vividly captured by the call to action by Alegría and colleagues:<sup>30</sup> "Efforts to develop a more comprehensive understanding of the optimal time and dosage of certain interventions could inform future policy and program planning." Findings from our work underscore the need for additional research to examine the dose response in mental health treatment among African Americans with depression. Such research might shed light on dose response—research that may well impact the minimal number of sessions required to achieve clinically significant changes in depression symptoms.

Such work could inform policies and programming aimed at improving quality of mental health services and improving mental health outcomes for target populations.

We examined mental and physical health status at 6 and 12 weeks during the intervention and at 3 and 6 months post-intervention. Both groups showed parallel changes in mental health scores, suggesting increasing levels of mental wellness. Physical health scores indicated a general decline for OHDC group, whereas the CWD maintained stability, though not statistically significant. Furthermore, the measures of physical health scores showed little difference in dose but, in general, were lower for OHDC subjects than CWD subjects.

These findings showing no response to physical functioning are consistent with research in depression showing that depression in African Americans is often chronic with associated disability. In a national survey examining the prevalence, persistence, treatment, and disability of depression, Williams et al<sup>1</sup> found chronicity of depression was higher for African Americans (56.5%) than for White adults (38.6%), leading to an overall greater degree of functional impairment among African Americans. These data show the need for intervention research to explore integrating physical health wellness in depression interventions.

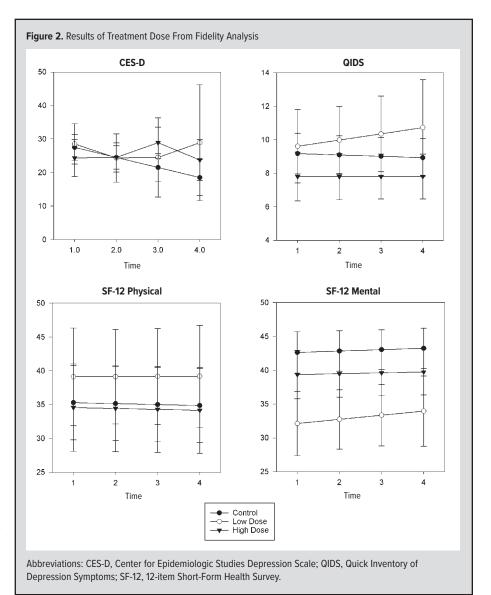
#### Limitations

There are a few limitations in our study. First, the study cohort is homogeneous, ie, only African American adults, which may limit the generalizability of the results to other racial and ethnic groups.

Due to difficulty with recruitment and attrition, we were challenged in getting our required sample size, which compromised power; thus, our findings should be interpreted cautiously. There was higher-than-expected missing data, which may have been due to measures being self-administered. More oversight was needed to reduce the risk of missing data. This research was conducted in a Midwestern city, which limits generalizability to African Americans in other regions.

#### CONCLUSION

This clinical trial examining the efficacy of a culturally adapted depression intervention designed for African American adults with



depression demonstrates the potential of the Oh Happy Day Class. In sum, both interventions were effective in reducing symptoms of depression. However, higher doses of OHDC showed greater reduction in depression symptoms, providing evidence of effectiveness of a culturally adapted intervention designed for African Americans. Given this is the first clinical trial of the OHDC, more research is needed to explore its full impact. We recommend conducting studies with larger samples of African Americans across various geographic regions to increase generalizability of findings.

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# Differences in Utilization of Perinatal Psychiatric Teleconsultation Line Between Primary Care and Mental Health Providers

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#### **ABSTRACT**

**Purpose:** Teleconsultation has been a newly recognized avenue by which to provide psychiatric services to perinatal populations being treated either by psychiatric or primary care providers. The Periscope Project (TPP) is a business-hours teleconsultation line providing enrolled clinicians with access to a subspecialty-trained psychiatrist, as well as community resources and provider education. This study examines the differences in consultation between enrolled providers.

**Methods:** Encounter data were entered into REDCap by TPP's team members. Data were analyzed using summary statistics. Satisfaction information was attained by follow-up survey.

**Results:** During the first 24 months of program activity, TPP had a total of 737 referred encounters, 70.4% from primary care and 20.5% from psychiatry. There were statistically significant differences between psychiatric and primary care providers in terms of recommendations for use of certain types of medications and use of diagnostic screenings, as well as differences in what providers would have recommended in absence of TPP's involvement.

**Conclusions:** Differences in enrollee's rationale for consultation allows for better understanding of the needs of front-line providers. Tailoring educational information and even teleconsultation information based on provider group can allow for more efficient patient care and resource utilization. Providers across the spectrum found TPP beneficial, indicating that continued availability to all providers caring for women of reproductive age is important.

#### INTRODUCTION

One in 7 women in the United States struggle with depression during pregnancy and postpartum periods. The number of affected mothers climbs higher when other disorders, such as anxiety, bipolar disorder, schizophrenia, and substance use disorders are included, and resulting complications affect everyone

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involved, including mothers and their children, families, and even care providers. The National Center for Health Workforce Analysis estimates that by 2030, the supply of adult psychiatrists will decrease by 27%. Given that more people today are seeking mental health care than previously, we cannot address even general psychiatric needs through a traditional service model, let alone provide adequate and timely subspecialty care for perinatal populations. 6

In July 2017, the PERInatal Specialty Consult Psychiatry Extension (PERISCOPE) Project (TPP) launched in Wisconsin as a business-hours real-time teleconsultation line for all providers caring for preconception, pregnant, or postpartum women, including obstetric, primary care (internal and family medicine and pediatricians), and psychiatric

physicians and advanced practice providers (APP). Information regarding project design, implementation, and descriptive characteristics from the first 24 months of program activity has been reported previously.<sup>7</sup> For the remainder of this paper, "primary care providers" encompasses MD/DO, physician assistant, nurse practitioner, and midwifery providers in the fields of obstetrics, pediatrics, and internal and family medicine. "Psychiatric providers" encompasses MD/DO, physician assistant, and nurse practitioner providers in the psychiatry and behavioral health settings.

Data are reviewed regarding the differences in consultation questions between provider types over the first 2 years of program activity. This information can highlight current differences in practice, support standardized curriculum development,

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Table 1. Represented Provider Type and Patient Status at Time of Consultation				
	n	Psychiatry No. (%)	Primary Care No. (%)	
Provider type				
Physician (MD/DO)	383	90 (59.6)	293 (56.5)	
Nurse practitioner (NP)	139	58 (38.4)	81 (15.6)	
Midwife	136	0 (0)	136 (26.2)	
Physician assistant (PA)	12	3 (2.0)	9 (1.7)	
Total	670	151	519	
Patient status				
1st trimester	164	45 (31.7)	119 (23.6)	
2nd trimester	149	26 (18.3)	123 (24.4)	
3rd trimester	106	26 (18.3)	80 (15.8)	
Postpartum lactating	107	18 (12.7)	89 (17.6)	
Postpartum not lactating	52	0 (0)	52 (10.3)	
Preconception	40	22 (15.5)	18 (3.6)	
Interconcpetion	6	2 (1.4)	4 (0.8)	
Other	23	3	20	
Total	647	142	505	

<b>Table 2.</b> Current Symptoms and Diagnostic Concerns Reported by Enrolled
Provider to TPP Team Members at Time of Consultation

	n	Psychiatry No. (%)	Primary Care No. (%)
Current symptoms <sup>a</sup>			
Depressive <sup>b</sup>	323 (48.2)	52 (34.4)	271 (52.2)
Anxiety <sup>b</sup>	273 (40.7)	38 (25.2)	235 (45.3)
Mania	7 (1.0)	2 (1.3)	5 (1.0)
Appetite	2 (0.3)	0 (0)	2 (0.4)
Suicidality	12 (1.8)	2 (1.3)	10 (1.9)
Sleep changes	51 (7.6)	6 (4.0)	45 (8.7)
Psychotic <sup>b</sup>	36 (5.4)	18 (11.9)	18 (3.5)
Mood liability	46 (6.9)	14 (9.3)	32 (6.2)
Irritability	16 (2.4)	3 (2.0)	13 (2.5)
No psychiatric symptoms <sup>b</sup>	91 (13.6)	40 (26.5)	51 (9.8)
Diagnostic concerna			
Mood disorder	445 (66.4)	97 (64.2)	348 (67.1)
Anxiety disorderb	248 (37)	32 (21.2)	216 (41.6)
Psychotic disorderb	34 (5.1)	17 (11.3)	17 (3.3)
Substance use disorderb	44 (6.6)	16 (10.6)	28 (5.4)
ADHD <sup>b</sup>	45 (6.7)	17 (11.3)	28 (5.4)
Sleep disorder	15 (2.2)	2 (1.3)	13 (2.5)
Other	31 (4.6)	7 (4.6)	24 (4.6)

Abbreviations: TPP, The Periscope Project; ADHD, attention-deficit/hyperactivity disorder.

encourage routine screening, and provide direction for analysis of programmatic cost benefit.

#### **METHODS AND MATERIALS**

#### Triage

Initial calls to TPP are triaged by a coordinator who is trained to provide community resources with specific knowledge regarding availability within Wisconsin. The triage coordinator also opens an encounter with the database REDCap (Vanderbilt University, Nashville, Tennesee). Information gathered includes deidentified patient descriptors such as age, pregnancy and lactation status, geographic location of the clinic, diagnoses, number/type of psychotropics, provider type, and rationale for call (assistance with diagnosis, medications, community resources, or referral information). This study was approved by the institutional review board of the host institution; as no direct patient contact occurred, providers completed an online waiver of consent on enrollment to TPP. Data presented here correspond to the first 24 months of programming, July 1, 2017 through June 30, 2019.

Note that while TPP was launched to focus on utilizers within the state of Wisconsin, no eligible utilizer was denied access based on geographic location. Thus, a minority of utilizers were located in states other than Wisconsin though are grouped into these data without delineation.

#### **Satisfaction Surveys**

Following encounters with TPP, utilizers are sent a survey via email. The survey is brief and requests responses regarding provider satisfaction, ability to extrapolate knowledge to care for other patients, and whether the gained knowledge was effective to assist with initial patient.

#### **Data Analysis**

HIPAA-compliant data were stored in REDCap and deidentified, relevant statistics to this study were imported into EXCEL (Microsoft, Redmond, Washington) for the designated time range. Basic summary statistics were then calculated using summation formulas within EXCEL. Statistical significance was defined as a resulting P value of < 0.05.

#### **RESULTS**

#### **Provider Type Utilization**

Over the first 2 years of program activity, TPP had a total of 737 referred encounters, 70.4% from primary care and 20.5% from psychiatry. Table 1 delineates provider type and patient status. Provider type contains possible categories of physician (MD/DO), physician assistant, nurse practitioner, or midwife. The majority of utilizers were physicians. Patient status is delineated as preconception, trimester of pregnancy, or postpartum status, as well as lactation status. Of note, no psychiatric providers consulted on a nonlactating postpartum patient, while 10.3% of primary care providers consulted on a patient in this category. Psychiatric providers were more likely to consult regarding preconception patients; this category comprised 15.5% of psychiatric consults vs only 3.6% of primary care consults.

#### **Diagnoses and Screening**

Table 2 displays information around both current symptoms and diagnostic concerns. It is important to note that these are not

<sup>&</sup>lt;sup>a</sup>Current symptoms and diagnositic concerns are not mutually exclusive categories. Some patients presented with multiple symptoms.

<sup>&</sup>lt;sup>b</sup>Notes the difference is statistically significant.

mutually exclusive categories and utilizers could report multiple concerns while consulting on a given patient. Of note, no psychiatrists consulted for a screening tool question, whereas 0.8% of primary care providers did so. No psychiatrists reported using a validated screening tool to assess for depression during patient visit, though 28.8% of primary care visits did.

In terms of current symptoms, primary care was more likely to consult regarding depression (52.2% vs 34.4%) and anxiety (45.3% vs 25.2%), whereas psychiatric providers were more likely to consult for psychotic symptoms (18% vs 3.5%) or for a patient without current psychiatric symptoms (26.5% vs 9.8%). In terms of diagnosis, these trends continue, with primary care patients more often meeting criteria for an anxiety disorder (41.6% vs 21.2%) and psychiatry patients more often meeting criteria for a psychotic disorder (11.3% vs 3.3%), substance use disorder (10.6% vs 5.4%), or attention-deficit/hyperactivity disorder (ADHD) (11.3% vs 5.4%).

#### **Rationale for Consultation**

A total of 15.2% of consults involved diagnostic criteria information, with primary care being significantly more likely to do so (7.5% vs 1.3% of contacts). More than 90% (91.8%) were seeking medication information (multiple questions could be asked during same consult), with rates being similar between psychiatric and primary care utilizers. Questions were rarely raised surrounding screening tools (<1% of calls), and 3.1% of calls were follow-ups from a prior encounter (3.7% of primary care contacts vs 1.3% of psychiatric contacts).

#### **Medication Interventions**

Table 3 displays medication information. A majority of patients were taking psychotropic medications at time of consult; psychiatrists' patients were more likely to be prescribed psychotropic medications than primary care patients. Nonsignificantly different rates of use were seen between utilizers for medication classes, including selective serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors (SNRI), and benzodiazepines. Significantly disparate rates of use were seen for atypical antipsychotics and mood stabilizers between the 2 provider groups, with psychiatric providers utilizing them more often.

In addition to types of medications utilized, data were gathered to assess whether recommendations were to increase or decrease medications. A total of 10.8% of primary care contacts and 6% of psychiatry contacts resulted in recommendations to increase medication dosage as a result of contact, whereas 1% to 2% of each had recommendations to decrease dosage. Primary care consultations were more likely to have medications added (3.7%) than psychiatric ones (1.3%). Medications were changed in 4% to 5% of both groups. Psychiatrists were more likely to receive recommendation to taper/discontinue medications (9.3%) than primary care

**Table 3.** Current Psychotropic Medication Being Utilized by Enrolled Provider's Patient at Time of Consultation

	n	Psychiatry No. (%)	Primary Care No. (%)
Taking any psychiatric medication	399	95 (67.4)	244 (49.1)
at time of consultation <sup>a</sup>			
SSRI	182	43 (28.5)	139 (26.8)
SNRI	23	5 (3.3)	18 (3.5)
Tricyclic	1	1 (0.7)	0
Other antidepressant	62	15 (9.9)	47 (9.1)
Atypical antipsychotica	65	28 (18.5)	37 (7.1)
Typical antipsychotic	2	2 (1.3)	0 (0)
Benzodiazepines	53	16 (10.6)	37 (7.1)
Mood stabilizer <sup>a</sup>	54	28 (18.5)	26 (5.0)
Stimulant	41	14 (9.3)	27 (5.2)
Medication-assisted treatment	16	6 (4.0)	10 (1.9)
Sleep aids	18	7 (4.6)	11 (2.1)
Anxiolytic	22	5 (3.3)	17 (3.3)
Opioids	2	0 (0)	2 (0.4)
Other	19	8 (5.3)	11 (2.1)

Abbreviations: SSRI, selective serotonin reuptake inhibitors; SNRI, serotonin norepinephrine reuptake inhibitors.

<sup>a</sup>Notes the difference is statistically significant.

physicians (3.6%). No medication changes were recommended in 14.3% of primary care contacts and in 28.5% of psychiatric contacts.

#### **Options in Lieu of TPP**

Requesting physicians were also asked what they would have done if TPP had not been available for consultation that day. Just 1.5% of primary care providers and 3.3% of psychiatric providers reported that they would have discontinued medications in this situation; 13.9% of primary care would have started a medication versus 8.6% of psychiatric providers, and 40.7% of primary care encounters would then have referred patients for mental health consultation vs 2% of psychiatric providers who would have referred to further subspecialty level care. Eight percent to 10% of both groups would have consulted with another provider. Psychiatrists reported that in 36.4% of cases, they would have done more independent research, which is higher than 8.9% of primary care providers who would have done the same. Of primary care consults, 1.3% would have recommended patients go to the emergency department (n=7), whereas none of the psychiatric providers would have referred similarly.

#### **Teleconsultation Response Data**

For both primary care and psychiatric providers, there was no significant difference in route of contact (telephone vs email), time spent on phone during consultation, or survey response. All utilizers either agreed or strongly agreed that they were satisfied with services received, felt they could now more effectively manage their patient, and that they could incorporate learned information to help better care for other patients in future.

#### **DISCUSSION**

Differences between utilizers occur for many reasons. First, the inherent differences in populations served are important. Psychiatrists are more often caring for the chronically mentally ill, those struggling with psychotic or bipolar disorders, severe substance use disorders, or treatment-refractory anxiety or depression. This aligns with the differences seen in presenting symptoms and resulting diagnoses in Table 2. As such, psychiatrists typically are using newer psychotropics, augmentation agents, or second- or third-line medication choices for a given condition. Unfortunately, didactic education in the specific subspecialty of perinatal mental health is newer; even in today's curriculum, the amount of training varies widely between programs. The National Curriculum in Reproductive Psychiatry was conceived in 2013 and first piloted during the 2018-2019 academic year (http://ncrptraining.org/). Given how recent this has been implemented, many psychiatrists do not feel comfortable counseling patients on specific risks regarding psychotropic agents in pregnancy. For psychiatrists, TPP allows for psychoeducation regarding use of these medications in pregnancy. This knowledge can certainly then be applied to similar patients on a provider's panel. For those in primary care, the training in medication management of psychotropics in pregnancy is even more limited. Thus, consultations typically focus on more common psychotropics, such as SSRIs; these were the highest number of represented medications and are first-line agents for control of a variety of mental illnesses, such as depressive disorders, anxiety disorders, posttraumatic stress disorder, and obsessive-compulsive disorder.

As noted above, psychiatrists were more likely to consult regarding psychotic illnesses, whereas primary care more often focused on depressive and anxiety symptomatology. Without TPP, patients with a stable illness who can be safely managed by their primary provider would have been referred to mental health, possibly increasing the wait time for a patient with refractory or more severe disease who requires subspecialty-level management. By utilizing TPP, patients can more appropriately stay with their existing care team, allowing for evidence-based practice and knowledge gain in a setting where the patient is already known and comfortable, or TPP can serve as a bridge to more specific levels of psychiatric care without delaying initiation of care.

Psychiatric providers are more likely than primary care providers to consult regarding preconception management. Given the movement towards having all providers assess a patient's plan for pregnancy within the next year, TPP can also support any provider in preconception management of psychotropic medications.<sup>8</sup> This will allow for an overall improvement in maternal and fetal outcomes and an increase in evidence-based management of psychotropics.

Primary care utilization more often results in recommendations to increase medications, whereas psychiatric consultants

more often receive recommendations to decrease medications. This information is beneficial in that it affects differential educational resources and trainings between the 2 groups. Psychiatric utilizers are more often caring for patients using stimulants and benzodiazepines, which carry a dose-dependent risk in pregnancy unlike antidepressant medications and thus require a more detailed risk/benefit discussion.<sup>9,10</sup> As such, TPP can seek to offer more detailed trainings for psychiatric providers to educate on those specific risks, as well as nuances of tapering or discontinuing those medications classes in anticipation of or during pregnancy or lactation. Primary care utilizers—who are most often prescribing SSRI or SNRI agents—can receive more focused education on risks of those medications, as well as the risks of untreated maternal symptoms or illnesses, which can be overlooked. In summation, though utilizers are at times prescribing significantly different medications and receiving different management recommendations, consultative services can still serve to benefit both populations in their patient care.

Other overt differences in groups are revealed by use and knowledge of screening tools. The 2015 recommendations from the American College of Obstetrics and Gynecology to screen all pregnant and postpartum women for depression, as well as directives from other national institutions such as the American Medical Association and the US Preventive Services Task Force to screen all patients for depression routinely, aim to to increase use of validated screening tools.<sup>11,12</sup> These tools (specifically the Edinburgh Postnatal Depression Scale [EPDS], Patient Health Questionnaire [PHQ]-9, and PHQ-2) generate a numeric score that is utilized both as a screen and a rough indicator of severity of illness. However, these tests are not diagnostic tools, and the goldstandard for diagnosis of an illness remains a thorough psychiatric interview. This, then, indicates the likely reason for the high use of screening tools in a primary care setting and the lack of such in psychiatric settings. There remains, though, a benefit in psychiatric professionals also utilizing such tools, given that the ability to track a numeric score over time does allow for an objective measure of symptom severity. As patients increasingly seek care across health systems and from a variety of provider types and specialties, there is value in quantitative information being available and interpretable by multiple providers.

It is also important to know that from the primary care subset, providers reported they would have sent the patient to the emergency department for further assessment in 7 cases. As emergency psychiatric services are also uncommon in most hospitals, this could have resulted in a few different, though costly, interventions. On the one hand, the patient could have been released to outpatient care, with a possible significant wait time to see a psychiatric specialist; this could result in a delay of needed care and sequalae. At the opposite end of the spectrum, the patient could have been referred for inpatient treatment. While inpatient level of care is necessary at times, it should be utilized when indicated and not

as a default plan due to lack of resources. TPP was of assistance in these 7 cases, such that the patient was not then referred for emergency services and more costly care when consultation was of sufficient benefit.

#### CONCLUSION

These data brings to light the differences in consultation between primary care and psychiatric providers. As a service that seeks to support all those caring for reproductive-age women, it is imperative to understand the different needs of utilizers in order to best promote evidence-based care, improve the knowledge base of providers, and encourage an efficient service that can continue to be utilized real-time.

Our analysis implies that primary care (OB/GYN, internal and family medicine, and pediatrics) consults focus predominantly on the more common psychiatric illnesses (depressive and anxiety disorders) and more typically involve first-line medications. Availability of TPP to this group resulted in avoidance of ER visits in several cases, as well as maintenance of patient within their current medical care setting instead of referral to behavioral health for management. Psychiatric and behavioral health clinicians saw more psychotic and alcohol and other drug abuse (AODA) illnesses than primary care. They were less likely to use screening tools and more likely to taper or discontinue medications. For these psychiatric providers, TPP served as a reference point in place of additional solo research into these topics. Though utilizers vary in terms of type of patient seen, management of medications, and subsequent recommendations, consultation was nonetheless rated to be beneficial across the board, and it is strongly recommended that such services be available to any health care provider caring for preconception, pregnant, or postpartum and lactating patients.

Future studies could assess further the related outcomes between precisely which medications were changed by a provider in an individual encounter, so as to better determine management types. For instance, are psychiatrists titrating or tapering benzodiazepines in pregnancy? What about primary care providers? This can further inform understanding on type of patient population and disorders being treated. Additionally, more detailed analysis of the cost-savings benefit of our program can bring to light additional ways to decrease health care spending while maintaining high-quality patient care and improving outcomes for mothers, babies, and families.

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### Patient Preferences for Diagnostic Imaging: CTA vs MRA When Diagnosing Pulmonary Embolism

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#### **ABSTRACT**

**Objective:** To identify preferences regarding choice of diagnostic imaging (computed tomographic angiography [CTA] vs magnetic resonance angiography [MRA]) for the evaluation of pulmonary embolism.

Methods: We conducted 4 focus group discussions with residents of 2 Wisconsin cities. Community members ≥18 years old were recruited via telephone using a commercially available telephone database. The discussions were audio recorded and professionally transcribed. Three investigators (a research specialist, emergency physician, and qualitative methodologist) independently analyzed these transcripts using inductive thematic coding to identify the overarching themes and underlying concepts. Intercoder discrepancies were resolved through consensus discussion by the reviewers.

Results: Focus groups were held over a 3-month period and included 29 participants (16 female). Ages were well represented: 18-30 (n=7), 31-40 (n=8), 41-55 (n=6), and 56+ (n=8) years old. Analysis revealed 3 central themes: time, risk, and experience. Participants who preferred CTA commonly cited the need for immediate results in the emergency department. When nonemergent scenarios were discussed, the option to undergo MRA was considered more strongly; participants weighed additional details like radiation and diagnostic accuracy. Regarding risks, discussants expressed concerns from multiple sources, including radiation and intravenous contrast. However, understanding of this risk varied across the groups. Prior experience with medical imaging—both personal and indirect experiences—carried considerable weight.

**Conclusions:** Preferences regarding imaging choice in the diagnosis of pulmonary embolism were mixed, often reliant on vicarious experiences and an exaggerated notion of the difference in timing of imaging results. Participants frequently used incomplete or even incorrect information as the basis for decision-making.

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#### **INTRODUCTION**

Chest pain and shortness of breath are 2 of the most common presenting complaints for patients seen in the emergency department (ED), accounting for 10.8 million of the 136.6 million ED visits in the United States annually.1 Concern for possible pulmonary embolism (PE) in these patients is historically driven by the dire effects that may result from missing the diagnosis, namely heart failure and death.<sup>2-4</sup> Though the incidence of venous thromboembolism (VTE) is substantial (900,000 cases in the US annually),5 most patients who undergo diagnostic imaging for the evaluation of possible PE end up not having this disease. In fact, PE is only present in 5% to 10% of the patients undergoing imaging evaluation, which is usually computed tomographic angiography (CTA) of the chest.6 Though CTA has high diagnostic accuracy for the diagnosis of PE,7-9 it is associated with 2 potentially hazardous exposures: ionizing radiation and intravenous iodinated contrast.

More recently, magnetic resonance angiography (MRA) has emerged as an ionizing radiation-free imaging alternative to CTA. Due to several studies reporting that its sensitivity is inferior to CTA, particularly the PIOPED III trial, <sup>10</sup> some have advised that MRA be reserved for use at centers that routinely perform MRA well and only for patients with contraindications to CTA. This has greatly limited the potential for wide-scale adoption of MRA as a first-line imaging test for suspected PE. However, other diagnostic efficacy studies evaluating the accuracy of MRA for the diagnosis

of PE have shown that "diagnostic quality" images are obtained as frequently for MRA as they are for CTA, and the accuracy of MRA is similar to that of CTA.<sup>11,12</sup> In fact, when accounting for patient-oriented clinical outcomes (ie, death, missed VTE, and major bleeding), data from the University of Wisconsin (UW) – Madison show that patients fare better after MRA than CTA.<sup>12</sup> The discrepancy between the PIOPED III findings and those at UW likely have origins in the treatment of subsegmental pulmonary emboli (SSPE), a vascular filling defect commonly missed by MRA but more frequently visualized by CTA.<sup>13</sup>

Recently, the American College of Chest Physicians has called into question the value of universally treating these clots, identifying risk groups in which clinical surveillance is recommended over anticoagulation. Additionally, the Society for Academic Emergency Medicine Consensus Conference in 2015 (Diagnostic Imaging in the Emergency Department: A Research Agenda to Optimize Utilization) recommended that alternative diagnostic strategies to the current standard of CTA for the diagnosis of PE should be investigated in an effort to decrease the burden of harmful exposures associated with such scans.

Given the paucity of evidence regarding the patient-oriented benefit of treating SSPE, this area of clinical equipoise would benefit from studying patient preferences regarding the choice of medical imaging, particularly MRA versus CTA, when patients are tested for possible PE. Specifically, it would be valuable to know how patients value the small long-term risk associated with CTA use compared with the unknown, but likely low, risk associated with not diagnosing SSPE. There have been no studies to date answering this question. Therefore, the purpose of this study was to ascertain patient perceptions of PE and the differences between MRA and CTA, as well as assess their preferences regarding imaging modality selection in the diagnosis of PE.

# **METHODS**

# **Study Design**

This study sought to understand the knowledge and opinions regarding the use of diagnostic imaging tests (ie, MRA and CTA) in the context of being evaluated for PE in the ED. Due to the limited availability of existing literature on this topic, we took an exploratory, qualitative approach. Focus group discussion was chosen as the best method to elicit a wide range of opinions, while giving participants the opportunity to discuss the presented topics in depth. We consciously chose not to enroll patients in the ED for 2 reasons: (1) time constraints and potential privacy issues of interviews in the ED would yield suboptimal conditions, resulting in limited exploration of discussants' perspectives; and (2) we did not want to interfere with individual provider's decision-making (be it shared or not) regarding the diagnostic evaluation being pursued in the ED. This study was approved by the institutional review board of the coordinating university.

Table 1. Gender and A	ge Range of Pa	rticipants	
Age Range (years)	Men	Women	Age Range Totals
18-30	3	4	7
31-40	3	5	8
41-55	3	3	6
56+	4	4	8
Gender Totals	13	16	29

# **Study Setting and Population**

This study used a purposive sampling strategy in order to recruit a diverse range of ages and equal gender representation. Participants were drawn from the general public of each city, though were required to be English-speaking adults. Since anyone could be faced with an emergent problem that would require an ED visit for diagnostic imaging, we did not constrain recruitment beyond these basic demographics.

Recruitment took the form of telephone calls to a randomized list of known telephone numbers purchased from a professional sampling firm (Survey Sampling International; Shelton, CT). The telephone sample consisted of a mix of landline and cellular telephone numbers of current residents of either Madison or Milwaukee, 2 metropolitan areas in Wisconsin. The recruiters were professional telephone interviewers at the University of Wisconsin Survey Center. The telephone recruiters called the selected telephone numbers, explained the study objectives and the focus group format, and invited eligible candidates to participate. Confirmation letters were sent to the participants via US mail and reminder telephone calls were made 24 hours before the focus group discussions. Each participant was compensated \$50 at the end of the discussion. By design, 11 participants were recruited for each focus group, with the anticipation that 6 to 8 people would actually attend each group. Table 1 shows the gender and age range of the 29 individuals who attended the groups; 2 were held in Madison and 2 in Milwaukee.

# **Study Protocol**

The principal investigator (MDR), in collaboration with co-investigators with expertise in conducting focus group discussions (KDC, EAJ, MNS), created a discussion guide (Appendix), which was used in all groups. Each discussion lasted approximately 90 minutes. Initial questions in the discussion were open-ended, eliciting participants' knowledge/experience regarding the diagnosis and treatment of PE, as well as with CTA and MRA. We then used the deliberative discussion method to introduce participants to the pros and cons of CTA and MRA, <sup>16</sup> including the potentially harmful exposures of CTA scans and the risks of missing and not treating a PE, particularly as it relates to MRA. In addition, to provide context for participants to render an opinion, the guide included discussion of a clinical vignette about a hypothetical 22-year-old woman presenting to the ED with chest pain and trouble breathing. Participants were asked whether they would

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# Table 2. Quotes Exemplifying the Major Theme of Time

# **Subtheme: Emergencies**

- "Yup, and for me, that's what it's going to come down to. How much time do I have before this could potentially be fatal? Do what's quickest, what's most expedient."
- 2. "Yeah, and if she does develop cancer, deal with the cancer later. Deal with the patient now."
- 3. "I agree with everybody that you want to be involved, but I think, like you said, if it's that emergency, going back to your emergency room situation, chest pain, whatever, I'm just whatever the doctor says, just do it."
- 4. "... but if it was him [the doctor] coming in and saying, we're just going to do a CT scan just to figure out what's going on, I would be gung-ho for it, just because it's in the chest area. I have four kids. I'm not ready to go yet."

#### **Subtheme: Nonemergent**

- 5. "I was just going to say I would think it's kind of, consider also the situation. If you come into an emergency room, you don't have time to go through a whole big MRI. And the CT scan, the speed, the quickness of it, sounds like you've got to make a decision quick. But, if you had, well, 'we're trying to diagnose something, let's see what this is' then maybe the MRI would be, you know, a little more efficient."
- "Yeah, but it's clear to me, I think they got more information because they were doing a breast MRI. So there was much clearer information than, well, mammography..."
- 7. "I guess it would depend on, you know, the situation and which test. Sometimes you hear things that, oh, well, they didn't see anything. I can think of a situation with a cousin where he had cancer of the pancreas. They did not see anything on the CT, and then I think something came out on the MRI. So then in my mind I'm thinking, okay, well, in some situations maybe the CT isn't the answer, and then you have to go to the MRI."

Abbreviations: MRI, magentic resonance imaging; CT, computed tomography.

choose CTA or MRA for the vignette patient. One of the authors (KDC) moderated all groups, and at least 2 of the authors were always present.

#### Measurements

Principal data of interest were the themes that emerged based on participant responses and opinions derived from the moderator-guided focus groups. All discussions were audio recorded and professionally transcribed. Secondarily, the age and gender of each participant was documented.

## **Data Analysis**

The analysis team consisted of a research physician with expertise in radiology and emergency medicine (MDR), a research specialist (RLB), and a qualitative research methodologist with extensive experience in focus group facilitation and analysis (KDC). The electronic transcripts were compiled and organized by discussion guide question and then imported into Dedoose qualitative analysis software (version 7.5.9, SocioCultural Research Consultants; Los Angeles, CA).<sup>17</sup> All transcripts were coded – that is, participants' verbatim transcript responses were assigned to 1 or more categories of similar responses. Coding was done inductively and independently by all authors, using conventional content analysis to identify major themes in the responses to each question.<sup>18</sup> This

method of analysis derives the codes directly from the raw transcripts rather than using codes generated *a priori*. The coding team met regularly to compare their independent coding and to develop consensus codes and themes.

#### **RESULTS**

# **Characteristics of Study Subjects**

Twenty-nine individuals participated in this research project: 15 from Madison and 14 from Milwaukee. Participant age and gender details are shown in Table 1.

#### **Main Results**

After thorough collaborative analysis of the transcripts from the 4 focus groups and resultant coding structures, 3 central themes emerged: time, risk, and experience.

## Theme 1: Time

Discussants frequently noted time differences between acquiring the images for MRA versus CTA as an element that influenced their decision-making. Notably, we did not provide this information in the deliberative discussion; participants came with this as a preconceived notion. In emergencies, participants believed the time spent in the scanner (CTA or MRA) to be a variable that had a significant impact on a patient's outcome. In these time-sensitive instances, we observed partiality towards CTA because of its perceived speed. One participant said, "I like the speed of the CT scan. It seems to be much, much quicker for the patient."

The importance of time persisted, even as the facilitator—following the discussion guide—described some of the risks of CTA, such as radiation exposure and iodinated intravenous contrast administration. These risks did not affect some participants, as one said, "I guess to me, since I don't have a preference about radiation, I would probably go with the faster, hypothetically faster operation." Many participants reiterated the idea that fast results were a top priority. One group member said, "I think the reward is more worth the risk, because it's that time, those couple of minutes, that it might take to transport her from one to the other—those couple of minutes, you know, while she's in the MR machine could be the end for her."

As the facilitator further described the clinical vignette, the element of time continued to be considered. Participants were asked to decide which imaging modality should be used in this fictional scenario. Among those wanting to pursue CTA, 1 person said, "She had trouble breathing. Right then and there, you've got to go for the quick solution." As the conversation progressed, the facilitator helped participants explore their decision-making process for nonemergent events. In these scenarios, many participants said they felt that MRA would be a better option. One participant believed MRA to have better diagnostic capabilities, as they described their thoughts regarding when each of the imaging options should be used (Table 2, quote 5). Other references to nonurgent MRA experiences were described, including a partici-

pant who said, "I had an MR for my left knee. It was a small meniscus tear. That was my experience with it. Pretty short and sweet."

#### Theme 2: Risk

Participants referenced multiple sources of perceived risk within the discussions. The most commonly discussed subthemes were radiation, iodinated contrast, interpretation of risk, and patient anxiety. Regarding radiation, generally the participants either were explicit about desires to avoid it or they did not believe they would be affected by the exposure (Table 3, quotes 1-4). For example, 1 participant said, "...I don't really have enough...radiation. I would assume that my body would, you know, get rid of it eventually or not have any serious negative effects…"

Within 1 discussion, the relative radiation dose of a single CT scan was shared (ie, 1 CT scan of the abdomen/pelvis delivers the same amount of radiation as 100 to 500 chest x-rays).19 This new knowledge caused some participants to change their mind about which scan they would prefer. Specifically, 1 participant commented, "Yeah. I'd have changed my opinion if I had known the 500 x-rays. I didn't know it was that much." Another said, "And I guess if the doctor would have said to me, it's 100 to 500 chest x-rays, then I would have chosen the MR because I didn't know that when I answered the question in the beginning." Participants with strong wishes to avoid radiation shared comments such as, "Even though I don't like MRs and they're very uncomfortable, I would definitely choose the one without radiation." Radiation risk was a prominent topic within these discussions, with participants ranging in their degree of exposure avoidance.

Iodinated intravenous contrast administration elicited similarly strong opinions from participants. Frequently, they stated 1 of 2 sentiments: either they wanted to avoid contrast entirely or they did not believe they would be harmed by the injection. Persons with previous experi-

## Table 3. Quotes Exemplifying the Major Theme of Risk

#### **Subtheme: Radiation**

- "[when asked about getting a CT scan] I think it would be a chance I'd want, might have to take because
  if there was really considerable seriousness of this and that it's really not going away and there's nothing else to try, because again, like you said, if you do the MRI, you may end up having to do the CT scan
  anyway. So I guess I would chance it."
- 2. "So I kind of feel like I wouldn't be worried about radiation. We've been doing MRIs and using radiation for x-rays for quite a long time now..."
- 3. "But if they can detect the stuff with an MRI, probably go with that first because it gets rid of the radiation and stuff, you know. Gets that out of the picture."
- 4. "Yeah, I'd have changed my opinion if I had known the 500 x-rays. Wow. I didn't know it was that much."

# **Subtheme: Iodinated Intravenous Contrast**

- "...the stuff they put in my arm that made me feel really warm and like I was chewing on a penny and I didn't like the feeling."
- 6. "But the CT was a little scary because of the injection."
- 7. "Maybe I, you know, having had both, if I don't have to have that stuff injected, I mean, that's creepy.
- 8. "CT is tricky for me because they can't put iodine dye in me, so they don't tend to use, find the X-rays particularly useful."
- 9. "But the kidney damage, I'm not really as worried about. Because on one of the things the doctors stress when you get a CT scan is to, afterwards, drink plenty of water to flush out the dye out of your kidneys and stuff. And if you're doing what the doctor tells you, and you're flushing your kidneys out, I don't think there's that high of a chance of getting kidney damage from it."
- 10. "I mean, if it were me, I would probably want to get to the bottom of it, and my kidneys are the least of my issue if I have healthy kidneys to begin with. So I would go with the CT scan."

#### Subtheme: Interpretation of Risk

- 11. "I think if the doctor is recommending this new MRI scan that would catch even small ones potentially, that might be a good option for somebody who had that sort of a risk just to at least consider just because they could catch it, you know, and then there wouldn't be the extra added risk of cancer."
- 12. "So I'm assuming that like she's got a problem here, nd that probably means she has a big blood clot, or it wouldn't be this much of a problem. So I would say, go with the MRI because it's going to catch the big clot, and it has no other risks. So if I were to go with the CT, maybe it will catch everything, but I also have the chance of getting radiation and cancer later on or kidney damage later on when I think the MRI could probably catch what it needs to."
- 13. "I think she should have the CT. For one, she's her age, she's 22, and she's having chest pains at 22 years of age. You know, so that would be really good for her to get the CT, so they can catch it right away. It's one of the best ways. You know, she may be exposed to a little radiation. However, they say it's safe levels of radiation. You never know. It all depends on the body...some people don't get, they don't get the exposure to the radiation sometimes. It may not affect them, so I think the CT would be good for her because of her age too."
- 14. "So if it's a very, very small chance of that, I'm wondering, I would definitely go with that, because the likelihood is very, if it's very, very rare, I want the most, you know, I want detection... [regarding picking CT]... Because if it [downstream risk of cancer] is something very, very rare, which I don't know if we can confirm or deny that, but I would want the CT..."
- 15. "Well, if it were me, I would be clear with the doctor. I would say, use whatever gives you the absolute best, most information no matter what these minor risks are. I would absolutely say that. In your judgment, what is the absolute best for you to find whether there's a problem or not? It doesn't matter which one. That's what I would say absolutely."
- 16. "I guess I feel like since there's, I mean, and like she was saying, like [name redacted] said, some of them, sometimes there's one that, you know, is going to be able to find something that the other scan might not. So, if it comes down to having both, you know, I'll have both."
- 17. If you don't find anything, keep testing."

# **Subtheme: Patient Anxiety**

- 18. "I needed the anti-anxiety because I am claustrophobic, and that's like the worst."
- 19. "Maybe that's something we should be offering to everybody going in. Some kind of anti-anxiety..."
- 20. "When I was younger, I didn't have claustrophobia. Now that I'm older I have developed it somehow, so being in there for a while, having to lay still, even though it only went up to my knees, if it had gone for much longer or they had pushed me in any further, I would have started to feel a little anxiety."
- 21. "I'd rather be with the CT scan... scary inside that tunnel [referring to MRI]."

Abbreviations: MRI, magentic resonance imaging; CT, computed tomography.

#### Table 4. Quotes Exemplifying the Major Theme of Experience

#### **Subtheme: Direct Experience**

- 1. "I don't have a preference. I am under the impression that, and not for any kind of scientific reason, I'm under the impression that the MRI is better. It's like a better picture. It's more detailed. It shows the soft tissue. Again, I have no idea if that's right, and so at the end of the day, I would do whatever my doctor told me to do. I don't really have enough...radiation. I would assume that my body would, you know, get rid of it eventually or not have any serious negative effects..."
- 2. "But you know, I've never really heard of anything, and I've never, when I got my MRI, they didn't say, well, we're going to use this much radiation, so they didn't even explain those risks to me. It was more important to have the MRI. So I kind of feel like I wouldn't be worried that much about the radiation. We've been doing MRIs and using radiation for x-rays for quite a long time now."
- 3. "And then the interesting thing is they always ask you if you have any metal, you know. I'm not sure if I have like shrapnel or anything in me, and then they have to kind of figure out whether it's worth it to go and do the scan or to not do the scan. So it's kind of frightening in that sense. And then they injected some liquid into me like with that but just to be able to see something better in the frame. That's my experience with it. It wasn't really fun, but it wasn't as bad as I thought it was going to be."

#### Subtheme: Indirect Experience

- 4. "I can think of a situation with a cousin where he had cancer of the pancreas. They did not see anything on the CT, and then I think something came out on the MRI."
- 5. "Men, you know, don't go to the doctor. They don't want to hear. They don't want to deal with the problem. They'll just go right through it. My mom went right through her problems. She wasn't going to go back. I mean, one of the things happens is if have a bad experience one time, you know, with one of these techniques, for whatever reasons, you're very shy about doing that again. And so it's what you're willing to, you know, a lot of people just go right on and don't want to have to deal with it either from an emotional standpoint or a financial standpoint or whatever. They can live with the pain or their inconvenience."
- "I know there's open MRIs, so I haven't really experienced the open one yet, but just the noise itself being so loud, I think I would prefer maybe the CT better."
- 7. "Just heard of them, and, you know, seeing the MRI thing like in the movies, whatever. How realistic that is, I don't know."

Abbreviations: MRI, magentic resonance imaging; CT, computed tomography.

ence receiving contrast shared vivid descriptions of these events. One participant said, "I felt like I was wetting my pants. It was kind of disturbing" while another said, "But then they put that injection, yeah, it felt like my whole body was on fire." These participants were clear that receiving contrast was not an enjoyable experience (Table 3, quotes 5-7). Others mentioned existing medical conditions for which receiving contrast was contraindicated (Table 3, quote 8). In each group, however, there were members present who did not share these concerns about contrast. They believed following their physician's orders regarding postscan care would be enough to keep their kidneys healthy (Table 3, quotes 9-10).

Beyond radiation and contrast administration risks, another subtheme present was interpretation of risk. The facilitator told participants that the health risks associated with missing a SSPE by either CTA or MRA was unknown, though CTA scans could

detect smaller PEs with greater accuracy than MRA. Participants were then asked to opine on 2 scenarios: being able to detect SSPEs more accurately but requiring exposure to ionizing radiation (the case of CTA) versus an unknown risk of a false-negative test result regarding the presence of a small clot (SSPE) but with no ionizing radiation exposure (the case of MRA). The influence of this unknown risk on participants' perceptions varied (Table 3, quotes 11-15). During discussions about the clinical vignette, a participant voiced the following concern, "What if it's like a tiny blood clot—really, really small—and that new MR doesn't catch it in time, and then she just... those precious moments are like gone." Others had more confidence in MRA. One said, "... would still say go with the MR, because I don't feel like the smaller ones would be as important." As might be expected, those participants preferring CTA were anxious about the possibility of missing any sized PE. One participant said, "So it just seems to me, why would you take a chance with the MR if you have like 100% certainty with the CT scan?"

The last prominent subtheme of risk discussed in the focus groups was anxiety. Participants expressed anxiety towards both imaging modalities; however, MRA received more scrutiny as it was regarded as more involved than CTA. Like the difference in image acquisition time mentioned previously, the process of image acquisition was not discussed by the facilitator. Nonetheless, participants had preconceived notions of what each imaging modality entailed. The design of an MR scanner (mostly enclosed space) was a major limitation for many due to being claustrophobic. The severity of claustrophobia among participants varied: for some, it was a significant concern; for others, the fear could be easily managed with medication (Table 3, quote 18). In 1 group, participants discussed the idea of a prescan sedative. They recommended medication be available as an option for all patients undergoing MR imaging (Table 3, quote 19). A few people also described having an easier time managing their claustrophobia when in an "open" MR scanner (Table 3, quote 20). Regarding their own size, 1 participant commented, "And because I'm big, you don't fit in the tube so well. You've got to go in the big tube." Participants expressed important hesitations over different components of MR scanning, which inevitability factored into their decision-making process (Table 3, quote 21).

# Theme 3: Experience

Participants' prior experience with diagnostic imaging was the final theme to have an influence on their decision-making. Within each of the groups, discussants' experiences and impressions of these imaging events varied greatly. Some had absolutely no experience, while others had significant experiences to share. Those with repeated experiences typically had chronic medical conditions or employment in health care, though none were physicians or nurses. Among the participants who identified as having no experience with imaging, 1 person shared that for no particular

reason, he believed MRA to be better than CTA (Table 4, quote 1). Another participant, with experience undergoing both kinds of imaging, said, "That was just my experience with MRs is they're noisy coffins. CT scans are relatively easy. They're open. Other than that, they are what they are. They're very loud." Sometimes, participants' experience with medical imaging led to them gaining misinformation. In particular, a comment was made about the radiation dose received during an MR exam (Table 4, quote 2). Not all experiences were negative; 1 participant spoke favorably about their experiences, aying, "And I've had experiences with people that were really good, like the first CT, you know, the guy just explaining, okay, this is exactly what's going to happen. This is how you're going to feel." Others also mentioned being similarly surprised when their MR experiences did not meet their negative expectations (Table 4, quote 3).

The most common indirect imaging experiences referenced in discussions were those of friends and family members (Table 4, quotes 4-5). These events held particular weight for those without direct experience. One participant referenced a sister's experience saying, "So I just like experienced all of this stuff in the hospital being there with her. I mean, I haven't experienced an MR personally myself, but just knowing how beneficial it was for her, because she was really sick." Knowledge of these indirect experiences frequently motivated participant preferences (Table 4, quote 6). While deliberating the risks of CTA, 1 participant said, "It's hard to say. Me personally, wanting to do less-invasive stuff because there is cancer in some of my immediate family, that's what I've always leaned away from." It was common for participant decision-making to reflect the positive or negative perception that they observed indirectly in another person's imaging event. Other indirect experiences mentioned were social media, television, and movies, but these sources generally had neutral effects on participant opinion (Table 4, quote 7).

# **DISCUSSION**

In this study, we sought to identify preferences and opinions held by the general public about diagnostic imaging for PE. Specifically, we aimed to ascertain what their preconceived notions were about MRA and CTA, as well as assess their preferences for choice of imaging test after we provided basic information about the potential benefits and drawbacks of each imaging technique. Across all 4 focus group discussions, the major themes present were time, risk, and prior experience (either direct or indirect). Participants frequently used these themes to develop or rationalize their decision-making process.

Frequently, discussants would allude to their impression that people coming to the ED needed immediate imaging since they could be facing a life-threatening emergency (Table 2, quote 4). We observed participants placing a high degree of importance on finding any abnormality that could explain their symptoms while discussing the mock scenario (Table 3, quotes 14-15). Interestingly, the possibility of false-positive findings did not enter

the narrative at any point. Further, discussants seemed to conceptualize PE as 1 uniform disease process, ie, a potentially deadly clot that causes severe symptoms. The full spectrum of disease—particularly the entity of SSPE—was not in their awareness until we disclosed it later during the deliberative discussion. Moreover, discussion regarding the costs associated with medical imaging was limited, even though discussants suggested potentially undergoing both imaging tests in tandem to fully ensure that PE was not present (Table 3, quotes 16-17).

When we presented participants with the fact that PE exists on a spectrum of severity and that physicians do not have a uniform approach for the treatment of SSPE, many of the discussants changed their preference from CTA to MRA (Table 3, 4). Posed with this additional background information, several participants simply stated that they would trust whatever the doctor recommended, while others wanted to be more engaged in the decision-making process. The shift in preference from CTA to MRA given the new information underlines the importance for shared decision-making in clinical contexts such as this, where there is more than 1 reasonable choice of diagnostic evaluation. In fact, a recent survey of emergency medicine physicians reported that there was more than 1 acceptable treatment option for over half of their patients, yet the shared decision model was applied in only 58% of those cases.<sup>20</sup>

Further echoing this concept, Rodriguez et al investigated patient opinions regarding CT imaging and radiation exposure. They proposed a variable threshold for what patients determined to be an acceptable risk of CT radiation.<sup>21</sup> Within our focus group discussions, participants demonstrated a similar shifting tolerance for risk acceptance. Multiple factors influenced the theoretical circumstances in which they would accept or reject increased risks, namely either radiation from CTA or the possibility of a false-negative MRA result. These findings suggest that providing patients with more information regarding their diagnostic imaging choices may be necessary in order for them to meaningfully participate in shared decision-making.

A previous study regarding patient knowledge of risks and radiation dose of medical imaging reported only 14% understood the relative radiation exposure of a CT scan compared to a chest x-ray, and 23% were aware that MR scans did not use radiation.<sup>22</sup> These data continue to highlight the problem that patient awareness of radiation exposure from CTs and their long-term risks is low. For imaging events such as SSPE, wherein the increased benefit of a CT scan is unclear, patients need to have an informed understanding of the potential health costs of undergoing such imaging. Working to increase public knowledge surrounding diagnostic imaging risks and benefits stands to have significant impact on overall public health.

There are several limitations to our study. First, participants were not screened for prior visits to the ED, whether they worked in health care or had prior experience with diagnostic imaging, and we acknowledge these experiences may have been factors in the

decision of whether or not to participate in the study. Secondly, since the discussants represent only 1 state, the opinions presented here may have been geographically homogenous. Third, though we observed many redundant experiences and opinions in our discussions, we did not conduct a formal assessment of thematic saturation prior to ending the study. Finally, the use of the deliberative discussion method - which, for our objectives, required the explanation of complex topics such as the risks of PE and the pros and cons of diagnostic imaging - may have introduced bias. However, under the direction of our qualitative research experts, every attempt was made to introduce concepts in a neutral and comprehensible way. Respondents were encouraged to discuss the issues thoroughly and to arrive at their own conclusions. Finally, though "groupthink" is sometimes observed in focus group discussions, we attempted to limit this by restricting the number of participants per discussion group.

# **CONCLUSIONS**

We found that patients often have preconceived notions of the potential benefits and drawbacks of imaging tests, particularly MRA and CTA, and frequently rely on both personal and vicarious experiences to inform these opinions. Not surprisingly, these are often based on incomplete, and at times inaccurate, information. Their perception of underlying potential disease processes appears to be skewed to the direst of circumstances, perhaps in contradiction to the belief of the treating physician. Once people learn that diseases—particularly PE—exist on a spectrum of severity and, therefore, do not usually pose an imminent life threat, patients' preferences for medical imaging modalities may change.

In clinical circumstances where there is a reasonable choice of diagnostic imaging strategies, as in the case of the evaluation of PE, we suggest that engaging patients in shared decision-making is both possible and desired by patients. When pursuing this, however, the burden to confirm that patients are utilizing accurate information falls on the physician. Therefore, it is advisable to have an open discussion with patients regarding their baseline knowledge of medical imaging, their true risk of disease, and their level of clinical stability to ensure a fruitful conversation.

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# Therapeutic Efficacy of Yoga for Common Primary Care Conditions

Adrienne Hampton, MD; Megan Bartz, MD

# **ABSTRACT**

**Introduction:** Yoga is a popular form of exercise that uses body postures, meditation, and breathing techniques and has been shown to have many health benefits.

**Objective/Methods:** Our goal for this review is to orient health professionals to the evidence-based uses of yoga most relevant to primary care. We conducted a PubMed search that included meta-analyses, reviews, systematic reviews, and randomized controlled trials.

**Results:** Results were limited to English language and publication between 2010 and 2020. Yoga was found to help decrease hypertension, relieve back pain, promote overall well-being, and improve mental health.

**Conclusions:** Yoga is a relatively safe and effective option for patients interested in therapeutic lifestyle change to promote well-being and to help manage hypertension, back pain, and overall mental health.

**INTRODUCTION** 

Yoga is a system of health-promoting attitudes and practices arising out of Hindu philosophy. In the West, the elements of yoga most emphasized and widely practiced are breath control practices, bodily postures, and meditation.<sup>1,2</sup> Increasingly, Americans are practicing yoga for overall wellness and to treat specific health conditions. A 2017 survey of US adults ages 18+ found that 1 in 7 Americans had practiced yoga in the past 12 months.<sup>3</sup> As such, primary care clinicians may encounter questions about yoga, including the health benefits and safety of this practice. To orient health care professionals to the evidence-based uses of yoga,

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we review current literature on the efficacy of yoga to address commonly encountered health-related concerns. A 2018 systematic review of the top reasons for primary care visits found that—in descending order—hypertension, upper respiratory tract infection, depression/anxiety, back pain, and routine health maintenance are the 5 top reasons for visits to primary care clinicians in developed countries.<sup>4</sup> Our review focuses on these conditions, excluding upper respiratory tract infection.

## **SEARCH METHODS**

We completed a PubMed search using the key terms "yoga" and each reported condition, and "yoga and safety." The search parameters included meta-analyses, reviews, systematic reviews, and randomized controlled trials (RCT). We limited our inquiry to English language and publication between 2010 and 2020 for search dates February 1, 2020 through May 29, 2020. Two reviewers evaluated articles for inclusion. From this initial search, we prioritized meta-analyses and reviews with adult study populations, though 1 included study includes incarcerated youth. High quality RCTs were included where meta-analyses and reviews were not available.

# **PATIENT CASE: Linda**

Linda is a 61-year-old woman who comes to see you for a routine health maintenance visit. She has a history of hypertension that she prefers to manage without pharmaceuticals. Additionally, she notes her mother suffered a series of devastating falls, and she'd like a health maintenance activity to support healthy mobility into advanced age. Based on what she's heard of the health benefits of yoga, she asks if yoga might be a good activity to try.

Author/Year	Study Design	Study Populations	Outcomes	No. of Studies/ Subgroups	Sample Size	Results (95% CI)  P value	Controls
Chu, et al, 2016 <sup>6</sup>	Meta-analysis	Healthy adults and ASCVD risk, metabolic syndrome, diabetes, CAD	BMI, kg/m <sup>2</sup>	8	654	MD -0.77 (-1.09 to -0.44) P<0.00001	Nonexercise
			SBP, mmHg	22	1470	MD -5.21 (-8.01 to -2.42) P=0.0003	
			LDL, mg/dl	12	751	MD -12.14 (-21.80 to-2.48) P=0.01	
			HDL, mg/dl	12	751	MD 3.20 (1.86 to 4.54) <i>P</i> <0.00001	
Hartley, et al, 2014 <sup>7</sup>	Meta-analysis	Adults with ASCVD risk factors, HIV, menstrual irregularities, and healthy adults	HDL, mg/dl	5	207	MD 3.09 (0.77 to 5.41) P=0.01	Nonexercise
			Triglycerides, mg/	dl 5	207	MD -23.91 (-38.97 to -9.74) P=0	
			DBP, mmHg	8	444	MD -2.90 (-4.52 to -1.28) P=0	

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; MD, mean difference; CAD, coronary artery disease; SBP, systolic blood pressure; LDL, low density lipoprotein; HDL, high density lipoprotein; DPB, diastolic blood pressure.

Author/Year	Study Design	Study Populations	Outcomes N	lo. of Studies/ Subgroups	Sample Size	Results (95% CI)  P value	Controls
Sivaramakri- shan, et al,	Meta-analysis	Healthy adults mean age 60+	Balance	7	265	ES 0.70 (0.19 to 1.22) P=0.01	Nonexercise
2019 <sup>8</sup>			Lower limb strength	7	485	ES 0.45 (0.22 to 0.68) P< 0.001	
			Lower body flexibility	7	431	ES 0.50 (0.30 to 0.69) P< 0.001	
			Depression	8	450	ES 0.64 (0.30 to 0.95) P< 0.001	
			Perceived mental healt	n 9	554	ES 0.60 (0.33 to 0.87) P< 0.001	
			Perceived physical hea	th 5	400	ES 0.61 (0.29 to 0.94) P< 0.001	
			Sleep quality	4	353	ES 0.65 (0.41 to 0.88) P< 0.001	
			Vitality	3	196	ES 0.31 (0.03 to 0.59) P= 0.03	
			Lower body flexibility	3	225	ES 0.28 (0.01 to 0.54) P= 0.04	Exercise
			Lower limb strength	3	225	ES 0.49 (0.1 to 0.88) P=0.01	
Tulloch, et al, 2018 <sup>9</sup>	Meta-analysis	Adults, mean ages 60+, 74% female, community- and facility-dwelling,	HRQOL	12	752	SMD 0.51 (0.25 to 0.76) P<0.001	Nonexercise
		healthy with OA, cancer history, Parkinsons disease, COPD, chronic back pain	Mental well-being	12	752	SMD 0.38 (0.15 to 0.62) P = 0.001	

# **HEALTH MAINTENANCE AND WELL-BEING**

According to national survey data from 2012, 78% of people practicing yoga in the US are practicing for general health and disease prevention. 5 Yoga has shown benefit for several indicators of wellbeing in otherwise healthy individuals.

Yoga may be an effective intervention for atherosclerotic car-

diovascular disease risk reduction. In a 2016 meta-analysis of 32 RCTs with healthy adults and adults with cardiovascular disease risk factors, diabetes, metabolic syndrome, and coronary artery disease (CAD), asana-based yoga practice was shown to improve cardiovascular risk factors including body mass index (BMI), systolic blood pressure (SBP), low density lipoprotein (LDL) and

Author/Year	Study Design	Study Populations	Outcomes	No. of Studies/ Subgroups	Sample Size	Results (95% CI)  P value	Controls
Hagins, et al, 2013 <sup>18</sup>	Systematic review, meta-analysis nonexercise	Prehypertensive or hypertensive adults	Blood pressure	17	1013	SBP -4.17 mmHg (-6.35 to -1.99) P=0.0002 DBP -3.62 mmHg (-4.92 to -1.60) P=0.0001	Exercise and nonexercise
Cramer, et al, 2014 <sup>19</sup>	Systematic review, meta-analysis	Prehypertensive or hypertensive adults	Blood pressure	7	452	SBP -9.65 mmHg (-17.23 to -2.06) P=0.01 DBP -7.22 mmHg (-12.83, -1.62) P=0.01	Nonexercise
Cramer, et al, 2014 <sup>20</sup>	Systematic review, meta-analysis	Healthy, nondiabetic adults with risk of CVD or adults with diabetes mellitus type 2	Blood pressure	17	SBP 952 DBP 991	SBP -5.85 mmHg (-8.81 to -2.89) P<0.01 DBP -4.12 mmHg (-6.55, -1.69) P<0.01	Nonexercise
Wu, et al, 2019 <sup>21</sup>	Systematic review, meta-analysis	Adults	Blood Pressure	49	3517	SBP weighted mean effect size -0.47 (-0.62 to -0.32, -5.0 mmHg) $P$ <0.001 DBP weighted mean effect size -0.47 (-0.61 to -0.32, -3.9 mmHg) $P$ <0.001	Nonexercise

high density lipoprotein (HDL) cholesterol compared to nonexercise controls. Notably, no difference was observed between yoga and other exercise interventions<sup>6</sup> (Table 1). A 2014 Cochrane review evaluating yoga for the prevention of cardiovascular disease reported improvements in diastolic blood pressure, HDL cholesterol, and triglycerides with yoga interventions<sup>7</sup> (Table 1).

Yoga shows promise as a health maintenance activity for older adults. A large 2019 meta-analysis of the effects of yoga on physical functioning (17 trials) and health-related quality of life (20 trials) in older adults demonstrated that yoga practice is associated with improved balance, flexibility, and strength compared to inactive controls. Compared to active controls, results for strength and flexibility favored yoga interventions. Results for health-related quality of life also favored the yoga interventions in the domains of depression, perceived mental health, perceived physical health, sleep quality, and vitality as compared to nonactive controls8 (Table 2). In 2018, Tulloch et al published a meta-analysis of 12 RCTs in people 60+ years of age (n=752)examining the effects of yoga on health-related quality of life and mental well-being. They found a significant medium-sized effect on health-related quality of life and a small, statistically significant effect on mental well-being9 (Table 2). In a 2016 metaanalysis (n = 307), results for yoga trended toward improved balance and mobility in persons 60 years or older, though results did not reach statistical significance.<sup>10</sup> A 2019 pilot RCT with 81 participants 55+ years of age with a diagnosis of mild cognitive impairment showed improvements in memory for both the yoga and a memory training intervention, where only the yoga participants showed statistically significant improvements in executive functioning compared to participants in the memory training group.<sup>11</sup> In a 2014 RCT of peri- and postmenopausal women, yoga showed a modest positive effect on menopauserelated quality of life.<sup>12</sup> These results demonstrate that yoga can help older adults improve their physical functioning and quality of life.

In a systematic review of 5 RCTs examining the effects of yoga on workplace well-being, 4 studies evaluating yoga interventions showed statistically significant reductions in workplace stress, and no adverse events were recorded. One study did not report results.<sup>13</sup>

In a 2015 meta-analysis examining the effects of yoga on incarcerated women and youth, participants in yoga programs showed improved behavioral functioning (10 trials) and psychological well-being (9 trials), with longer programs tending to show more robust results.<sup>14</sup>

# **HYPERTENSION**

According to America's Health Rankings in 2019, 30.8% of Wisconsin adults have been told they have high blood pressure by a health professional.<sup>15</sup> The Wisconsin Chronic Disease Quality Improvement Project found that patients with hypertension and with Wisconsin health plans and national commercial health plans had controlled blood pressure an average of 68.6% and 62.2%, respectively.<sup>16</sup> As of 2017, high blood pressure was estimated to account for \$68 billion in medical care expenses per year in the US.<sup>17</sup> Yoga has been considered as a treatment to improve blood pressure control.

There have been 4 systematic reviews and meta-analyses in the last several years looking at patients with high blood pressure and yoga<sup>18-21</sup> (Table 3). All of the reviews have shown some improvement in both SBP and diastolic blood pressure (DPB), though they have not always been consistent in the amount of change seen. This is likely due to the low number of studies in this area, high or unclear risk of bias in most of the studies

included, and high degree of heterogeneity. The 3 reviews that looked at yoga vs exercise as a control showed that there was no statistical difference between these interventions. 18-20

In the 2013 systematic review and meta-analysis by Hagins et al, yoga was found to decrease SBP by -4.17 mmHg (P=0.0002; 95% CI, -6.35 to -1.99) and DBP by -3.62 mmHg (*P*=0.0001; 95% CI, -4.92 to -1.60).18 Subgroup analysis showed further reduction of SBP (-8.17 mmHg) and DBP (-6.14 mmHg) when yoga contained all 3 elements (postures, breathing, and meditation) compared to yoga that contained <3 of these elements.18 The systematic review and meta-analysis in 2014 studying yoga and hypertension by Cramer et al showed a reduction in SBP of -9.65 mmHg (P=0.01; 95% CI, -17.23 to -2.06) and DBP of -7.22 mmHg (*P*=0.01; 95% CI, -12.83 to -1.62).19 Another meta-analysis by Cramer et al looked at patients with cardiovascular risk factors and found that yoga vs usual care or no intervention was associated with a decrease in SBP of -5.85 mmHg (P<0.01; 95% CI, -8.81 to -2.89) and DBP of -4.12 mmHg (*P*<0.01; 95% CI, -6.55 to -1.69). Furthermore, in nondiabetic patients with high cardiovascular risk factors, they found that SBP was decreased by -10.00 mmHg (P<0.01; 95% CI, -16.42 to -3.59) in the yoga group vs usual care/no treatment.<sup>20</sup> Between groups assigned to yoga and to exercise, no significant differences in blood pressure outcomes were observed. 18-20

In the most recent systematic review and meta-analysis, a meta-regression analysis was done to determine which elements of yoga elicited the greatest blood pressure effects. Reductions of SBP were statistically significantly greater for studies including breathing techniques and higher initial blood pressures. The additive model created for SBP (samples with hypertension, breathing techniques, and average methodological study quality and controlled for publication bias) showed a decrease in SBP of -11.3 mmHg (95% CI, -14.6 to -8.1).<sup>21</sup> Reductions of DBP were statistically significantly greater for studies including meditation, practicing ≥ 4x per week, and higher initial blood pressure. The additive model created for DBP (samples with hypertension, meditation, average methodological study quality, and yoga practiced >3x per week) showed a reduction of DBP by -5.5 mmHg (95% CI, -7.4 to -3.8).<sup>21</sup>

Despite the high amount of heterogeneity and high risk of bias in the randomized controlled trials noted in most of the meta-analyses, all have found a statistically significant decrease in blood pressure with yoga. This suggests that there is evidence that yoga can decrease both SBP and DBP in meaningful amounts ranging from 4 mmHg to 11 mmHg and 3 mmHg to 7 mmHg, respectively.

However, as with most lifestyle modifications, questions remain about the feasibility and the likelihood that patients will implement these changes in their lives. A matched controlled study by Wolff et al looked at adult patients who were matched by SBP and whether a yoga class vs at-home yoga were more effective in lowering blood pressure.<sup>22</sup> The yoga at-home group was given a CD and a manual by a health professional who was not a qualified yoga instructor. Interestingly, the at-home yoga group showed a

decrease in DBP by 4.4 mmHg compared to the control (treatment as usual). This is in contrast to no improvement in blood pressure in the yoga class group compared to the control, suggesting that an at-home practice could be a feasible lifestyle change.<sup>22</sup> Another study by Sarah et al looked at male patients who were hospitalized in Germany for noncardiac or pulmonary diagnoses and with SBP >135 and <165 mmHg.23 These patients underwent inpatient yoga practice during rehab prior to discharge. The study was evaluating whether telerehabilitation (including telephone check-ins) vs no further support increased the likelihood of continued compliance with yoga practice. It was found that adherence was statistically significantly higher in the telerehabilitation group vs the control group (60.5% vs 29.3%, P<0.0001 at 6 months and 56.0% vs 23.9%, P = 0.014).<sup>23</sup> This suggests that phone check-ins can be useful in supporting patient adherence to this lifestyle modification.

Overall, yoga has been shown to decrease SBP by 4 mmHg to 11 mmHg and DBP by 3 mmHg to 7 mmHg and is a feasible option for patients to do at home with some support from primary care providers.

#### **PATIENT CASE: Linda continued**

You discuss the benefits of yoga with Linda. At a follow-up 4 months later, she states that she has been practicing yoga about 3 times a week and finding joy in this practice. Her blood pressure is under control and she thanks you for your recommendation.

# **PATIENT CASE: Mark**

Mark is a 50-year-old male with a history of depression who presents to your office to discuss low back pain. He has had low back pain for years. He has tried many different treatment modalities including NSAIDs, acetaminophen, lidocaine patches, Icy Hot, and physical therapy. He is wondering if there is anything else that can be done to help with his pain. He also has a nephew with opioid use disorder and would like to avoid any more medications. His wife has been doing yoga and he's wondering if this would help with his back.

# **BACK PAIN**

Back pain is estimated to generate \$100 billion in health care costs annually,<sup>24</sup> and back pain consistently ranks among the top 3 diagnoses in claims prevalence and cost for Quartz Health Solutions, a major Wisconsin health insurance company.<sup>25</sup>

Yoga has been studied extensively for chronic low back pain and function. <sup>26-28</sup> A 2019 meta-analysis of 13 RCTs evaluating the effectiveness of yoga for low back pain demonstrated that yoga practice significantly decreased pain intensity (standardized mean difference [SMD] -0.33; 95% CI, -0.47 to -0.19, *P*<0.001)26 (Table 4). In a 2013 meta-analysis of yoga for low back pain and pain-related function, yoga was shown to improve pain based on what the reviewers deemed moderate quality evidence from 6 high quality RCTs. Short-term improvements in back-related disabil-

Author/Year	Study Design	Study Populations	Outcomes	No. of Studies/ Subgroups	Sample Size	Results (95% CI)  P value	Controls
Zou 2019 <sup>26</sup>	Meta-analysis	Adults with chronic low back pain	Pain intensity	10	1179 <i>P</i> <0.001	SMD -0.33 (-0.47 to -0.19) nonexercise	Exercise and
Cramer <sup>27</sup> 2013	Meta-analysis	Adults with chronic low back pain	Pain intensity + pain bothersomeness	6	584	SMD -0.48 (-0.65 to -0.31) P<0.01	Exercise and non-exercise
		(short-term)	Back-specific disability	y 8	689 <i>P</i> <0.01	SMD -0.59 (-0.87 to -0.30) nonexercise	Exercise and
Wieland <sup>28</sup> 2017	Meta-analysis	Adults with chronic low back pain	Back-specific function (short-term)	5	256	SMD -0.45 (-0.71 to -0.19) P=0.00070	Nonexercise
			Back-specific function (long-term)	2	365	SMD -0.26 (-0.46, -0.05) P=0.015	Nonexercise

ity were also observed<sup>27</sup> (Table 4). In a 2017 Cochrane Review, 9 trials compared yoga to nonexercise controls. Yoga was associated with improved function at short- and long-term follow-up, with moderate and small effect sizes, respectively. Yoga was associated with improved pain at short-, intermediate-, and long-term follow-up as well; results were statistically significant but did not meet the authors' threshold for clinical significance<sup>28</sup> (Table 4). The same Cochrane review compared yoga to exercise controls (4 trials), and the authors found no difference between yoga and nonyoga exercise for back-related function. For pain, yoga participants demonstrated statistically and clinically significant improvement at intermediate-term follow-up (1 trial) but not short-term follow-up. No long-term follow-up results were reported for this comparison.<sup>28</sup>

In addition to meta-analyses, yoga for back pain also has been evaluated in 2 large systematic reviews in the past 10 years. In a 2017 review of 14 RCTs, functioning was significantly better in the yoga group compared to education intervention controls at short-term (5 trials) and long-term (4 trials) follow-up. When compared to exercise, yoga tended to be associated with small improvements in pain and functioning, though results were not always statistically significant.<sup>29</sup> In a 2020 systematic review published by the US Agency for Healthcare Research and Quality, when compared to attention or wait-list controls, yoga showed improved function at short-term (8 trials) and intermediate-term (3 trials) follow-up. Additionally, when compared with attention or wait-list controls, yoga was associated with improved pain at short-term (7 trials) and intermediate-term (2 trials) follow-up. There were no differences between yoga and other exercise for pain or function at short- or intermediate-term follow-up.<sup>30</sup>

A 2017 review on the cost-effectiveness of various nonpharmacologic therapies for low back pain suggests that yoga is a cost-effective therapy for chronic low back pain. However, these results must be interpreted with caution in the United States as the studies reviewed were carried out in Europe.<sup>31</sup>

Overall, there is a growing body of literature demonstrating

that yoga is a moderately effective means of treating chronic low back pain.

# **PATIENT CASE:** Mark continued

Mark also notes that his mood isn't as good as it used to be, despite continuing to take his selective serotonin reuptake inhibitor (SSRI) regularly. His wife has been saying that yoga has been helping her mood. He's wondering if there is any truth behind this.

# **MENTAL HEALTH**

Anxiety and depression are, together, the third leading chief complaint for primary care visits in developed countries,<sup>4</sup> and in 2018, 7.2% of adults had an episode of major depressive disorder in the last year.<sup>32</sup> In a national survey on yoga use, 84.7% of people stated that practicing yoga reduced their stress levels, and 67.5% of people stated that practicing yoga made them feel better emotionally.<sup>5</sup> One proposed mechanism of the feeling of decreased stress levels is that practicing yoga has been found to increase  $\gamma$ -aminobutyric acid levels in the thalamus.<sup>33</sup> While most of the randomized control trials studying yoga and depression/anxiety have high risk of bias and heterogeneity, there is some evidence that yoga can be effective in treating these conditions.<sup>34-38</sup>

A systematic review and meta-analysis looking at yoga and depression found that there was moderate evidence for short-term effects of improving severity of depression with yoga vs usual care (SMD -0.69; 95% CI, -0.99 to -0.39; P<0.001)<sup>34</sup> (Table 5). There was also limited evidence for improvement of depression for yoga vs relaxation and yoga vs aerobic exercise, though smaller than yoga vs usual care.<sup>34</sup> Another systematic review for patients with major depressive disorder found that there was no difference between yoga and exercise or antidepressant medication (imipramine) for treatment of depression.<sup>35</sup> This particular systematic review was flawed in that it analyzed very few studies that had few participants. However, given that exercise and antidepressant medications are known to improve depression, it is reasonable to

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Author/Year	Study Design	Study Populations	Outcomes	No. of Studies/ Subgroups	Sample Size	Results (95% CI)  P value	Controls
Cramer <sup>34</sup> et al, 2013	Systemic review, meta-analysis	Adults with depression	Various depression scales	5	284	SMD -0.69 (-0.99 to -0.39) P<0.001	Usual care
	,			3	109	SMD -0.62 (-1.03 to -0.22) P=0.003	Relaxation
				2	159	SMD -0.59 ( -0.99 to -0.18) P= 0.004	Aerobic exercise

Author/Year	Study Design	Study Populations	Outcomes	No. of Studies/ Subgroups	Sample Size	Results (95% CI)  P value	Controls
Cramer <sup>36</sup> et al, 2018	Systematic review, meta-analysis	Adults with diagnosis of an anxiety disorder	Improvement of anxiety based on various scales	3	169	SMD -0.43 (-0.74 to -0.11) P=0.008	No treatment
				3	79	SMD -0.86 (-1.56 to -0.15) P=0.02	Active controls

suggest that yoga can also improve depression in those with major depressive disorder.

For anxiety, there is even less research available; however, a recent systematic review and meta-analysis found that there was evidence for short-term benefits of yoga on anxiety compared to no treatment (SMD -0.43; 95% CI, -0.74 to -0.11; P=0.008)<sup>36</sup> (Table 6). Even greater effects were found for yoga compared to active controls like progressive muscle relaxation (SMD -0.86; 95% CI, -1.56 to -0.15; P=0.02).<sup>36</sup> In a more recent RCT looking at yoga vs no treatment for anxiety in college students, there was a statistically significant improvement of anxiety symptom scores in those in the yoga group.<sup>37</sup>

While there is at least modest evidence for improvement in the short term for both anxiety and depression with yoga, very few studies have looked at long-term benefits. One such study followed patients with cancer for 6 months after the end of a yoga intervention to see if there were decreases in depression and anxiety scores.<sup>38</sup> Overall, both symptoms of anxiety and depression were statistically significantly improved compared to their baseline scores prior to the yoga intervention. In addition, 69% of patients in the study were still practicing yoga at 6-month follow-up, likely due to reported subjective benefits.<sup>38</sup>

Overall, there is moderate evidence that yoga could be an additional tool to treat anxiety and depression.

# **PATIENT CASE: Mark continued**

Mark's daughter attends classes at a "power yoga" studio, and their website depicts highly flexible young adults in challenging positions, including headstand. Mark asks if you advise this type of yoga for him.

# **SAFETY**

In clinical trials, yoga has generally been shown to be a safe activity. Only about 2.2% of participants experience yoga-related adverse events, and only 0.6% of participants experience serious adverse events.<sup>39</sup> These numbers are comparable to usual care or other exercise interventions.<sup>40</sup> The most common adverse event reported with respect to yoga practice for back pain is temporarily increased pain.<sup>30,41</sup> Serious adverse events include stroke and glaucoma, although these complications are rare.<sup>42</sup>

The wide variety of yoga interventions studied and variations in reporting generally preclude assessment of risk by specific type of yoga.<sup>39</sup> However, certain postures have demonstrated increased risk of adverse events. The yoga practices most frequently associated with serious adverse events are headstand, shoulder stand, lotus position (where the practitioner is seated and the legs are crossed such that both feet rest on the opposite thighs), postures requiring the placement of 1 or both feet behind the head, and intense, forceful breathing practices.<sup>42</sup> These practices are generally not recommended for a medical population and may only be considered on a case-by-case basis for advanced yoga practitioners under the guidance of a certified yoga instructor.

Overall, yoga is regarded as being as safe as other exercise or usual care and can be safely practiced by most people under the direction of a certified instructor.

# **PATIENT CASE: Mark Continued**

Mark returns to your clinic 3 months later and states that he has been practicing yoga with his wife 3 to 4 times per week. He has not gone to the power yoga class with his daughter. He states that his mood has improved overall since starting yoga. While he still has some back pain, he also feels that yoga has improved both his mobility and pain.

## **CONCLUSIONS**

To date, yoga shows promise as a relatively safe and effective option for patients interested in therapeutic lifestyle change to promote well-being and to help manage hypertension, back pain, and overall mental health. However, our review is limited by number of studies, small sample sizes, poor quality data, and risk of bias. Additionally, there are many different types of yoga and different elements of yoga practice, such as meditation, breathing, and postures. Preliminary data suggest that a mix of these elements in the treatment of hypertension could be more beneficial than only practicing 1 or 2 of these elements of yoga. These results indicate that more studies are needed to determine the optimal components of a yoga intervention for a given health condition, dosing of the intervention, and delivery method. Additionally, more studies are needed to discern the safety and efficacy profiles of different styles of yoga, which vary widely in emphasis on the different components of yoga and level of exertion. Still, the cur-

rent data in aggregate are encouraging, and we hope clinicians will feel more comfortable considering yoga as a therapeutic option for the top conditions seen in primary care.

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Condition	Evidence	Level of Evidence	Comments
Hyperlipidemia	Yoga practice improves HDL, LDL, triglycerides	Level 2	Compared to nonexercise controls 6,7
Well-being in older adults	Yoga practice improves HRQOL, physical functioning in older adults	Level 1	Compared to nonexercise controls <sup>8-1</sup>
Workplace stress reduces workplace	Yoga practice in the workplace stress	Level 1	Consistent results across varied work settings including health care <sup>13</sup>
Well-being in incarcerated populations	Yoga practice improves behavior, mental well-being in incarcerated women, youth	Level 2	Longer programs show more benefit <sup>14</sup>
Hypertension	Yoga practice improves SBP, DBP	Level 1	Compared to nonexercise controls <sup>18-2</sup>
Back pain	Yoga practice improves chronic back pain, overall function	Level 1	Effect sizes generally small to moderate vs nonexercise controls <sup>26-30</sup>
Depression	Yoga practice improves symptoms	Level 1	Compared to nonexercise and non-
of depression		controls and ne period <sup>34,3</sup>	
Anxiety of anxiety	Yoga practice improves symptoms mus	Level 2 cle relaxation	When compared to no treatment,

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; HRQOL, health-related quality of life; SBP, systolic blood pressure; DBP, diastolic blood pressure; SR, systematic review; RCT, randomized control trial.

Level 1 - SR/meta-analysis of RCTs with consistent findings. High-quality individual RCT. All-or-none study. Level 2 - SR/meta-analysis of lower-quality clinical trials or of studies with inconsistent findings. Lower-quality clinical trial. Cohort study. Case-control study.

Level 3 - Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), or case series for studies of diagnosis, treatment, prevention, or screening.

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# SARS-CoV-2 Cycle Thresholds, Poverty, Race, and Clinical Outcomes

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## **ABSTRACT**

**Background:** Poverty and high viral load are associated with worse outcomes among COVID-19 patients.

**Methods:** We included patients admitted to Froedtert Health between March 16 and June 1, 2020. SARS-CoV-2 viral load was proxied by cycle-threshold values. To measure poverty, we used Medicaid or uninsured status and residence in socially disadvantaged areas. We assessed the association between viral load and length of stay and discharge disposition, while controlling for demographics and confounders.

**Results:** Higher viral load was associated with longer length of stay (coefficient -0.02; 95% CI, -0.04 to 0.01; P=0.006) and higher likelihood of death (coefficient -0.11; 95% CI, -0.17 to -0.06; P<0.001). Poverty, residence in disadvantaged areas, and race were not.

**Discussion:** This study confirms a relationship of viral load with in-hospital death, even after controlling for race and poverty.

## INTRODUCTION

The current gold standard for diagnosis of coronavirus disease 2019 (COVID-19) is the reverse transcriptase-polymerase chain reaction (RT-PCR) test. This test provides a cycle threshold (Ct) value, a proxy indicator of viral load. Evidence suggests that viral

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load is higher in patients with more severe clinical presentations, on the first day of symptoms, and in fatal cases.<sup>2,3</sup>

Another poor prognostic factor among patients with COVID-19 is poverty, as shown by our research group<sup>4</sup> and others.<sup>5,6</sup> Specifically, we found that poverty is associated with requiring intensive unit care, even when controlling for race/ethnicity, age, body mass index, and comorbid conditions. Given that poverty is likely a proxy for nonclinical issues (ie, reduced access to care, housing density, and/or essential worker status), we were interested in the extent to which poverty accounted for the relationship between viral load and clinical out-

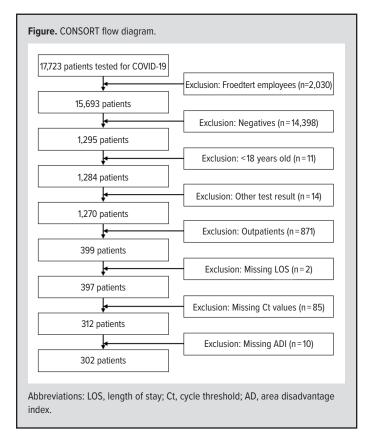
comes. Therefore, the purpose of this study was to examine the association between SARS-CoV-2 viral load and clinical outcomes while adjusting for poverty and race among COVID-19 patients.

#### **METHODS**

# Setting, Study Design, and Testing Methodology

This cross-sectional study was performed at Froedtert Health and the Medical College of Wisconsin (FH and MCW) and included all consecutive, unique patients hospitalized for at least 24 hours with a positive SARS-CoV-2 RT-PCR test between March 16 and June 1, 2020 (Figure). The study was approved by MCW's Institutional Review Board and a waiver of informed consent was granted.

COVID-19 tests were performed at FH and MCW's microbiology laboratory (Wisconsin Diagnostic Laboratories) using the Centers for Disease Control and Prevention's (CDC) methodology for RT-PCR tests (n = 107), Roche Molecular Systems



SARS-CoV-2 Nucleic Acid Test (n = 68), and Cepheid Xpert Xpress SARS-CoV-2 tests (n = 127).<sup>7</sup>

Combined nasopharyngeal/oropharyngeal swabs were collected using a dual swab system and placed into viral transport media. The CDC SARS-CoV-2 assay was performed by extracting RNA using the eMag (bioMerieux) according to the manufacturers' product insert. RT-PCR was performed according to CDC protocol.<sup>7</sup> Roche Molecular Systems SARS-CoV-2 Nucleic Acid test and Cepheid Xpert Xpress SARS-CoV-2 test were performed and interpreted in accordance with emergency use authorization protocols (Doc Rev 3.0 and 2.0).<sup>7</sup>

Viral load, measured by Ct values, was obtained by direct interrogation of laboratory testing equipment. To harmonize viral loads obtained from different platforms and to ensure that the choice of Ct target did not influence our results, we included indicators for the test type in all multivariable analyses.

# **Variable Definitions**

Information on acute care length of stay (LOS) and post-acute discharge disposition were obtained from electronic medical records. Discharge disposition was classified into 3 mutually exclusive categories: discharged home (with or without home health care), discharged to a skilled nursing facility, or death. We obtained demographic characteristics (age, sex, race), symptoms on admission (presence of fever, cough, shortness of breath, sore throat, diarrhea, nausea, vomiting, or abdominal pain, changes in mental status, and olfactory changes or taste changes), comorbidities

(hypertension, diabetes, chronic heart disease, chronic lung disease, and chronic kidney disease), primary and secondary health insurance, body mass index (BMI), and smoking history. Race was based on self-reported data, where individuals were classified as African-American, White, Hispanic, or Other (Native Hawaiian or Pacific Islander, Native American or Alaska Native, and Asian).

In the absence of individual-level information on income, we used lack of health insurance or enrollment in Medicaid as our individual-level indicator of poverty. Finally, the patients' address of residence was obtained using the ZIP code lookup tool, as previously described.<sup>4</sup> Their 9-digit ZIP codes were then used to classify individuals as living in socially disadvantaged areas based on a score of 7 or higher on the Area Deprivation Index (ADI).<sup>4</sup>

# **Statistical Analysis**

For descriptive analysis, patients were stratified into 2 groups based on the distribution of Ct values seen in the study. Specifically, patients with Ct values <26 were defined as having high viral loads, while those with Ct values  $\ge26$  were defined as having low viral loads. Categorical variables were described as count (percentage) and continuous variables as mean (standard deviation [SD]) or median (interquartile range [IQR]). Pearson's chi-square test was used to compare categorical variables, Student t test for means, and Mann-Whitney-U test for medians. In the multivariable analyses, viral load was analyzed as a continuous variable.

LOS, a continuous variable, was analyzed using linear regression techniques applied to the logarithmic transformation of the dependent variable to minimize the influence of outliers. For discharge disposition—an unordered 3-category variable—we used a multinomial logistic regression. All analyses were conducted in Stata version 16 (StataCorp) and SPSS (version 24.0; SPSS Inc., Chicago, IL). To adjust for longitudinal effects of community spread, we stratified our observation period by weeks, including it as an independent variable.

## **RESULTS**

A total of 302 patients were hospitalized for COVID-19 during the study period. Table 1 shows summary statistics for the cohort. Overall, 161 (53.3%) patients were male and 172 (57%) were ≥60 years old. Slightly over half were poor as measured by having Medicaid or no health insurance (n=156, 51.7%). The mean BMI was 31.9 (SD 9.1), and 124 (41.1%) patients reported having a history of smoking. The median hospital LOS was 6 days (IQR 3-11). Regarding discharge disposition, 54 (17.9%) patients died, 199 (65.8%) were discharged home, and 49 (16.2%) were discharged to nursing homes.

Patients with high viral loads (ie, Ct values  $\leq$  26) were older (65.6 [SD 16] vs 56.7, [SD 19]; P<0.001) and were more likely to be poor (81 [SD 57%] vs 75 [SD 46.9%]; P=0.078) than those with low viral loads. Patients with high viral loads also experienced a greater acute care LOS (8 [IQR 4-13] vs 5 [IQR 2-8];

P<0.001) and were more likely to die (39 [SD 27.5%] vs 15 [SD 9.4%]; P<0.001) than those with low viral loads.

# SARS-CoV-2 Viral Load, Poverty, and Health Care Utilization

Table 2 shows the parameter estimates from our multivariable models. After controlling for race, socioeconomic status, and potential confounders (ie, age, sex, comorbidities, BMI, ADI), viral load was significantly associated with longer LOS (coefficient -0.02; 95% CI, 0.04 to -0.01; P= 0.006). Patients with higher viral loads were also more likely to die during hospitalization (coefficient -0.11; 95% CI, -0.17 to -0.05 0.95; P<0.001). Neither poverty, residence in a disadvantaged area, nor race were associated LOS or in-hospital death. Viral load was not a significant predictor of discharge to a skilled nursing facility among those discharged alive from the hospital, but poverty was a significant predictor (coefficient 2.83; 95% CI, 1.18 to 4.49; P < 0.001). Neither residence in a disadvantaged area nor race were significantly associated with discharge to a skilled nursing facility.

In addition to viral load, age ≥60 (coefficient 0.42, 95% CI, 0.16 to 0.67; P<0.001), male sex (coefficient 0.29; 95% CI, 0.07 to 0.50; P<0.001), and higher BMI (coefficient 0.02; 95% CI, 0.01 to 0.03; P < 0.001) were independently associated with longer LOS. Relative to those discharged home, COVID-19 patients discharged to a nursing home were more likely to be 60 years or older (coefficient 1.97; 95% CI, 1.04 to 2.90; *P*<0.001), male (coefficient 0.87; 95% CI, 0.10 to 1.63; *P*<0.001), poor (coefficient 2.83; 95% CI, 1.18 to 4.49; P<0.001), and have 1 to 2 comorbidities (coefficient 0.29; 95% CI, 0.05 to 0.54; P<0.001).

# **DISCUSSION**

In this cross-sectional study of hospitalized COVID-19 patients, we found that higher viral loads were associated with longer LOS and greater in-hospital mortality. Poverty, residence in a disadvantaged area, and race

Table 1. Characteristics of Patients Hospitalized	d for COVID-19	, Overall and by Vira	ıl Load	
Characteristics	Total N=302	High Viral Load N=142	Low Viral Load N=160	P value
Age (mean, SD)	60.89,18.22	65.61,16.05	56.71,19.03	<0.001
≥60 years old, N (%)	172 (57)	95 (66.9)	77 (48.1)	0.001
Sex: male, N (%)	161 (53.3)	71 (50)	90 (56.3)	0.28
Race, N (%)				
African-American/Black	177 (58.6)	78 (54.9)	99 (61.9)	0.22
White	84 (27.8)	46 (32.4)	38 (23.8)	0.09
Other	12 (4)	1 (0.7)	11 (6.9)	0.01
Hispanic, N (%)	29 (9.6)	17 (12)	12 (7.5)	0.19
Residence in socially disadvantaged area (ADI ≥ 7), N (%)	186 (61.6)	80 (56.3)	106 (66.3)	0.08
Poverty status: uninsured or Medicaid, N (%)	156 (51.7)	81 (57)	75 (46.9)	0.08
Comorbidities, N (%)	150 (51.7)	01(37)	73 (40.3)	0.00
None	59 (19.5)	32 (22.5)	27 (16.9)	0.216
1-2	131 (43.4)	54 (38)	77 (48)	0.077
>3	112 (37.1)	56 (39.4)	56 (35)	0.426
Body mass index (mean, SD)	31.9 (9.1)	32.05 (9.81)	31.77 (8.53)	0.794
History of smoking/current smoker, N (%)	124 (41.1)	59 (41.5)	65 (40.6)	0.871
Days to symptoms onset (median, IQR)	2 (0-5)	1(0-4)	2 (1-7)	< 0.001
Symptoms, N (%)				
Fever	103 (34.1)	53 (37.3)	50 (31.3)	0.266
Cough	197 (65.2)	95 (66.9)	102 (63.7)	0.57
Shortness of breath	124 (41.1)	58 (40.8)	66 (41.3)	0.94
Diarrhea, nausea, vomiting, abdominal pain	42 (13.9)	24 (16.9)	18 (11.3)	0.16
Other symptoms	173 (57.3)	77 (54.2)	96 (60)	0.31
Outcomes, N (%)				
Length of stay (median, IQR)	6 (3-11)	8 (4-13)	5 (2-8)	<0.001
Discharge disposition, N (%)				
Nursing home discharge	49 (16.2)	29 (20.4)	20 (12.5)	0.062
Home or other nonmedical setting discharge	199 (65.9)	74 (52.1)	125 (78.1)	< 0.001
Death	54 (17.9)	39 (27.5)	15 (9.4)	<0.001

Abbreviations: ADI: area disadvantage index; IQR: interquartile range; ICU, intensive care unit. Patients with Ct values < 26 were categorized as having high viral loads, while those with Ct values ≥ 26 as low viral load.

**Table 2.** Multivariate Analysis of Length of Stay, Death, and Discharge Disposition Among COVID-19 Positive Patients

	Length of Stay Coefficient (95%)	Discharge Disposition (Relative to Discharge Home)				
		Death Coefficient (95% CI)	Nursing Home Coefficient (95% CI)			
Viral load	-0.02a (-0.04 to -0.01)	-0.11a (-0.17 to -0.05)	-0.02 (-0.08 to 0.03)			
Health insurance						
Medicaid or uninsured	0.05 (-0.24 to 0.33)	0.93 (-0.12 to 1.97)	2.83ª (1.18-4.49)			
Medicare	-0.07 (-0.42 to 0.28)	0.85 (-0.29 to 1.98)	1.13 (-0.60 to 2.85)			
Age ≥60 years	0.42a (0.16 to 0.67)	1.46a (0.60 to 2.32)	1.97a (1.04 to 2.90)			
Sex: male	0.29a (0.07 to 0.50)	0.22 (-0.48 to 0.92)	0.87** (0.10 to 1.63)			
African American/Black	-0.09 (-0.34 to 0.15)	0.19 (-0.61 to 0.98)	-0.71 (-1.56 to 0.14)			
1-2 comorbidities	0.06 (-0.01 to 0.13)	0.01 (-0.22 to 0.24)	0.29a (0.05 to 0.54)			
Body mass index	0.02a (0.01 to 0.03)	0.03 (-0.01 to 0.07)	-0.02 (-0.06 to 0.02)			
Days to symptoms onset	-0.001 (-0.02 to 0.02)	-0.04 (-0.11 to 0.04)	-0.09 (-0.18 to 0.01)			
Area disadvantage index	-0.02 (-0.05 to 0.03)	-0.02 (-0.14 to 0.11)	-0.06 (-0.19 to 0.08)			
Week block	-0.007 (-0.07 to 0.06)	0.13 (-0.07 to 0.34)	-0.01 (-0.24 to 0.23)			

Viral load was measured by cycle threshold values

alndicates statistical significance at  $P \le 0.05$ .

were not associated with increased LOS or mortality when viral load was included in the model. Although patients who were discharged to a nursing home had higher viral loads, poverty rather than viral load was a significant predictor of nursing home discharge.

Studies have explored the relationship between SARS-CoV-2 viral loads and in-hospital clinical outcomes.<sup>2,3,8</sup> Similar to our findings, others found an association between viral load and mortality after adjusting for race, age, and other variables. Our study builds upon the existing literature, as we found that high viral load was still associated with mortality, even after adjusting for poverty, residence in a disadvantaged area, and race. We also noted an association between viral load and LOS while controlling for sex, age, race, and other demographic variables—a finding that is inconsistently reported in the literature.<sup>9,10</sup>

Our study has several limitations. The research was performed at a single health system over a relatively short study period, and therefore may not be generalizable to other areas. The SARS-CoV-2 test samples were taken at different points during each patient's clinical course and measured by different platforms. These issues, however, are unlikely to have influenced our findings as analyses of the number of days from onset of symptoms to the day of testing indicated no association between these 2 variables (data not shown). Additionally, we controlled for test type in our multivariable models.

In conclusion, viral load, measured indirectly by Ct values, was independently associated with in-hospital death—even after controlling for race and poverty. Although these socioeconomic factors increase the likelihood of COVID-19 infection, they do not influence the effect of viral load on clinical outcomes.

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# Collective Action: The Medical College of Wisconsin COVID-19 Vaccination Program

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# **ABSTRACT**

The Medical College of Wisconsin (MCW) COVID-19 Vaccination Program facilitated early vaccination efforts in metro Milwaukee, Wisconsin from December, 2020 through April, 2021. Goals of the program were to work with clinical partners to ensure rapid vaccination availability for the institution's frontline workforce, to support state public health agencies in offering a vaccination opportunity for underserved and higher education community members, and to train vaccinators. A key component of the program was the MCW COVID-19 Vaccination Clinic, and 88% of MCW's workforce was fully immunized against COVID-19 with the 2-dose, mRNA vaccine by April 30, 2021. Within the MCW clinic, 219 pharmacy and medical students learned to administer vaccinations, and 12,450 community vaccinations were administered.

# **BACKGROUND**

In November 2020, despite the use of masks and social distancing, COVID-19 was surging in Milwaukee, Wisconsin, and health care personnel were highly stressed. In anticipation of the Food and Drug Administration's emergency use authorization for the 2-dose Pfizer-BioNTech COVID-19 mRNA vaccine, the Medical College of Wisconsin (MCW) considered how to structure an institutional program for COVID-19 vaccination. MCW employees and trainees number about 9,000, including physicians, clinical personnel, educators, students, staff, and researchers. For context, 24.1% of the regional adult inpatient market in Milwaukee is

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cared for in Froedtert Hospital and MCW facilities.

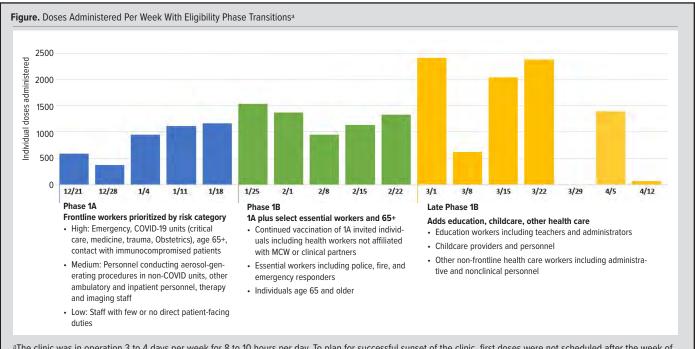
Ann Nattinger, MD, MPH, was appointed to lead MCW's vaccination program. After consultation with other leaders, she determined that the MCW program would utilize clinical partner vaccination sites; additionally, MCW would develop an independent vaccination site on the Milwaukee campus. The program had 3 main goals: (1) engage with clinical partners to ensure rapid vaccination availability for the institution's frontline workforce;

(2) support state public health agencies in offering vaccination opportunities for underserved and higher education community members; (3) train medical and pharmacy student vaccinators to support subsequent public health community vaccination efforts.

# **METHODS**

# **Development of the Covid-19 Vaccination Program**

MCW worked closely with health care partners that were planning vaccination sites, including Froedtert Hospital, Children's Wisconsin, and the Clement J. Zablocki VA Medical Center (VAMC), to assure accountability for initially targeted Phase 1A groups. Children's Wisconsin and VAMC offered vaccinations to MCW personnel and house staff with responsibilities at those sites; Froedtert Hospital (which provides occupational health services for MCW personnel) and MCW agreed to provide vaccinations to all eligible personnel of either organization, as well as trainees. Due to anticipated early vaccine shortages, MCW and Froedtert Hospital worked cooperatively to determine prioritization of Phase 1A personnel based on the Wisconsin Department of Human Services (DHS) criteria, and also by relative level of risk regardless of position (Figure). For example, all personnel working in the emergency department (ED), including physicians,



<sup>a</sup>The clinic was in operation 3 to 4 days per week for 8 to 10 hours per day. To plan for successful sunset of the clinic, first doses were not scheduled after the week of March 1, except for a limited number scheduled the week of March 15. Only second doses were scheduled for the week of March 22 and beyond. The week of March 29 was intentionally not scheduled. The week of April 12 offered 1 makeup clinic date for second dose appointments.

**Box.** Organizations That Provided Referrals and/or Prescreened Community Patient Lists<sup>a</sup>

Alverno College
America's Black Holocaust Museum
Boys & Girls Clubs
Bright Horizons Day Care
City of Milwaukee
HealthyMKE.comb
Herzing University
Local faith-based organizations
Medical College of Wisconsin
(including essential contract workers in food service, utilities, and cleaning)
Milwaukee Academy of Science (K-12)
Milwaukee Area Technical College
Milwaukee School of Engineering

Milwaukee Urban League
Mount Mary University
NAACP of Milwaukee
Next Door Foundation/Head Start
St. Augustine Prep (K-12)
ThriveOn Collaboration
Versiti Blood Center of Wisconsin
Wauwatosa Health Department
Wauwatosa Police and Fire
Wauwatosa School District
WeGive MKE Food
Wisconsin Lutheran College
YMCA

<sup>a</sup>Medical College of Wisconsin leadership worked with leaders of established community, business, education, and faith-based partnerships to help identify eligible, vulnerable populations for vaccination. In several cases, these leaders arranged technology support and transportation.

<sup>b</sup>HealthyMKE.com provided referral lists for frontline health care providers who were not affiliated with an established health care system, such as local dentists, physical therapists, and other private practice health care providers who were Phase 1A eligible.

nurses, trainees, and support staff, were considered at equally high risk for exposure.

Initially, Froedtert Hospital emailed invitations to Phase 1A eligible persons at Froedtert Hospital and MCW that permitted scheduling at either location. Beyond Phase 1A, MCW developed an independent ticket system that issued vaccination invitations to

lists of eligible individuals provided by local organizations (Box). These lists included independent ("unaffiliated") health care providers, individuals age 65 years and older, community members, and MCW personnel as they became eligible. MCW leadership also identified eligible recipients, including local opinion leaders whose vaccination might positively influence others to be vaccinated, as opportunities became available.

# **Clinic Planning and Organization**

MCW submitted its vaccination site application to the state in November, 2020. A secure location with ultra-cold freezers and holding refrigerators was identified. Protocols for remote temperature monitoring, safety, and inventory management were developed, as well as a secure transportation process.<sup>2</sup> Documentation procedures were developed to screen for vaccine contraindications and to ensure rapid uploading of vaccinations to the Wisconsin Immunization Registry (WIR).

Based on prior School of Pharmacy flu clinics, an open model clinic space utilized plexiglass partitions with appropriately distanced vaccination stations. This permitted ideal patient flow and easy oversight by clinic leaders and preceptors. A "compounding station" was used for trained individuals to dilute the vaccine with saline and fill individually dosed syringes. These syringes were then distributed across the vaccination stations for effective inventory management. Since the vaccine was stored frozen, vials had to be used within 120 hours of thawing and within 6 hours of dilution.<sup>3</sup> This required careful planning to ensure appropriate amounts of usable vaccine were ready for clinic. Before vaccina-

tion, patients checked in for appointment confirmation and to receive required paperwork, including the COVID-19 vaccination form, the Pfizer-BioNTech COVID-19 vaccine fact sheet for recipients and caregivers,<sup>3</sup> and information on the Centers for Disease Control and Prevention's V-safe after vaccination health checker.<sup>4</sup> Postimmunization, patients remained in a designated monitoring area for 15 to 30 minutes for observation. Here, patients were invited to provide feedback on their satisfaction with the clinic experience (likert scale 1-10; 10=best) via materials posted in the area. All areas underwent sanitization immediately following patient contact throughout the operations.

# **Program Staffing**

Program leads were identified from the Office of Research, the School of Pharmacy, and the President's Office. These leads managed invitations, trained and scheduled volunteers, entered data into WIR, managed inventory, and oversaw daily clinical and compounding operations. Licensed volunteer vaccinators included School of Medicine and School of Pharmacy faculty, nurses, advanced practice providers, and community volunteers. Compounders included School of Pharmacy and School of Medicine researchers and faculty; all doses were rechecked by licensed pharmacists. MCW public safety, receiving, compliance, communications, human resources (HR), finance, and legal offices provided additional support.

# **RESULTS**

A total of 19,393 doses were administered to 9,944 individuals. Of these, 3,817 MCW employees, students, and residents were vaccinated in the clinic (other personnel were vaccinated at clinical partner sites), and 6,127 unique community members were vaccinated. No episodes of anaphylaxis occurred, although 2 patients were transported to the Froedtert Hospital ED for observation after displaying immediate allergy symptoms. With careful attention to inventory management, no vaccine doses expired. With mitigation efforts, no doses were wasted at the end of clinic days due to overpreparation (Table). Of the 203 respondents to the patient satisfaction survey, the mean score was 9.8 (SD = 0.77). Ratings of 9 or 10 were given by 96.6% of respondents. Nearly 300 internal and external volunteers directly supported the clinic in vaccinator or other capacities, offering over 5,000 hours of service. The clinic served as an important bridge to fill an urgent, critical need for vaccination availability. However, as community capacity for vaccinations increased, and because the volunteerbased operation was never intended as an ongoing health care facility, the vaccination clinic ceased operations in April, 2021.

The School of Pharmacy standard curriculum provides didactic and laboratory training in immunization administration to pharmacy students, and the School of Medicine rapidly developed a new COVID-19 vaccination curriculum for medical students.<sup>5</sup> The clinic was the site for completion of experiential training for

Method	Phase
Offer vaccinations to clinic volunteers	1A
Seek referrals for at-risk populations (immunocompromised, older age groups) from institutional leaders to maintain an ongoing standby list	1A
Seek employees who are on-campus at end of clinic day for immediately available referrals	1A, 1B
Contact local businesses and partner organizations at the end of clinic day for immediately available referrals	1B
Seek employee referrals to maintain an ongoing voucher list (offer vouchers at the start of clinic day for referred individuals to return at	1B

<sup>a</sup>Clinic days often resulted in extra doses exceeding the number of patients seen. It was uncommon that persons attending a given clinic presented in multiples of 6, and most vials of Pfizer vaccine yielded 6 doses once opened. For this reason, between 1 and 5 standby recipients frequently were needed.

219 students (56 pharmacy students and 163 medical students).

In January, 2021, MCW agreed to a request from DHS to host a regional vaccine hub to complement direct shipping in supplying vaccine to various community vaccination sites. Under this partnership, MCW provided workspace and ultra-cold storage. The hub was staffed by DHS personnel and a Wisconsin National Guard Team supporting health care emergency readiness coalition (HERC) Region 7. At the time of writing, more than 600,000 vaccine doses had traversed the MCW hub, which was still active.

# **DISCUSSION**

end of day to wait on standby)

With the collaboration of clinical partner vaccination sites at Froedtert Hospital, Children's Wisconsin, and VAMC, the overall MCW COVID-19 vaccination program was a highly effective workforce program, resulting in the vaccination of 7,488 MCW employees, students, and residents (88%) by April, 2021. Operationalized within 1 month, the clinic provided almost 20,000 vaccinations during the first 4 months of availability of vaccine when relatively few vaccinators were available. Over 200 students of medicine and pharmacy were trained in COVID-19 vaccination techniques, many of whom went on to provide vaccination services with various community agencies in Wisconsin.

Internal and external volunteers were essential to clinic operations. Volunteers adhered to personal protective equipment requirements and no cases of COVID-19 were identified as a result of participating in this clinic. Perhaps due to the strong engagement of the volunteer workforce, patients reported extremely positive experiences in the clinic, commenting on the efficient procedures and caring staff.

The MCW program highlights the challenges of applying generic and rapidly changing interim public health guidelines during an emerging public health threat to specific clinical situations for small populations of patients, health care personnel,

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and community members. For example, having quantified levels of risk among health care providers would have simplified the task of equitably assigning risk categories. Risk assessment would be improved if HR records included identification of employees working in patient care areas, including any patient-facing role and extent of that role (ie, patient contact hours per day). Confirming patient eligibility based on state guidelines also presented challenges, and the clinic ultimately functioned on an honor system.

The efforts to prevent wasted doses were part of the program contributing to the efficient use of a limited resource during a public health emergency to maximize benefit to all community members. Factors such as inclement weather and no-show appointments made the daily patient counts difficult to predict. During Phase 1A, it was straightforward to find willing individuals available to take prepared doses at the end of the clinic day. Throughout the phases, this required increasingly more creative solutions (Table), which resulted in zero wasted doses due to overpreparation.

Though other similar community and volunteer-based clinics likely existed in early 2021, the literature on the subject is limited. A COVID-19 vaccination clinic at The Brooklyn Hospital Center<sup>6</sup> and an influenza clinic at the University of Sydney<sup>7</sup> also reported utilization of students to administer vaccines.

Regarding lessons learned, the early incorporation of students in development of procedures would be extremely useful, as well as the utilization of mitigation strategies to avoid wasted doses. Additionally, the use of predominantly internal volunteers allowed us to move more rapidly than if we recruited externally. The use of volunteers, however, is not a long-term solution as there is an increased risk of burnout.

In summary, a health sciences university developed and executed a COVID-19 vaccination program staffed by internal and external volunteers, in collaboration with local and state health departments to address a community-wide public health threat.<sup>8</sup> The program served multiple constituents and was well received by all stakeholders.

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# Outcomes of an Interprofessional Patient Safety Fellowship Program

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# **ABSTRACT**

**Background:** Interprofessional training for patient safety is essential in developing leaders and advocates who are versed in patient safety science and interprofessional collaboration. We describe an interprofessional patient safety fellowship program and its outcomes over 8 years.

**Methods:** Programmatic data were reviewed and a survey was sent to all program graduates with a known email address (N=18).

**Results:** Fellows obtained interprofessional skills, knowledge, and methods of patient safety science, as well as preparation as patient safety experts through didactic and experiential training. Program outcomes included sustained quality improvements, publications (n=8), presentations (n=29), and recruitment of graduates into quality and safety leadership positions (67%).

**Discussion:** Facilitators and barriers that influenced the success of the fellowship program were noted at institutional and individual levels. The development and sustainability of interprofessional safety training programs depends on concerted efforts by leadership, academic-practice partnerships, and committed faculty and learners.

# **BACKGROUND**

There is a critical need for an expert, interprofessional workforce to lead current and future patient safety initiatives in health care. Some progress has been made in designing and establishing interprofessional training programs that focus on patient safety, quality improvement (QI), and teamwork knowledge and skills.<sup>1,2</sup> These advanced training programs are necessary for developing

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leaders and clinicians who are well-versed in building reliable and safe health care delivery systems through interprofessional collaboration. Nevertheless, challenges remain to establish and sustain such training programs due to multiple factors at the institutional and individual levels. 1-4

We describe a postgraduate interprofessional patient safety fellowship program that has successfully incorporated interprofessional education (IPE) and patient safety training into 1 integrated program. Fellow and programmatic outcomes are shared, along with facilitators and barriers experienced over the course of program maturation.

# **Program Description**

An interprofessional patient safety fellowship program that provides a wide range of primary, secondary, and tertiary care to eligible veterans is offered at a Midwestern Veterans Affairs (VA) medical center. The program has had continuous funding since 2011 from 2 VA sources. In 2011, the Chief Resident in Quality and Safety (CRQS) training (a physician-only program) was expanded into an interprofessional patient safety fellowship program that supported additional positions for a graduate-degreed nurse and pharmacist. Based on the program's success, continued funding was awarded for 2 positions through the VA National Center for Patient Safety (NCPS).

The goal of this program is to develop clinical, administrative, and academic leaders who will serve as patient safety and IPE champions, with expertise in the areas of system redesign and patient safety science. Fellows are provided a stipend with benefits—similar to other federal awards—that covers 100% protected time. The fellowship faculty are composed of an interprofessional

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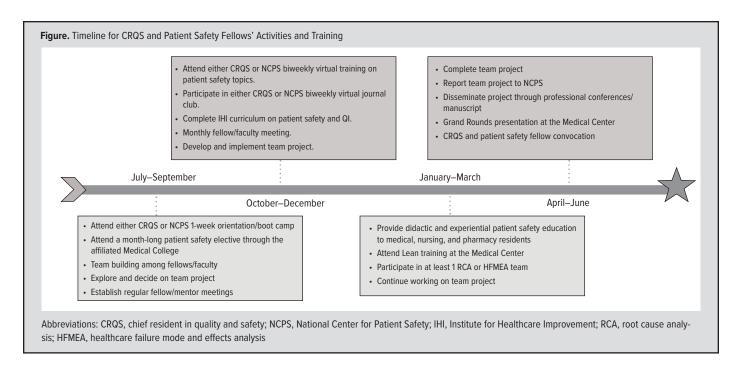


Table 1. Leadership Positions Taken by Graduates after Completing the Interprofessional Patient Safety Fellowship Program Anesthesiologists/ Nurses **Pharmacists Physicians** Other Health Care Discipline High reliability Associate Medical Performance organization lead director of college faculty improvement medical resicoordinator Medication safety Public health dency program coordinator project lead FRP coordinator and division QI Program chair at System medication director safety officer nursing college VA, medical Area pharmacy Nurse scientist/ college faculty manager, medicaprogram coorwith specialty tion safety dinator x2 fellowship x4 Patient safety Clinical nurse manager specialist Medication safety pharmacist (infusion pumps) Advanced clinical pharmacist, medication safety Abbreviations: EBP, evidence-based practice; QI. quality improvement.

team that includes physician, nurse, and pharmacist leaders, as well as patient safety managers.

# **Program Structure and Content**

During this 1-year full-time fellowship, a comprehensive training program is provided at the national and local levels (Figure).<sup>5-8</sup> The combined curriculum provides the fellows with rich didactic and experiential training in patient safety and teamwork among 16 patient safety fellows across 7 sites. Each cohort is expected to jointly design and complete 1 QI project that meets an orga-

nizational safety need. Several strategies have been put in place to promote the development of interprofessional teamwork and decision-making among the fellows. As a team, the fellows share a common office space; together they actively learn, teach, and conduct QI projects throughout the year. The faculty-fellow group meets monthly to review project ideas, discuss patient safety topics, and track progress toward project outcomes. The patient safety curriculum provided at the affiliated medical college also allows the fellows to interact with clinicians from 2 other academic medical centers.

# **METHODS**

Programmatic data were evaluated and an anonymous survey was sent to graduates with known email addresses (N=18). The survey included 7 questions using a 5-point Likert scale (1=low/strongly disagree to 5=high/strongly agree) and an open-ended section for comments.

# **RESULTS**

# **Programmatic Outcomes**

The goal for our interprofessional patient safety training program is to prepare leaders, mentors, and educators versed in patient safety and QI. Within 8 cohorts, 27 fellows graduated from the program (100% completion) and 67% (18/27) obtained administrative, clinical, or educational leadership roles in patient safety and quality (Table 1). Some graduates took positions at this VA and are now faculty for this program. Overall, 42% of the graduates were retained by the VA: 5/8 nurses, 2/7 pharmacists, 4/11 physicians. Of note, 67% (18/27) of the graduates remained in Wisconsin, and many of those who moved out of state took positions closer to family.

#### **Fellow Outcomes**

Fellows developed increased knowledge and skills in safety and QI science, as demonstrated by their improvement projects. Each cohort successfully completed a team improvement project focused on a medical center's safety priority. These capstone projects demonstrate fellows' accomplishments in teamwork and patient safety and have brought sustained improvement to the medical center. For example, 1 cohort completed an inpatient insulin pump management project using Healthcare Failure Mode and Effects Analysis (HFMEA) methodology to identify over 50 failure modes and causes. Outcomes included an insulin pump note template for the electronic medical record (EMR), order set, development of a policy/procedure and interdisciplinary education resources. Another project added a note template to the EMR, ensuring accurate verbal/telephone orders and documentation of read-back; this improves patient safety, reduces the use of recall, and saves nursing time without an increase in physician workload. All patient safety and QI projects have been disseminated through multiple avenues, including 29 poster or paper presentations and 8 publications in peer-reviewed journals.

The survey had a 44% response rate (8/18). Respondents indicated "high/strongly agree" in response to 5 of 7 questions regarding their perceptions about the training. All respondents strongly agreed that their patient safety knowledge increased and that they acquired new skills (4.9-5.0). They rated their level of knowledge as high for factors influencing patient safety, systems-thinking to improve patient safety and quality, and QI methods (4.7-4.8). Their ability to use data for patient safety evaluation was moderately high, as was their level of confidence to lead patient safety projects (4.0, 4.4, respectively).

The 8 respondents also shared their accomplishments regarding new patient safety skills, leadership techniques, and the teamwork skills they developed from the fellowship (Table 2). All fellows commented on the effect the fellowship had on their career and professional development. One said the fellowship directly contributed to their ability to lead an Agency for Healthcare Research and Quality/Institute for Healthcare Improvement grant to address the COVID-19 pandemic in nursing homes. Two graduates remarked on the invaluable experiences of working with people from different professions, which allowed them to develop the skills, ability, and confidence to lead changes within a complex system. Several graduates said that the fellowship changed their views on patient safety and opened new doors for their career.

# **Facilitators and Barriers for Interprofessional Safety Training**

Implementation of interprofessional safety training is not easy, and a variety of facilitators and barriers have been noted in the literature and with our program (Table 3).<sup>4,9</sup> For fellows, a deep commitment to patient safety is a motivator to further their training and education. Meanwhile, a strong alignment between the

Table 2. Responses to a Postfellowship Survey

#### Examples of new patient safety skills learned during the fellowship:

- Using the Swiss cheese model when dealing with a complicated patient situation
- Using root cause analysis, run charts, HFMEAs, Lean, PDSA, A3
- · Using data to illustrate an issue, support the need, and demonstrate change

## Examples of leadership techniques cultivated during the fellowship:

- Developed confidence. Learned how to identify and engage stakeholders.
   Learned skills to lead or facilitate complex Ql/research projects
- Best practices for communication with colleagues and peers; communication methods that are critical in leadership, including the 4-step assertive tool
- Establishing expectations and deferring to expertise. "As the year progressed, more people wanted help with things—being able to say 'I don't have time right now, but would be happy to help in 2 weeks' or 'Thanks for reaching out; I know someone who may be able to help' were key in my success."

## Examples of teamwork skills developed during the fellowship:

- The ability to get a team on board for a project
- How to advocate, negotiate, and delegate among an interprofessional team
- How to resolve differences among team members
- Team facilitation
- Communication and balancing the talents of the team

Abbreviations: HFMEA, Healthcare Failure Mode and Effects Analysis; PDSA, plan, do, study act

Institutional Level	Fellow Level						
Facilitators							
<ul> <li>Leadership commitment</li> <li>Culture of safety</li> <li>Faculty with patient safety/</li> <li>Quality improvement expertise</li> </ul>	<ul> <li>Commitment to patient safety</li> <li>Alignment between institutional and fellow's interest</li> <li>Paid position with protected time</li> <li>Experience in a different medical center</li> </ul>						
Ba	arriers						
Lack of funding     Lack of experts/mentors	<ul><li>Competing priorities</li><li>Workload distribution</li><li>Pre-existing hierarchy</li><li>Low stipend</li></ul>						

institution's needs and the fellows' interests is a critical facilitator supporting the fellows' attempts to lead improvement efforts.

A variety of barriers are listed in Table 3, including the low stipend amount. Some fellows have a part-time position to supplement their income. Another potential barrier found in the literature related to interprofessional learning is the preexisting hierarchy in the health care system, where the physician may be defaulted into a leadership role on the interprofessional team.<sup>4</sup> This has not been our experience, possibly due to initial and ongoing purposeful planning. For example, the program director intentionally identified an interprofessional faculty team, and a core competency for interprofessional collaborative practice<sup>8</sup> is embedded within our fellowship structure and curriculum.

Facilitators and barriers exist at the institutional level as well. The overall institutional safety culture and environment can con-

tribute greatly to the success of the program and the development of fellows.<sup>3,10</sup> For our program, the strong commitment to patient safety and support from leadership have been recognized as key facilitators. The availability of qualified faculty and mentors is vital to the sustainability of our fellowship program.<sup>1-3</sup> In addition to VA faculty, our academic affiliate is able to provide needed training. Lastly, financial resources are critical in sustaining the training program. There are many resources from the medical center that support the fellows, including poster development, graphic design, high-quality video recording, and conference registration with travel costs.

## **DISCUSSION**

Health care quality and safety are expected by patients, families, clinicians, and society. However, this cannot occur in professional silos, as patient safety depends on multiprofessional collaboration.<sup>1,11</sup> Our program has demonstrated that providing patient safety training using an interprofessional framework leads to health care professionals adept in their ability to collaborate interprofessionally and foster improvements in patient safety.

Interprofessional learning needs to be multifaceted and built into all aspects of training, including structural, environmental, and procedural components, to provide an authentic experience for fellows. The program director and faculty have intentionally structured core learning activities based on components of the interprofessional collaborative practice competencies.<sup>8</sup> Successful interprofessional collaboration is reinforced through daily interactions among the fellows and role modeled by the interprofessional faculty team.<sup>12</sup>

Our fellows, like their counterparts reported in the literature, expressed difficulty in finding time to attend all required training and to master the extensive patient safety knowledge and skills in the allocated time frame. Systematic strategies are required to address the finite amount of time available with increasing opportunities, experiences, and competencies being offered or expected. Last, program evaluation is a component that needs strengthening. A robust and systematic evaluation is needed in order to demonstrate individual and health care system outcomes, as well as the return on investment.

# CONCLUSION

A team approach is critical in achieving patient safety and providing quality care throughout the health care continuum. Interprofessional training programs for patient safety are a viable and important component in developing leaders who are equipped with the knowledge and skills for patient safety and QI, as well as interprofessional collaboration. Many graduates of this program continue their career paths as leaders in patient safety and QI in clinical practice and education. Nevertheless, challenges and obstacles remain for the training program. A concerted effort involving supportive leadership, a well-established faculty team,

and overall institutional engagement are vital for success of interprofessional training programs.

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# Pericarditis as a Secondary Complication of COVID-19 in a Renal Transplant Patient

Taylor Brockman, BS; Leilani Hernandez, MPH; Tej Mehta, MD; Bipin Thapa, MD, MS, FACP

# **ABSTRACT**

**Introduction:** A wide range of complications from COVID-19 are being reported, including cardiac complications.

Case Presentation: A 71-year-old woman with systemic lupus erythematosus complicated by focal segmental glomerular sclerosis status post kidney transplant presented with worsening left-sided chest pain after receiving treatment for COVID-19 pneumonia at an outside hospital. She was subsequently diagnosed with acute pericarditis, likely secondary to viral infection with COVID-19, and was successfully treated with aspirin and colchicine for 90 days without complications.

**Discussion:** NSAIDs and colchicine are mainstays in acute pericarditis treatment. Though treatment presented a potential challenge given this patient's prior kidney transplant, aspirin and colchicine proved to be effective in treating her case of COVID-19-associated pericarditis.

**Conclusion:** This report has implications for future treatment of renal transplant patients with COVID-19-related pericarditis and emphasizes the need for research into the pathophysiology of pericarditis in the context of COVID-19, including risk factors and treatment.

# INTRODUCTION

Since the first described cases in December 2019 in Wuhan, China, SARS-CoV-2—the virus responsible for the COVID-19 pandemic—has infected over 175 million people worldwide, with the death toll exceeding 3.8 million at the time of this publication.<sup>1,2</sup> It is now well-known that common clinical characteristics of COVID-19 include fever, cough, dyspnea, and fatigue. It is also well understood that individuals with comorbid medical conditions, such as hypertension, diabetes, and other cardiovascular

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conditions, are more likely to have a severe progression of and worse prognosis from the disease.<sup>3</sup>

As the novel coronavirus continues to affect the global population, other presentations and complications are emerging. Neurologic, dermatologic, and cardiac complications all have been reported. Cardiac presentations have included acute myocardial injury, myocarditis, acute heart failure, and acute myocardial infarction.<sup>4,5</sup>

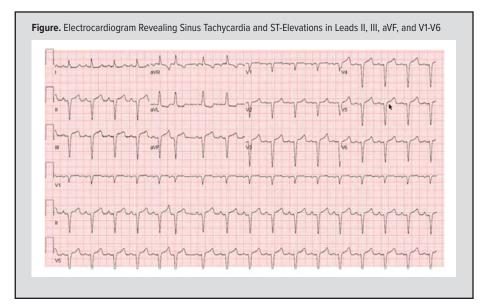
This case report describes a case of COVID-19-associated pericarditis in an elderly woman with a complex medical history and discusses potential treatment options for future cases of COVID-19-related pericarditis, specifically in patients

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with systemic lupus erythematosus status-post renal transplant.

# **CASE REPORT**

A 71-year-old woman with a history of systemic lupus erythematosus complicated by focal segmental glomerular sclerosis status post living related donor kidney transplant in 2005, Hepatitis C, type 2 diabetes mellitus, asthma, and obstructive sleep apnea presented to the hospital with chest pain and shortness of breath. Her home medications included allopurinol, amlodipine, insulin, metformin, metoprolol, mycophenolate mofetil, spironolactone, tacrolimus, and trazodone. Notably, she was discharged 1 day prior from a different hospital after a week-long stay where she was treated for COVID pneumonia with remdesivir for 5 days and dexamethasone 6mg daily for 7 days. She did not receive convalescent plasma, and intubation was not necessary. She also was noted to have acute metabolic encephalopathy, likely secondary to her COVID infection, which resolved by the time of discharge.



Upon arrival to the hospital, the patient endorsed a week-and-a-half long history of intermittent left-sided burning/sharp chest pain that radiated to her neck and left shoulder. The pain was exacerbated while supine and with deep inspiration and improved on sitting upright and leaning forward. On examination, she appeared anxious and uncomfortable. She was afebrile, hypertensive to 173/88 mm of Hg, had a regular heart rhythm but was tachycardic with pulse of 105/minute, and tachypneic to 22/minute. Palpation over her sternum revealed reproducible pain. On cardiac exam, she was noted to have a friction rub that was more noticeable when learning forward. The remainder of the exam was largely unremarkable.

Initial labs revealed elevated lactic acid to 2.3 mmol/L (reference range 0.5-2.0 mmol/L), a high-sensitivity troponin level of 283 ng/L (reference range < 10 ng/L), unremarkable complete blood cell count and basic metabolic panel, including a creatinine of 0.75 mg/dL (reference range 0.50-1.10 mg/dL). Labs also demonstrated elevated ferritin to 615.0 mg/dL (reference range 18.0-340.0 mg/dL), elevated C-reactive protein to 1.60 mg/dL (reference range 0.00-0.50 mg/dL), and elevated D-dimer to 2.59 mg/L (reference range < 0.69 mg/L), suggesting the presence of inflammation. Electrocardiogram (ECG) showed diffuse ST segment elevations in leads II, III, aVF, and V1-V6 concerning for acute coronary syndrome (Figure). The patient was subsequently started on clopidogrel and a heparin drip. Contrast transthoracic echocardiogram revealed severe left ventricular hypertrophy, no wall motion abnormalities, no pericardial effusion, and left ventricular ejection fraction (LVEF) of 64%. This study was largely unchanged from her most recent previous echocardiogram done in 2019, aside from a previously normal-sized left ventricle. LVEF in 2019 was 62%. Within 2 hours of admission to the transplant medicine team, troponin decreased to 142 ng/L. Based on presentation, physical examination findings, down-trending troponins, ECG and echocardiogram findings, it was determined that her symptoms were likely secondary to pericarditis rather than acute coronary syndrome. Clopidogrel and heparin

were discontinued, and she was started on aspirin 650 mg 3 times daily and colchicine 1.2 mg twice daily for the first day of treatment, followed by 0.6 mg twice daily for 90 days. The primary team also discussed this plan with her outpatient transplant nephrologist prior to initiating, who agreed with the treatment regimen and recommended continuing home immunosuppression regimen.

The patient's chest pain improved over the course of her admission, and she remained hemodynamically stable. She was discharged on day 4 of hospitalization with close follow-up scheduled with her primary care physician for aspirin taper and monitoring for potential treatment side effects. On follow-up chart review, there were no

reported complications from her treatment by her outpatient medical teams.

# **DISCUSSION**

Acute pericarditis is defined as inflammation of the pericardium that may present with or without concomitant pericardial effusion. The diagnosis is made with 2 of the following criteria: (1) typical chest pain—usually pleuritic and positional in nature, (2) pericardial friction rub on physical exam, (3) ECG changes consistent with pericarditis—new PR depression or ST-segment deviations, and (4) pericardial effusion.<sup>6</sup> Most cases of acute pericarditis are triggered by viral infections, though it is well-known that acute pericarditis also can result secondary to systemic inflammatory or autoimmune conditions, such as systemic lupus erythematosus.

Our patient met criteria for acute pericarditis diagnosis as she had typical chest pain and ECG changes, as well as a friction rub on exam. Current Centers for Disease Control and Prevention guidelines recommend treating COVID-19 pneumonia with up to 10 days of dexamethasone in patients requiring supplemental oxygen.<sup>7</sup> Our patient received only 7 days of dexamethasone treatment prior to discharge from the outside hospital. We speculate this shorter course of corticosteroids, along with her predisposition as a patient with systemic lupus erythematosus, may have contributed to the development of her acute pericarditis. It is also possible that she had pericarditis earlier in her illness; the course of steroids received during her first hospitalization may have masked the original pleuritic chest pain.

Considering her complex medical history, including her previous kidney transplant, treatment presented a potential challenge. The mainstay of acute pericarditis treatment includes aspirin or NSAIDs, with colchicine as a potential add-on treatment to prevent recurrence.<sup>8</sup> Drug choice is dependent on contraindications or presence of other comorbid conditions.

It is well-known that NSAID use is contraindicated in patients with kidney disease. Though our patient had a history of livingdonor kidney transplantation, her current kidney function was within normal limits. The evidence for or against the use of NSAIDs in COVID-19 patients is still being debated, though the World Health Organization has declared there is no evidence to support the role of NSAIDs in progression or severity of the disease.9 There is also a paucity of evidence on use of colchicine in COVID-19 infection. Its use is limited by its toxicity, which ranges from mild gastrointestinal side effects to potentially fatal myotoxicity and rhabdomyolysis.<sup>10</sup> As colchicine undergoes both hepatic and renal metabolism, patients with hepatic or renal impairment are at increased risk of toxicity as are patients taking drugs that may inhibit these processes, including p-glycoprotein or CYP3A4 inhibitors. The calcineurin inhibitors cyclosporine and tacrolimus are inhibitors of p-glycoprotein and CYP3A4 and have been shown to potentially increase risk of colchicine toxicity when either is administered concomitantly with colchicine. 11-15 Our patient was taking tacrolimus as part of her immunosuppressant regimen at the time she presented with pericarditis, which presented a potential treatment challenge.

In other cases of COVID-19-associated pericarditis, colchicine, aspirin, and NSAIDs such as ibuprofen have been used and have shown success as treatment options. <sup>16–20</sup> Of particular importance to our case, there has been at least 1 other case of acute pericarditis secondary to COVID-19 infection in a kidney transplant recipient, who responded well and without complications to treatment with colchicine. <sup>19</sup> We were aware of the potential risks of using colchicine in this patient. However, given the previous case report demonstrating safe use of colchicine in a renal transplant patient on tacrolimus, we opted for treatment with both aspirin and colchicine due to our patient's higher risk for recurrence given her history of systemic lupus erythematosus, with close follow-up scheduled with her outpatient transplant team.

# CONCLUSION

This case highlighted a unique complication of COVID-19 infection in a patient with systemic lupus erythematosus status post renal transplant, which was treated effectively with aspirin and colchicine without complications. To our knowledge, this is the first reported case of COVID-19-associated pericarditis in a kidney transplant patient successfully treated with aspirin and colchicine. Though more research is needed to fully understand the pathophysiology of pericarditis in the context of COVID-19, including risk factors and treatment options, this case report adds to a growing body of evidence on how to manage this complication in patients with more complex medical histories.

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# Lessons Learned: COVID Management and Cultural Practices in the US Hmong Community

Maichou Lor, PhD, RN; Phia Xiong, MD

# **ABSTRACT**

**Introduction:** Racially and ethnically minoritized communities are disproportionately affected by the COVID-19 pandemic. Yet, it is not well understood how these communities are coping with and managing COVID-19. Research has shown that patients' cultural identities and practices can affect their health behaviors.

Case Presentation: We report the cases of 2 Hmong patients, a middle-aged man and an elderly woman, who were diagnosed with COVID-19. Both patients used a combination of traditional remedies and Western medical treatments to combat COVID-19.

**Discussion:** It is important to recognize how culture can affect COVID-19 treatment decisions in the Hmong population. The power of social networks in disseminating inaccurate information during the pandemic is something to be aware of within the Hmong community.

**Conclusion:** Hmong patients are likely to use traditional remedies passed along through virtual social platforms and word of mouth, due to poor access, limited health literacy, and low English proficiency skills. Culturally acceptable interventions are needed to improve access to health literacy interventions, including better translations of COVID-19 information for the Hmong community.

# **INTRODUCTION**

The COVID-19 pandemic has resulted in more than 36 million cases and half a million deaths in the United States. Racially and ethnically minoritized communities are disproportionately affected by COVID-19, yet it remains unclear how these communities are addressing this disease. The purpose of this paper is to share our observations to increase awareness on how culture can

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affect treatment decisions and to illuminate the Hmong community's response to COVID-19. As bicultural health care professionals from the Hmong community, we have witnessed how cultural orientations can influence the response to a novel disease crisis: COVID-19. Specifically, we share 2 case studies to highlight how the Hmong community copes with and manages COVID-19.

#### **CASE STUDIES**

We present 2 Hmong case studies that were shared with us from community members. Mrs H, a 76-year-old Hmong woman who lives in Wisconsin and has limited English proficiency, contracted COVID-19 from her family in July 2020 and was hospitalized. She has a medical history of high cholesterol, diabetes, hypertension,

and osteoporosis and has Medicare for health insurance. She has a Hmong family doctor whom she sees regularly, which allows her to be independent. She does not need her family members to accompany her or require interpreter services. She has no education and cannot read or write in either Hmong or English. She described that prior to her hospitalization, her family gave her several remedies—including a urine treatment—as part of her regimen. At home, she took her own urine mixed with warm water and another herbal supplement—vacomb, a dried white flower. This treatment information was obtained through word of mouth among family members who had previously contracted and recovered from COVID-19. Despite the treatments, Mrs H's shortness of breath worsened, which resulted in hospitalization. During her hospitalization, her family continued to bring her the urine treatment in the form of a soup. She continuously drank this concoc-

tion. She was in the hospital for 2 weeks before being discharged. She believed that the urine and oxygen treatments helped her recover from COVID-19.

Mr L, a 56-year-old man living in California, contracted COVID-19 in November 2020. He has private health insurance through his spouse and sees a Hmong family doctor. He has limited English proficiency; however, he can read and write proficiently in Hmong. Mr L's past medical history includes stage 3 chronic kidney disease, obstructive sleep apnea, asthma, gout, hypertension, transient ischemic stroke, hypothyroidism, and severe seasonal allergies. He described his COVID-19 symptoms as severe shortness of breath with a tight band-like sensation around the chest. He also noted some coughing, early satiety, lack of appetite, loss of smell, and diarrhea. He suspected he had contracted COVID-19 based on information from friends and family, who were previously affected by the disease. Based on his family's advice, he pursued testing and was confirmed positive. To treat his COVID-19, Mr L's wife and other middle-aged family members suggested that he take some over-the-counter antibiotics and herbal remedies, based on information they had heard through their own social networks. His wife, who listens to the local Hmong radio station, also made a urine concoction for him—as well as for herself—as a prevention, treatment, and cure for COVID-19. Adhering to both community and public health department recommendations, he drank the urine concoction about 3 times a day and self-quarantined for 14 days with his family.

# THE HMONG IN THE UNITED STATES

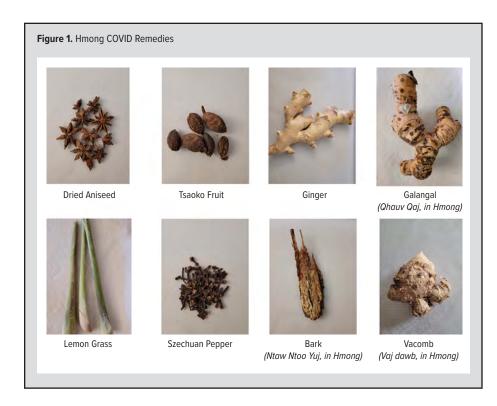
The Hmong are upland people from Laos in Southeast Asia who came to the US as refugees of the Vietnam War in the 1970s.2 According to the 2020 US Census, more than 330,000 Hmong live in the US.3 The largest Hmong populations are concentrated in California, Minnesota, and Wisconsin. The Hmong are a tightknit community from a primarily agrarian society, many of whom are unfamiliar with Western culture and medicine. Over 53% of Hmong have less than a high school education.<sup>4</sup> Hmong is traditionally and primarily an oral culture. A written Hmong language was only recently created in the 1950s,5 and most Hmong have not been formally educated to read and write this language. As a result, the written Hmong language remains unfamiliar to a majority of the population, especially the elderly. Over 21% of Hmong speak English less than well or not at all.6 These characteristics create multilayer barriers to health literacy, including understanding and accessing information about the evolving COVID-19 pandemic, which places the Hmong at higher risk for experiencing health disparities. Although materials are readily available in the Hmong language in states with large Hmong populations, they are effective only for those who have been educated to read the newly created language, which excludes many illiterate Hmong. Collectively, these factors seem to impact the ability of these vulnerable populations to process COVID-19-related information because the technique fails to account for the low health literacy. Compensatory behaviors may arise, such as greater reliance on social media and networks for information, since ideas are presented in a way that is easier for these populations to process, which can further exacerbate medical dissonance. This is evident in the 2 case studies, where it appears that a default back to traditional beliefs and practices occurs as a coping mechanism to reduce fear and uncertainty because information through their networks is more easily understood that provided by more official outlets.

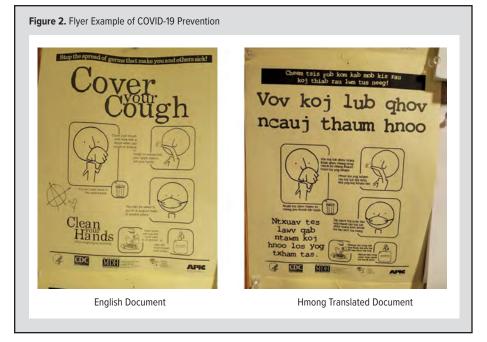
The Hmong's coping mechanisms and processing of information also are tied to their historical roots. Their history of trauma—of being constantly uprooted and persecuted without a country to call home—has instilled a strong ability to adapt to any crisis but also highlights their difficulty in accessing sustainable education.<sup>2</sup> During the pandemic, low health literacy due to decreased comprehension surrounding the disease state of COVID-19 has been pivotal in driving community members to develop new recipes containing traditional herbs to manage and treat COVID-19 symptoms.

# HERBAL TREATMENTS FOR COVID-19 IN THE HMONG COMMUNITY

We observed new recipe developments exchanged through social networks, wherein community members rely on the video or audio delivery of COVID-19 information through Hmong social media outlets on Facebook, radio stations, YouTube, and television shows, as well as through word of mouth. The information is being disseminated across state lines among Hmong communities, as seen in the 2 cases from California and Wisconsin. Since the Hmong culture is collectivist and highly values interdependence, the 2 individuals in the case studies illustrate the reliance on information and first-person experiences exchanged within their communities. As Mrs H's and Mr L's cases demonstrate, both have relied on and followed through with herbal treatments suggested by their relatives and members of the community who had experienced COVID-19. The reliance on their social networks for strategies is a result of their tight-knit communities and is consistent with tradition. This is not an uncommon phenomenon; research has shown that the spread of information in a social network is highly influential.7 After reviewing the various social media platforms, we learned that many listeners or viewers are middleaged to elderly non-English speakers. The recipes were shared by individuals, often those with relatives who had recovered from COVID-19.

The most consistently used—but not comprehensive—list of remedies includes a mixture of ginger, lemongrass, ginseng, galanga, szechuan pepper, vacomb, tsaoko fruit, dried aniseed, and ntaw ntoo yuj (a sprig of bark), depicted in Figure 1. Among websites where this recipe is found, the directions for creating and using the concoction are consistent: mix herbs together in a boiling pot of water, filter the liquid, and serve it warm. Although the





Hmong lack a scientific understanding of these herbs, some of these herbs—such as ginseng—have proposed physiologic mechanisms for their effect that provide protective properties against influenza and other respiratory illnesses such as COVID-19.8,9

Another popular COVID-19 remedy involves mixing the urine of the person taking the treatment with the herbs. Traditionally, Hmong people have held a strong cultural belief that urine has medicinal and healing properties. This cultural belief and practice reemerged during the COVID-19 pandemic. Instructions are to mix roughly 2 ounces of urine with warm water and vacomb.

#### **LESSONS LEARNED**

It is clear that cultural factors play a significant role in the choice to pursue alternative medical treatments. The case studies highlight not only the use of herbal medicinal remedies but also the traditional healing belief around drinking urine as a treatment for COVID-19. Additionally, the 2 cases show that Mrs H and Mr L seemed to blend both forms of medicine in a reasonable way appropriate for them. For example, Mrs H sought hospitalization when needed, while Mr L appropriately followed public health guidelines and stayed in quarantine.

Additionally, we learned that Hmong patients are likely to use traditional remedies (herbal or cultural practices that have been used consistently over time in the Hmong community to treat illnesses as they arise) disseminated through virtual social platforms and word of mouth, due to the lack of access to current COVID-19 health information, low health literacy, and limited English proficiency. Even though COVID-19 information is mobilized to various communities to increase implementation, it does not translate well into practice, and current methods are not effective in reaching all communities, including the Hmong. For example, COVID-19 information is not translated in a manner that is culturally comprehensible to the Hmong community. Existing COVID-19 information is delivered through flyers, posters, or pamphlets and often posted at clinics or hospital settings. Figure 2 depicts a flyer providing information on the prevention of the spread of COVID-19 in the Hmong language at a clinic. While there are efforts to translate English materials into other languages such as Hmong, the

quality of its translation is questionable. For example, on the flyer shown in Figure 2, the translation for "cover your mouth when you cough" is semantically incorrect in Hmong. Rather than vov (which, in Hmong, refers to covering a larger area, eg, the whole body), it should have been npog (which, in Hmong, refers to covering a smaller area, eg, the mouth). Such translation is considered culturally insensitive. It is possible that the translator may not have understood such cultural nuances due to a lack of fluency in the Hmong language. Although neither Mrs H nor Mr L are literate in Hmong, it is possible that similar types of transla-

tions or medical interpretations were given to both Mrs H and Mr L and that they may have not understood. This highlights the need for more culturally and acceptable health literacy interventions, including better translation of medical information for the Hmong community. Hence, it is critical for health care systems to use a rigorous process to select translators and interpreters and evaluate translated health information before dissemination. Such processes could include an interdisciplinary effort, such as translation/interpreting, education, linguistics, public health, medicine, and nursing to collaboratively create and evaluate translations of COVID-19 information.

The cases also posit that COVID-19 has affected Hmong patients' access to US health systems. Although Mrs H and Mr L have Hmong family doctors, surprisingly, they did not mention seeking advice from these doctors. A possible explanation for such behavior could be because the Hmong family doctors work in a private health care system that is limited by resources (eg, low number of staff members) and were unavailable to answer patients' questions or to see them. This is not an uncommon issue, since the COVID-19 pandemic has had a major impact on the capacity of health systems to continue the delivery of essential health services. However, the impact of COVID-19 may have impinged on the Hmong community to a greater extent due to the limited number of Hmong health care providers.

Furthermore, poor language (ie, English language proficiency) and literacy skills remain impediments to health care access for the Hmong, even during COVID-19. As the cases demonstrate, both Mrs H and Mr L sought traditional medicine first before seeking care from the US health care system, as well as relying on their social networks to gain verbal information about COVID-19.

# CLINICAL AND RESEARCH IMPLICATIONS FOR AMBULATORY CARE

Several clinical and research implications can be learned from the 2 cases described above. Although the pandemic is a unique phenomenon, it does not mean that behavior and practices will deviate from what is familiar and comfortable for communities. For the Hmong, this means turning to well-established cultural knowledge of herbal medicinal remedies to cope with and manage COVID-19. The use by Mrs H and Mr L of both traditional herbal remedies and Western medicine treatments suggests that the Hmong likely use holistic methods more frequently in treating and managing COVID-19. The use of traditional Hmong herbal remedies is common, yet evolving. 12,13 Additionally, the use of over-the-counter antibiotics purchased from local markets is frequent among Hmong members. A recent news article has documented the misbranding of medications sold at the Hmong Village Market in St. Paul, Minnesota.<sup>14</sup> Hence, it is critical that clinicians acknowledge the use of traditional herbal remedies and over-the-counter antibiotics and discuss such medicines with their Hmong patients to identify any potential harm or contraindication.

Some communities are disproportionately affected by COVID-19, adding to an already disproportionate health-related burden. For example, in the case of Mr L, who has stage 3 chronic kidney disease, hypertension, asthma, and COVID-19, his use of the urine treatment can confound the cause of his kidney disease, where the possibility exists of exacerbating an acute kidney injury on top of the chronic kidney disease. Therefore, it is vital that clinicians spend time with Hmong patients to thoroughly investigate whether their Hmong patients are taking urine concoctions at home and to provide education to Hmong patients.

The power of social networks in disseminating inaccurate information during the pandemic is another factor of concern. As seen in the cases of Mrs H and Mr L, all of their information sources were family and friends who had had COVID-19. Mrs H and Mr L shared that after receiving their positive test results, they were not contacted by a health care provider or public health department to discuss their COVID-19 diagnosis, leading them to rely on their immediate family members—particularly English-speaking adult children—and reach out to their social networks for information about COVID-19 and how to manage it. This lack of connection, access, and outreach from the public health system or health care educators may reinforce the distrust held by the Hmong and similar communities toward health care professionals. Research has shown that Hmong patients have a lack of trust in doctors due to fears of being studied<sup>15</sup> or conflicts between Hmong cultural values and beliefs and Western medical practices, as documented in the well-known book The Spirit Catches You and You Fall Down. 16 Community capacity-building is crucial in building trust and compliance and in ensuring health equity.

Some limitations must be acknowledged regarding the case studies in this research. The cases are first-person accounts shared from community members of their experiences during COVID-19, which limits our ability to describe specific medical treatments received during hospitalization or information about the over-the-counter antibiotics used. Additionally, we only presented 2 case studies, so generalizability may be limited to Hmong individuals with limited English proficiency. More research is needed to better understand the impact of COVID-19 on the Hmong community at large.

To ensure health equity, social and racial justice requires that all communities, including smaller communities that have been minoritized such as the Hmong, be included in research, funding, and national initiatives to address COVID-19. Asian subgroups that have language and cultural barriers are most at risk of being underserved and underrepresented in research due to the lack of funding and focus. Research funding could be directed toward creating and providing culturally and linguistically appropriate COVID-19 education interventions. Given the lack of research on Hmong traditional remedies, future research could study the impact of herbs such as vacomb on COVID-19 outcomes.

Additional funding could assist Hmong community health workers in bridging the gap between the Hmong community and the health care system, as well as help clinicians better understand any traditional remedies being used. We acknowledge that in states where certain subgroups are the majority, resources may be more readily available to address some of these disparities. However, in states where the subgroups are minoritized, access continues to be a challenge. Hence, education and opportunities for all communities are important to prevent misinformation and reduce disparities in care.

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# Adjunctive Minocycline for Treatment of Posttraumatic Stress Disorder

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# **ABSTRACT**

**Introduction:** Posttraumatic stress disorder (PTSD) is a chronic, debilitating anxiety disorder. While there is evidence that antibiotics such as minocycline may help to improve symptoms in some psychiatric disorders, no human studies have evaluated their potential as a treatment for PTSD.

**Methods:** We present results from 4 men aged 33 to 59 years who completed a 12-week pilot, prospective, nonrandomized, open-label clinical trial of adjunctive minocycline for veterans diagnosed with PTSD.

**Results:** All 4 patients showed reduction in PTSD symptoms at the end of the 12-week study, and 3 patients showed reduction in depression symptoms. Observed changes in inflammatory biomarkers are discussed.

**Discussion:** Previous studies have reported increased inflammation in PTSD, though evidence of a potential therapeutic effect of minocycline for PTSD has not been reported previously in humans.

**Conclusion:** These findings suggest that antibiotics like minocycline may help to reduce symptoms of PTSD, though further investigation is needed to confirm these findings.

## INTRODUCTION

Posttraumatic stress disorder (PTSD) is a debilitating disorder characterized by re-experiencing aspects of an original trauma, avoidance and numbing of trauma reminders, and general hyperarousal. Lifetime prevalence of PTSD in community samples is around 6.8%. A study looking at prevalence of current PTSD in Vietnam veterans was higher at 15%.

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Cumulative stress has been suggested to play an important role in the development of PTSD.2 For example, there is evidence that the risk of PTSD is greater in military units with longer deployments and shorter intervals between deployments.2 Studies have shown that the chronic stress associated with PTSD also may be related to chronic inflammation, observed through levels of proinflammatory markers.3 Elevated levels of these markers, such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor alpha (TNF-α), have been observed in patients with PTSD. Groer et al studied levels of inflammation in active military personnel and found that increased CRP levels were

associated with depression and PTSD symptoms.3 Another study comparing proinflammatory marker levels in 2 groups of combat-exposed veterans—one group with PTSD and one without found that the veterans with PTSD exhibited higher levels of the markers, even when accounting for depression as a comorbidity.<sup>4</sup> Elevated inflammatory cytokine activity may result from cortisol, a stress hormone, inadequately performing its regulatory functions.5 Low cortisol levels promote excessive catecholamine production, and increased levels of these catecholamines lead to excessive sympathetic activity. This overactive sympathetic response can accentuate flashbacks and lead to other PTSD symptoms.<sup>5,6</sup> PTSD has been linked to an increased risk of serious diseases, such as cardiovascular and autoimmune diseases.7 These diseases have an inflammatory aspect, further supporting the relationship between immune dysregulation and PTSD.7 Furthermore, in a prospective study, Eraly et al examined levels of CRP in active-duty military

Patient	Age/Sex	CAPS		CRP (mg/dL)		IL-6 (pg/mL)		TNF-α (pg/mL)	
		Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
A	33 y/male	23	15	< 0.5	< 0.5	0.83	1.04	1.4	1.14
В	39 y/male	40	29	1.5	1.0	1.59	1.29	1.4	1.19
С	59 y/male	29	18	1.0	8.0	1.79	2.56	0.97	1.26
D	46 y/male	34	30	< 0.5	< 0.5	0.87	1.68	0.78	0.93

Abbreviations: CAPS, Clinician-Administered PTSD Scale; CRP, C-reactive protein; IL-6, interleukin 6; TNF- $\alpha$ , tumor necrosis factor alpha; y, years.

personnel 3 to 6 months after returning from deployment. Those with elevated predeployment levels of CRP were more likely to develop PTSD, suggesting that individuals with more inflammation at baseline may be more likely to develop PTSD.8

The above studies suggest that the inflammatory response may serve as a potential target for treatment of individuals with PTSD. To our knowledge, the efficacy of anti-inflammatory medication has not been examined in patients with PTSD. However, a study using a rat model of PTSD showed that treatment with ibuprofen reduced both inflammatory cytokine levels and behavioral symptoms. Minocycline is a broad-spectrum tetracycline anti-biotic with anti-inflammatory and neuroprotective properties. It has been shown to reduce levels of proinflammatory markers and inhibit microglial cells. Microglial cells—the primary effector immune cells of the brain and a source of central proinflammatory cytokines—appear to play a key role in stress-induced behavioral changes in rodents. <sup>10</sup>

Several studies have reported evidence indicating that minocycline may help in treating symptoms of psychiatric disorders such as schizophrenia<sup>11,12</sup> and depression.<sup>13,14</sup> These treatments also could prove beneficial in treating health conditions associated with chronic inflammation that are often comorbid with PTSD, such as chronic pain, arthritis, diabetes, and cardiovascular disease.5 Two studies using animal models of PTSD have shown how the anti-inflammatory effects of minocycline may help to alleviate PTSD symptoms. 10,15 Decreased levels of cytokines were found in the animal models treated with minocycline compared to the control. 10,15 In addition, a recent study of fear conditioning in humans found attenuated fear memory in individuals administered doxycycline—another tetracycline antibiotic—suggesting that such medications may help to improve symptoms of PTSD.16 Despite these findings, to date there have been no published data on the efficacy of minocycline treatment in veterans with PTSD.

# **METHODS**

We reviewed existing medical records of patients who participated in a previous study conducted at the Nebraska-Western Iowa Health Care system. The study was a 12-week open-label pilot study to evaluate the efficacy of minocycline in treating PTSD. The data reported here were obtained from 4 patients who completed the 12-week study. The study enrolled veterans on a stable dose of psychotropic medications for a minimum of 8 weeks at the time of study entry. Use of statins was not permitted during the study. All patients were instructed to take 100 mg/day of adjunctive minocycline for 7 days, followed by 200 mg/day for the remainder of the study. They also were asked to report any changes in medi-

cations or behavioral therapies during the study period.

Data were collected using the following clinical measures: the Mini-International Neuropsychiatric Interview (MINI), used to screen for comorbid psychiatric disorders; the PTSD Checklist for DSM-5 (PCL-5), used to confirm diagnosis of PTSD; and the Beck Depression Inventory-II (BDI-II), which assessed depression symptoms in these patients. The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) was used to assess current (past month) PTSD symptoms. The Clinical Global Impressions-Severity (CGI-S) scale was used to assess overall severity of symptoms. Medical history and concomitant medications were noted. Laboratory samples collected include CRP, IL-6, and TNF-α. Review of medical records was performed as needed to obtain medical data and treatment history relevant to the study.

Primary efficacy measures included (1) change in CAPS-5 score from baseline to the end of study and (2) levels of the inflammatory markers CRP, IL-6, and TNF- $\alpha$  from screening to the end of the study. Secondary efficacy measures included change in BDI-II and CGI scores from baseline to the end of the study.

# **RESULTS**

Demographics and primary efficacy measure results are summarized in the Table. Patient A is a 33-year-old man diagnosed with PTSD in September 2014. He served active duty in the US Army from 2006 to 2014. Comorbid conditions included obstructive sleep apnea, tinnitus, lower back pain, and obesity. Prior to minocycline treatment, he took duloxetine 60 mg/day. Diagnosis of PTSD was clinically confirmed by his PCL-5 score of 38 at his screening visit. Starting with measures of primary efficacy, his CAPS score at baseline was 23 and reached 15 at the end of the study. CRP measurements remained below 0.5 mg/ dL at both visits, IL-6 increased from 0.83 pg/mL to 1.04 pg/ mL, and TNF- $\alpha$  decreased from 1.4 pg/mL to 1.14 pg/mL. His BDI-II started at 18 and dropped to 13 at end of study, so it was never above the threshold of 20 to indicate moderate/severe depression. Patient A's CGI-S score remained at the same value of 4 throughout the study, indicating that the severity of his clinical symptoms did not change.

Patient B is a 39-year-old man. He experienced several trau-

matic events as he served as a combat medic in Iraq from 2003 to 2005. He was diagnosed with PTSD in July 2013. He had previously received diagnoses of alcohol use disorder and cocaine use disorder. Medications he used prior to the study include sertraline 100 mg/day and prazosin 1 mg/day. Additionally, he participated in PTSD group therapy. He had a PCL-5 score of 38 at his screening visit, clinically confirming his diagnosis. His CAPS score decreased from 40 to 29. Changes in his inflammatory cytokine levels from the beginning to the end of the study were as follows: CRP, 1.5 mg/dL to 1.0 mg/dL; IL-6, 1.59 pg/mL to 1.29 pg/mL; and TNF-α, 1.4 pg/mL to 1.19 pg/mL. His BDI-II score of 11 did not meet the threshold for moderate/severe depression, but at the end of the study it had increased to 23, indicating depression. Patient B's CGI-S score was 5 at his initial evaluation and decreased to 4 by the end of the study.

Patient C is a 59-year-old man diagnosed with PTSD in September 2016. He witnessed traumatic events during his service as both a civilian and military firefighter emergency medical technician, including experience with dead and mutilated bodies. Along with PTSD, he experienced sciatic nerve pain, degeneration of intervertebral disk, and hearing loss. Patient C's medication taken prior to and during the study included 100 mg/day of the selective serotonin reuptake inhibitor sertraline and 4 mg/ day of the antihistamine cyproheptadine. For the study, Patient C received a PCL-5 score of 45 recorded at screening, which indicates a PTSD diagnosis (PCL-5 score ≥ 33). He also had a BDI-II score of 29 at the first visit, indicating moderate depression. Over the course of the study, data indicated a rise in concentrations for IL-6, 1.79 to  $2.56 \, pg/mL$ , and TNF- $\alpha$ , 0.97 to  $1.26 \, pg/mL$ . CRP levels dropped from 1.0 to 0.8 mg/dL. Patient C's BDI-II score at the end of the study measured 23, and his CGI-S score remained at 4 throughout the study. The CAPS score decreased from baseline measurement to end of study tests, 29 to 18.

Patient D is a 46-year-old man who was diagnosed with PTSD in January 2014. He served in active military from 1993 to 1997 in Haiti, Kuwait, and Bosnia as a reconnaissance scout. He attributes the cause of his trauma to experiences dealing with dead bodies, especially infants. Other than PTSD, Patient D was diagnosed with hyperthyroidism and hyperlipidemia. Medications taken prior to and during the study on stable dose included paroxetine 40 mg/day for anxiety and quetiapine fumarate 425 mg/ day for PTSD. At screening, he scored a 53 on the PCL-5, indicating a PTSD diagnosis. He also had a BDI-II score of 40 at screening, indicating severe depression. Concentrations of IL-6, CRP, and TNF-α measured from baseline to end of study were as follows: IL-6, 0.87 to 1.68 pg/mL; TNF- $\alpha$ , 0.78 to 0.93 pg/ mL. CRP levels stayed below 0.5 mg/dL for both measurements. Patient D's BDI-II score at the end of study measured 24, and his CGI-S score remained at 4 throughout the study. The CAPS score decreased from 34 to 30 at the end of study.

#### **DISCUSSION**

In this study, we hypothesized that minocycline treatment would be associated with reduced inflammation (measured by decreasing levels of inflammatory markers) and decreased PTSD severity, along with mood symptoms. All 4 patients had decreased CAPS scores by the end of the study, and 3 of the 4 patients had decreased scores on the BDI-II.

Consideration should be given to the biomarker results of the study, in which all 4 subjects' levels of CRP decreased or remained below 0.5 mg/dL, while 3 of the subjects' IL-6 levels and 2 patients TNF- $\alpha$  levels increased. The observed increases are contrary to minocycline's proposed mechanism of action.5,6 As IL-6 and TNF-α are among the main regulators of CRP release,<sup>17</sup> it was expected that elevations of CRP should mirror elevations of IL-6 and TNF-α. However, the results of this study showed the inflammatory markers diverge. While this finding was unexpected, it is not without precedent. Garvin et al discussed such a phenomenon where divergent patterning occurs.<sup>18</sup> The results may stem from the fact that kinetics between CRP and the other biomarkers differ in both release pattern and concentration. Additionally, CRP has a much longer half-life than IL-6 or TNF-α. Possibly, elevations in IL-6 and TNF- $\alpha$  without CRP could be attributed to various acute phase responses in individuals with differing subclinical inflammation. Whereas a subclinical infection would possibly not see a rise in all biomarkers, in a true clinical infection, all biomarkers would likely show a notable increase. Further studies utilizing larger samples of participants and measurement of inflammatory markers could help to better understand the interactions between these inflammatory factors.

Limitations of this research include the fact that it was an openlabel trial with no placebo arm. A 12-week treatment duration may have been too short to see long-lasting benefits, but future studies could address this by extending the trial length. Adjunctive minocycline was not associated with any serious adverse events or significant laboratory abnormalities in our cohort; however, it is important to pay attention to potential side effects from longterm antibiotic use.<sup>19</sup> No follow-up was done to evaluate patients' PTSD symptoms after the study, so we are unaware of long-term benefits regarding this intervention. Lastly, a larger sample size could create more generalizable information.

Further neuroprotective efforts also should be explored when considering minocycline treatment. Patients A, C, and D's BDI-II scores decreased by a notable margin during the study. Previous studies evaluating minocycline therapy for depression have reported significant improvement in symptoms.<sup>13,14</sup> Larger scale double-blind clinical trials should be considered in further research of this inexpensive and generally safe drug in PTSD.

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# Ganglion Cysts as a Cause of Ulnar Neuropathy at the Wrist

Bahram A. Nico, MD; Andrew J. Waclawik, MD

#### **ABSTRACT**

**Introduction:** The diagnosis of ulnar neuropathy at the wrist traditionally has depended primarily on clinical and electrodiagnostic findings. Magnetic resonance imaging (MRI) and ultrasound have emerged as very important diagnostic tools in diagnosis of focal neuropathies.

**Case Presentation:** We present clinical, electrodiagnostic, and MRI findings in 2 patients with ulnar neuropathies at the wrist caused by ganglion cysts.

**Discussion:** Ulnar neuropathies at the wrist are common, may present with different patterns of motor and sensory deficits, and can be misdiagnosed. Nerve conduction studies and needle electromyography are essential to assist with anatomical localization of possible lesions. The structural lesions may be well characterized by MRI.

**Conclusions:** We conclude that MRI is a very useful and important diagnostic tool that may help with diagnosis and therapeutic decisions in patients with ulnar nerve lesions at the wrist. It complements the neurological exam and electrodiagnostic studies. High resolution ultrasound may be an adequate alternative to the MRI.

#### INTRODUCTION

Entrapment of the ulnar nerve at the wrist is far less common than at the elbow. Entrapment in the Guyon's canal most frequently results from a ganglion cyst. Clinical examination and carefully performed electrodiagnostic studies can lead to a quick diagnosis and effective treatment in most cases. Nerve conduction studies (NCS) and needle electromyography (EMG) are most helpful in localizing the site of nerve injury. Understanding the anatomy of the ulnar nerve at the wrist is essential to accurately localize the

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lesion to the Guyon's canal, based on the pattern of clinical and electrophysiologic findings.3 However, not infrequently, the clinical symptoms and signs may not be straightforward for a reliable localization of the nerve lesion, and even the most diligent electrodiagnostic studies may not allow for confident confirmation of the site of the neuropathic process. Magnetic resonance imaging (MRI) or ultrasound may provide additional, clinically most useful information and help avoid diagnostic errors. By revealing a specific compressive lesion, such as a ganglion cyst, or other pathologies, it may help with selection of the appropriate treatment.4 We present 2 cases of ulnar neuropathies with

clinical and EMG findings consistent with nerve lesions at the region of the wrist. MRI in both cases revealed ganglion cysts originating from the pisotriquetral joint and compressing the ulnar nerves.

#### **CASE REPORTS**

#### Case 1

A 54-year-old woman was referred for evaluation of progressive right hand weakness and atrophy for 5 months. She had tenderness to palpation over the medial palmar aspect of the right hand. She denied any history of trauma to her wrist or hand. Her past medical history included non-Hodgkin lymphoma treated by chemotherapy, which was in remission.

Motor examination showed prominent atrophy of the right hand interossei and hypothenar muscles. She had moderate degree of claw hand deformity on the right side. The thenar muscles were well preserved. There was no atrophy of her forearm muscles. The strength of the dorsal and palmar interossei muscles was 4/5 by

	Normal		Patient 1		Patient 2	
	SNAP (μV)	LAT(ms)	SNAP(μV)	LAT(ms)	SNAP(mV)	LAT(ms)
R-Sensory						
Median	>15	<3.6	39	2.9	22	4.7
Ulnar	>10	<3.1	33	2.7	9	3.0
Radial	>19	<2.9	34	2.3	55	1.8
Median TC	>50	<2.3	61	2.2	17	3.5
Ulnar TC	>15	<2.3	18	2.0	6	3.4
DUC	>10	<2.8	17	2.1	12	2.6
	CMAP(mV)	LAT(ms)	CMAP(mV)	LAT(ms)	CMAP(mV)	LAT(ms)
R-Motor						
Median	>4	<4.5	5.8	3.7	5.7	7.7
Ulnara	>6	<3.6	5.7	2.6	4.0	4.2
Ulnar <sup>b</sup>	>7	<4.5	.07	4.0	0.5	6.5
L-Motor						
Ulnara	>6	<3.6	11.9	2.6	7.2	2.9
Ulnar <sup>b</sup>	>7	<4.5	14.0	4.0	5.8	4.0

Abbreviations: CMAP, compound muscle action potential (amplitude); DUC, dorsal ulnar cutaneous; SNAP: sensory nerve action potential (amplitude); LAT, latency; TC, transcarpal (mixed nerve action potential).

Abnormal values are in bold.

Medical Research Council (MRC) scale. Her long finger flexors and thenar muscles strength were normal. Muscle stretch reflexes and sensory examination were normal.

The pattern of abnormalities on neurologic examination indicated ulnar neuropathy at the wrist that was confirmed by NCS and EMG (Table). Median, ulnar, and radial sensory nerve conduction studies were normal. The sensory action potentials (SNAP) had normal amplitudes and latencies. Median motor compound muscle action potential (CMAP) had normal amplitude and latency, and motor conduction velocity was normal. Right ulnar motor study, with recording from the abductor digiti minimi (ADM), revealed small CMAP amplitude with normal latency. The ulnar motor conduction velocity in the forearm was normal. Inching around elbow did not demonstrate any focal slowing or change in CMAP morphology. Stimulating the ulnar nerve at the wrist and recording from right first dorsal interosseous (FDI) revealed severely reduced CMAP amplitude without any significant prolongation of the latency. Dorsal ulnar cutaneous SNAP was normal. Needle EMG revealed spontaneous activity in the right FDI and ADM and motor unit potential changes indicative of a chronic neurogenic process. Remaining right upper limb muscles including abductor pollicis brevis, flexor carpi ulnaris, flexor digitorum profundus IV/V, pronator teres, triceps, deltoid, and cervical paraspinal muscles were normal on needle EMG. The electrodiagnostic studies indicated severe right distal ulnar motor neuropathy at the wrist, with severe axonal injury. The pattern of clinical and electrophysiologic abnormalities was consistent with a lesion affecting the deep branch of the ulnar nerve in the Guyon's canal, distal to the superficial sensory

branch but proximal to the branch supplying the hypothenar muscles.

To confirm the suspected site of the ulnar nerve lesion and to identify possible structural abnormalities, MRI of the wrist and hand was requested. The MRI (Figure 1) revealed a  $9 \times 15 \times 9$  mm ganglion cyst arising from the pisotriquetral joint, extending into Guyon's canal and compressing the ulnar nerve in this region. Subsequently, the patient underwent surgical exploration with decompression of the right ulnar nerve at the Guyon's canal with removal of the large ganglion cyst. A follow-up neurological examination after 6 months showed complete recovery of her motor deficits, with normal muscle bulk and strength.

#### Case 2

A 54-year-old right-handed man was referred for evaluation of right hand weakness and atrophy. Onset of weakness was 6 months prior to our evaluation. He noted difficulty with activities such as pinching, grasping, and writing. Two months later he noticed muscle wasting in his right hand. For the last few years, he had intermittent tingling sensation in the distribution of the first 3 fingers of both hands. He had history of poliomyelitis as a child with residual weakness and atrophy of lower extremities and was using crutches to assist with ambulation.

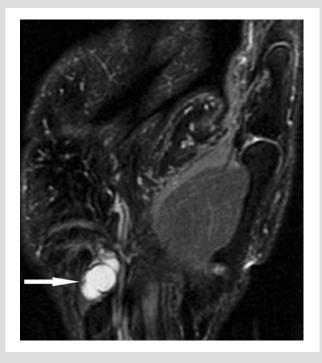
Examination revealed atrophy and grade 4+/5 (MRC scale) weakness of the right hypothenar and interossei muscles. Other upper extremity muscles had normal muscle bulk and strength. Muscle stretch reflexes in both upper extremities were normal, as was the sensory examination.

His NCS (Table) revealed decreased right ulnar SNAP (recording from the 5th digit) with normal latency. The right ulnar CMAP amplitudes (recording from the FDI and ADM) were reduced with prolonged latencies. Ulnar motor conduction velocities and inching around the elbow were normal. Ulnar transcarpal response had reduced amplitude and prolonged latency. Dorsal ulnar cutaneous SNAP was normal. Radial SNAP was also normal. He also had prolonged right median motor, sensory, and transcarpal latencies. The EMG study showed chronic and active neurogenic changes in the right FDI and ADM muscles. Flexor digitorum profundus IV/V, abductor pollicis brevis, pronator teres, triceps, deltoid, and cervical paraspinal muscles were normal. The NCS and EMG findings localized the ulnar neuropathy to the wrist, proximal to Guyon's canal affecting both motor and sensory branches. In addition, the patient had bilateral, relatively mild median neuropathies at the wrists, consistent with carpal tunnel syndrome. MRI of the right wrist (Figure 2) revealed 2 small ganglion cysts, 7.2 mm and 4.1 mm in diameters, respectively, in close approximation with the ulnar nerve, distal to the styloid process of the ulnar bone and adjacent to the proximal pisiform bone. The patient underwent surgical decompression of the right ulnar nerve at the wrist with removal of ganglion cysts. He did not return to the neuromuscular clinic for follow-up evaluation.

<sup>&</sup>lt;sup>a</sup>Recording from abductor digiti minimi.

<sup>&</sup>lt;sup>b</sup> Recording from first dorsal interosseous.

Figure 1. Patient 1, Magnetic Resonance Imaging of Right Wrist



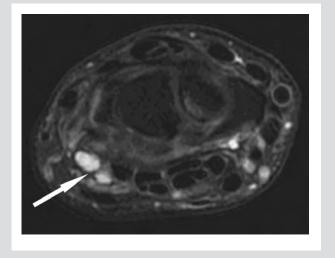
Coronal fat-saturated T2 image showing a multiloculated, fluid containing cyst originating from the pisotriquetral joint extending into Guyon's canal, compatible with a ganglion cyst (arrow). It exerts mass-effect compressing the ulnar nerve in this region.

#### **DISCUSSION**

These 2 cases demonstrate the importance of careful correlation of clinical findings and electrodiagnostic studies for specific localization of possible ulnar nerve lesions. In both cases, the MRI provided further information about the structural abnormalities causing ulnar nerve compressions. In both patients, ulnar nerve compressions were caused by ganglion cysts arising from the pisotriquetral joint. In the first case, the cyst compressed the deep motor branch in the Guyon's canal and, in the second case, the site of compression was proximal to the bifurcation of the motor and sensory nerve branches just proximal to the Guyon's canal.

The ulnar nerve enters the hand through Guyon's canal at the wrist. Nerve injuries at this site are seen less frequently than at the elbow. The ulnar nerve lesions at different sites along its course at the wrist and the hand may produce different patterns of symptoms and signs. Shea and McLain described 3 different types of ulnar neuropathy at the wrist, based on the anatomical course and clinical symptoms. These correspond to the 3 anatomical zones described by Gross and Gelberman in their cadaveric study, with the proximal zone I containing both motor and sensory fibers before their bifurcation, zone II containing the deeper motor fibers, and zone III containing the more superficial predominantly sensory fibers. Wu et al subsequently classified

Figure 2. Patient 2, Magnetic Resonance Imaging of Right Wrist



Axial fat-saturated T2 image demonstrates 2 ganglion cysts in close proximity to the ulnar nerve along the medial and volar aspect of the wrist (arrow).

ulnar neuropathies at the wrist into 5 types: type I, a mixed sensory and motor neuropathy occurring within the proximal end of the Guyon's canal; type II, a pure sensory neuropathy caused by a lesion of the superficial branch at the wrist; type III, a pure motor neuropathy due to a lesion of the deep branch of the ulnar nerve just distal to the superficial branch but proximal to the branch innervating the hypothenar muscles; type IV, a pure motor neuropathy with sparing of hypothenar muscles; and type V, with a pure limited distal motor neuropathy of ulnar nerve, in which the lesion occurs just proximal to the deep motor branches going only to the first dorsal interosseous and adductor pollicis muscles.2 According to Waugh and Pellegrini, the muscles most commonly affected in the ulnar tunnel syndrome (caused by compression of the ulnar nerve at the Guyon's canal) include the first palmar and dorsal interossei, the lumbricals to the ring and little fingers, and adductor pollicis.3

Etiologies of ulnar neuropathy at the wrist include acute and chronic trauma as the most common cause.<sup>7</sup> Other causes of ulnar neuropathy at the wrist include ganglion cysts, tumors, anatomic abnormalities, hypothenar hammer syndrome, fractures or dislocations, direct trauma during arthroscopy including other iatrogenic causes, rheumatoid arthritis, osteoarthritis, and tenosynovitis; it also may be more common in patients with carpal tunnel syndrome.<sup>3,8,9</sup> Physical labor and biking are associated with increased risk for ulnar neuropathy at the wrist.<sup>10</sup>

Entrapment of the ulnar nerve in Guyon's canal most frequently results from a ganglion cyst.<sup>2,11,12</sup> They are widely recognized as a mucoid degeneration of the wrist joint capsule that occasionally protrude into the Guyon's canal and induce entrapment neuropathies.<sup>13</sup> Seddon described a series of patients with motor symptoms caused by the ganglia compressing the deep

branch of the ulnar nerve. 14 Brooks observed that ganglion cysts arising proximal to the pisohamate ligament present with both motor and sensory symptoms, whereas those arising distal to this ligament tended to spare sensation. 15

Some patients with ganglion cysts at the Guyon's canal can present with a subacute onset of discomfort and pain at the wrist (as in case 1) with subsequent weakness with or without sensory symptoms, according to the anatomical location. <sup>16</sup> As in case 1, nearly 90% of all nontraumatic cases of pure motor weakness result from a ganglion cyst arising from the triquetrohamate joint. <sup>3</sup> Zone III lesions are most commonly caused by anomalous muscles or thrombosis of the ulnar artery. <sup>6</sup>

NCS and EMG are essential to differentiate ulnar neuropathy at the wrist from the more common ulnar neuropathy at the elbow or other neuropathic processes that may mimic ulnar neuropathy. It also helps with more specific localization of ulnar nerve lesions in the wrist. In the case of distal motor ulnar neuropathy, it is imperative to perform motor studies recording from the FDI muscle, in order not to miss involvement of the more distal deep motor branch after take-off of the hypothenar branch.<sup>7</sup>

Accurate anatomical localization and characterization of the lesion is crucial in planning the surgical approach. MRI has an important clinical utility in diagnosis of space occupying lesions causing ulnar neuropathies, such as ganglia, tumors, aneurysm or thrombosis, or congenital abnormalities. Its use has a particular importance value in patients presenting with subacute or chronic neurologic deficits of the hand without history of trauma when the NCS and EMG localize the lesion to the wrist. The ganglion cysts have signal intensity similar to that of waterbright on T2-weighted imaging or short tau inversion recovery and dark on T1-weighted imaging.<sup>17</sup> MRI images depict the ulnar tunnel in excellent detail.<sup>18</sup> High-resolution sonographic examination reveals ganglion cyst as a well-demarcated anechoic mass with posterior enhancement and without vascularity within the mass.<sup>13</sup> In some studies, MRI and ultrasound examinations were found to be equally effective in detecting ganglion cysts.<sup>4</sup> The ultrasound may be a cheaper and adequate alternative to the MRI. The resolution of ultrasound techniques has improved in recent years; however, the images frequently are not sufficiently anatomically precise, and many processes affecting peripheral nerves cannot be adequately assessed by the ultrasound. In addition to the aforementioned pathologies, the ulnar nerve lesions at the wrist are quite frequently associated with various systemic conditions affecting the bones, joints, ligaments, tendons, and soft tissues. In those instances, MRI provides markedly better and more complete information about specific pathologies and may be more helpful than ultrasound with planning of specific therapeutic interventions. Both imaging techniques have been used by physicians of different specialties for evaluation of focal neuropathies. Future research will help determine which technique should be used preferentially, depending on the observed clinical and electrodiagnostic abnormalities.

Ganglion cysts at the Guyon's canal causing motor deficits are subject to surgical interventions.<sup>19</sup> In a large series of patients with ganglion cysts causing peripheral nerve compression, only 58% had a good motor recovery; this was related to the severity of preoperative motor deficits,<sup>20</sup> which underscores importance of early diagnosis and therapeutic intervention.

All 3 elements of the assessment are very important to maximize the chances of successful management of ulnar nerve lesions at the wrist: (1) diligent clinical assessment, based on understanding of the ulnar nerve neuroanatomy and various patterns of the sensory and motor function abnormalities in ulnar nerve lesions at different locations; (2) additional confirmation of the neuropathic process and likely localization of the lesion by NCS and needle EMG; and (3) visualization and characterization of the possible structural lesion by MRI or ultrasound.

#### **CONCLUSIONS**

MRI is a very useful and important diagnostic tool that may help with diagnosis and therapeutic decisions in patients with ulnar nerve lesions at the wrist. It complements the neurological exam and electrodiagnostic studies. High resolution ultrasound may be an adequate alternative to the MRI.

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# Hypertensive Emergency Caused by Sexual Enhancement Supplements

Nathalie Abenoza, MD; Kimberly Stoner, MD, MS

#### **ABSTRACT**

**Introduction:** In the United States, major depression ranks second among all diseases and injuries as a cause of disability and 40% of patients using antidepressants experience sexual dysfunction.

**Case Presentation:** A 41-year-old woman with past history of depression and anxiety presented with hypertensive urgency after ingesting a sexual enhancement supplement—BioXgenic—for the first time. Shortly after, computed tomography showed a basal ganglia hemorrhage. After many weeks of rehabilitation, some cognitive deficits remained.

**Discussion:** The US Food and Drug Administration (FDA) does not regulate supplements. The sexual enhancement supplement ingested had monoamine oxidase inhibitor properties and precipitated a hypertensive emergency with an intracerebral hemorrhage. Reducing medication dosage, switching medication, using drug holidays, and changing the time of administration may help alleviate sexual side effects.

**Conclusion:** Physicians should inquire about dietary supplements and warn about the risks, encourage patients to report adverse effects to the FDA, and refer to the FDA's Tainted Supplements database for known adulterated supplements.

#### **INTRODUCTION**

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The dietary supplement market is larger than ever. In 2020, the global dietary supplements market was estimated at \$140.3 billion and is projected to continue growing and expanding due to rising health concerns and changing lifestyles. Pivotal legislation that laid the groundwork for this booming market included the 1976 "Proxmire Amendment" and the Dietary Supplement

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Health and Education Act (DSHEA) of 1994. The Proxmire Amendment, which became section 411 of the Federal Food, Drug, and Cosmetic Act,<sup>2</sup> prohibited the US Food and Drug Administration (FDA) from requiring and limiting potency of vitamins and minerals in food supplements and regulating them as drugs. The DSHEA created specific labeling requirements, provided a regulatory framework, and authorized the FDA to establish good manufacturing practice regulations for dietary supplements.3 It also established that dietary supplements are meant to supplement the diet; contain 1 or more dietary ingredients, including vitamins, minerals, herbs, amino acids, or other substances; are meant to taken by mouth; and are labeled as a dietary supplement. This distinction in labeling resulted in

different rules and regulations than those for food and drugs. Dietary supplements do not have to prove efficacy before reaching consumers, whereas drugs are tested for efficacy and safety before they can be sold. Dietary supplement labels may include a health claim, which purports to reduce risk of a disease or health-related condition; a nutrient claim, which describes the relative amount of a nutrient or dietary substance in a product; and a structure or function claim, which describes how a product may affect the organ systems of the body but cannot mention any specific disease. It also must include the following disclaimer: "This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease" on the label.<sup>3</sup>

Although dietary supplements may be "natural," as noted above, they are not regulated by the FDA and can have unex-

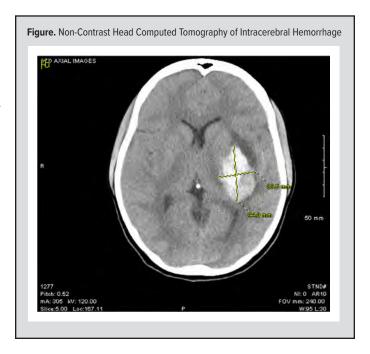
pected adverse effects and drug interactions, such as kidney toxicity,<sup>4</sup> liver toxicity,<sup>5</sup> anaphylaxis,<sup>6</sup> and drug interactions.

People turn to herbal supplements for many reasons, including sexual dysfunction. In the United States, major depression ranks second among all diseases and injuries as a cause of disability, and second-generation antidepressants are the first line of pharmacologic treatment. These include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), atypical antidepressants, and serotonin modulators. Unfortunately, many serotonergic antidepressants can interfere with different aspects of sexual functioning, including desire, arousal, and orgasm. In fact, a review of research studies showed that 40% of patients using antidepressants experienced some form of sexual dysfunction, which can negatively affect one's quality of life and lead to medication nonadherence. It also may prompt patients to try herbal supplements to improve sexual dysfunction.

#### **CASE PRESENTATION**

A 41-year-old woman with past history of depression, anxiety, substance use disorder in remission on medication-assisted treatment, and attention deficit hyperactivity disorder (ADHD) presented to urgent care with acute nausea, vomiting, flushing, and rash after ingesting a sexual enhancement supplement—BioXgenic—for the first time. Her home medications included bupropion 150 mg daily, clonidine 0.1 mg orally twice a day, as needed for anxiety, desvenlafaxine 200 mg daily, trazadone 100 mg nightly, lisdexamfetamine dimesylate 100 mg daily, and buprenorphine 8 mg daily. Within an hour of presenting to the emergency department (ED), her blood pressure was 201/108, pulse 61, respiratory rate 16, and oxygen saturation 100%. A urine drug screen was positive for amphetamines due to the lisdexaferamine dimesylate; she was not taking any illicit drugs and did not drink alcohol.

Within 2 hours of her arrival to the ED, she reported a headache and then became somnolent with a new facial droop and right-sided weakness on exam. Computed tomography (CT) showed a 3.8 cm left basal ganglia hemorrhage (see Figure), and she had a Glasgow Coma Scale score of 11 with incomprehensible speech. She was transferred to a neurological intensive care unit, where she was found to have anisocoria, disconjugate gaze with left adduction deficit, right upper and lower facial weakness, right-sided motor deficits, and a right extensor plantar reflex. Due to location of brain bleed, she was not a candidate for neurosurgical intervention and was treated supportively with mannitol, permissive hypernatremia, and antihypertensives. Upon admission, she was too obtunded for safe oral intake so feeding tube was placed, and all psychiatric medications were held initially. Throughout her 16-day hospital stay, she slowly improved and was discharged to inpatient rehabilitation with aphasia with intact comprehension, a mild right facial droop, intact cranial nerves, and right-sided hemiparesis. After many weeks of inpatient and outpatient rehabilitation, her speech was



comprehensible and motor function had improved enough for her to ascend a flight of stairs, but some subtle cognitive deficits remained.

#### **DISCUSSION**

Upon presentation, the patient's leading diagnosis included either an allergic reaction or a drug reaction due to the dietary supplement she had ingested about 2 hours prior. However, illicit drug use, reflex hypertension caused by clonidine, and alcohol withdrawal also were considered. A urine drug screen was ordered and was positive only for amphetamines caused by lisdexaferamine dimesylate, which she was taking for ADHD. A thorough social history also was taken to rule out any other illicit drug use and possible alcohol withdraw. Clonidine is known to cause reflex hypertension, but the patient's prescription history showed that it had been prescribed at a dose of 0.1mg orally twice a day as needed for anxiety 2 years earlier, and medication refill history indicated she was using less than 10 doses per month, so it is unlikely that this contributed to her hypertensive emergency. Although lisdexamfetamine can cause increased heart rate and blood pressure, she had been taking this medication for years, whereas she had just taken the herbal dietary supplement—BioXgenic—for the first time prior to admission. The emergency physician also spoke with poison control and was informed that the supplement is known to cause hypertension and tachycardia. Concerning ingredients listed on the supplement's label included American ginseng and epimedium, which is also known as "horny goat weed." Ginseng has been documented in scientific literature for causing adverse effects, including nausea, diarrhea, euphoria, insomnia, headaches, hypertension, hypotension, mastalgia, vaginal bleeding, and blood pressure abnormalities.8 Interactions also have been documented with the use of phenelzine, warfarin, clomipramine, imatinib,

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oral hypoglycemics, insulin, and caffeine, as well as about use in patients with hypertension or bleeding.<sup>9</sup> Epimedium is an herb used in traditional Chinese medicine to treat fatigue and sexual problems; known side effects include sweating or feeling hot, rapid irregular heartbeat, increased energy, and mood changes.<sup>10</sup>

Supplements may contain inconsistent amounts of active ingredients, have unknown potential side effects, or interact with prescribed medications, so they should be used with caution. A recent study identified unapproved pharmaceutical ingredients in herbal supplements from 2007 through 2016; 776 tainted dietary supplements were identified by the FDA, and 45.5% of these products were marketed for sexual enhancement.<sup>11</sup>

Our patient had a long history of refractory depression, which led to aggressive titration of her SNRI. Unfortunately, sexual side effects are often dose dependent. The sexual enhancement supplement she purchased contained herbs that likely interacted with her current medical regimen: ginseng and epimedium. These herbs may have contained monoamine oxidase inhibitor properties and precipitated a hypertensive emergency with an intracerebral hemorrhage. The antiplatelet effect of her serotonergic antidepressant also likely contributed to her hemorrhagic stroke. 12

#### CONCLUSIONS

In the United States, more than 50% of adults consume dietary supplements.11 Thus, physicians should always inquire about dietary supplement use and warn patients about risks. A systematic review of adverse effects, poisonings, and interactions of plant food supplements in 2014 found a total of 492 papers, with 81.7% described cases due to adverse effects directly associated with the botanical and 18.1% to interactions with conventional drugs. These papers identified 66 different plants used as supplements; the most sited were green tea, black cohosh, Cinnamomum zeylanicum (Ceylon cinnamon), bitter orange, Eastern purple coneflower, ginkgo/maidenhair tree, soybean, liquorice, devil's claw, St John's wort, ginseng, valerian, vitex or "chaste tree," and grape.9 The FDA relies on post-market surveillance to identify unsafe or contaminated supplements, so physicians should encourage patients to read dietary supplement labels, research the ingredients while keeping a close eye out for the botanicals mentioned above, and encourage patients to report to the FDA any adverse effects or complaints pertaining to dietary supplements. Physicians also should refer to the FDA's Center for Drug Evaluation and Research's Tainted Supplements database for known adulterated dietary supplements.13

Our patient experienced antidepressant-induced sexual dysfunction, which led her to purchase and ingest the supplement BioXgenic, precipitating a hypertensive emergency. Prescribing physicians should have candid conversations with patients about adverse effects of serotonergic antidepressants to determine if sexual effects are a concern. There is not a one-size-fits-all approach to managing antidepressant-induced sexual dysfunction, but reducing the medication dosage, switching medication, using drug holidays, and timing administration of medication to be further from the time of anticipated sexual activity may help to alleviate symptoms, prevent self-medication, and improve a patient's quality of life.

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Robert N. Golden, MD

## Mechanistic Health Disparities Research: Aligning Science With Solutions

Amy J.H. Kind, MD, PhD; Robert N. Golden, MD

ealth is not distributed equally. According to the National Institutes of Health (NIH), health disparities are experienced disproportionately by American Indians/Alaska Natives, Asian Americans, Blacks/African Americans, Hispanics/Latinos, and Native Hawaiians and other Pacific Islanders; socioeconomically disadvantaged populations; underserved rural populations; and sexual/gender minorities. Wisconsin is particularly challenged by these disparities, with worse health outcomes observed across all health disparities groups as compared to the national averages.

Therapeutics and interventions that effectively ameliorate disparities are critically needed. In the past, health disparities research focused primarily on documenting and describing the problem. As the field has matured, it increasingly aligns with action by embracing a precision-medicine approach—unlocking how social factors interact with biology to produce disease, and then designing solutions that are precisely tailored for targeted conditions, sys-

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tems, and populations. This area of "mechanistic" health disparities research illustrates the ways fundamental factors, such as race, ethnicity, and identity, interact with a complex array of geopolitical, socioeconomic, health

nature, mechanistic health disparities research is broadly inclusive. Any effective intervention in this area requires the unified action of diverse individuals toward a common goal. This is a welcome philosophy as, ultimately, the

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care, cultural, social, psychological, physiological, genetic, and cellular factors to produce disparate population health outcomes. Many of these factors are adversely influenced by systemic inequities, such as structural racism. Recognizing the urgent need to move beyond description, the NIH has endorsed this action-oriented, mechanistic health disparities research approach.

This emerging field brings together a diverse array of multidisciplinary research teams spanning cellular biology to sociology in order to better understand the role that structural processes and systems play in perpetuating disparities, as well as the biological pathways that these systems trigger to result in increased morbidity and mortality. By its

mitigation of health disparities is a responsibility we all share.

#### **Cutting-Edge Science**

Nationally, leading academic institutions are rapidly tailoring their infrastructure to align with NIH-promoted approaches to mechanistic health disparities research. Infrastructure capable of supporting this next-generation research enables the linkage of cellular and molecular mechanisms to community- and health-system-level factors. Modern, social-biological phenotyping allows for advanced characterization of the "exposome"—individual environmental, social, and biological exposures from before birth across the life course—to execute translational research that mechanistically links

these exposures to fundamental biological processes. Advanced analytic approaches capable of capturing the multiple levels, dimensions, interactions, and intersections for elucidating mechanisms of disparities from cell to community are made possible through the integration of emergent computational, statistical, "omic," and geoanalytic techniques, often applied across the life course. Through integrated, translational application of these approaches, new levels of rigor, validity, and generalizability can be attained for health disparities research.

#### **Center for Health Disparities Research**

To remain at the forefront of this revolution in health disparities research, we recently established the Center for Health Disparities Research (CHDR) at the University of Wisconsin-Madison. The center provides a next-generation, collaborative, research infrastructure and a means for delivering resources that address social-biological interactions, multilevel analytics, and mechanistic-focused system innovations. This, in turn, is expected to unlock opportunities for the development of new therapies, precision medicine approaches, and interventions capable of addressing the consequences of health disparities while also effectively targeting their complex, causal foundations.

CHDR's leadership team consists of Amy Kind, MD, PhD, director, CHDR, incoming director, Wisconsin Partnership Program, and professor, Department of Medicine, UW School of Medicine and Public Health (SMPH); Andrea Gilmore-Bykovskyi, PhD, RN, deputy director, CHDR, and assistant professor, UW School of Nursing; and Barbara Bendlin, PhD, deputy director, CHDR, and professor, Department of Medicine, SMPH. All are international leaders in mechanistic health disparities research with scientific backgrounds that span the translational research spectrum, resulting in diverse leadership that aligns with CHDR's mission, scope, and philosophy.

CHDR's mission is to catalyze research, clinical innovation, and educational activities in mechanistic-focused health disparities research; to accelerate the development of a robust, fully integrated health disparities research-and-practice community; and to bring the benefits of multilevel mechanistic

health disparities research across campus and to all corners of this state in fulfillment of the Wisconsin Idea. Housed in the SMPH, CHDR strategically complements existing cross-campus strengths in research, clinical care, and education domains, functioning as an interactive nexus to amplify the impact and reach of mechanistic health disparities research across key stakeholders that have aligned vision and foci. CHDR will provide the latest educational programming and tools to promote incorporation of a mechanistic lens for a diverse array of learners. We expect CHDR's infrastructure to become a cornerstone of health disparities research operations, attracting philanthropy, research funding, faculty, and learners in a synergistic manner that advances solutions, innovations, and cures.

#### **Research to Action**

Since the center's establishment in fall 2021, the CHDR team has already made key strides. CHDR recently was awarded a \$28.5 million NIH R01 grant to lead a 22-site national mechanisticfocused health disparities research study. This project, "The Neighborhoods Study," will establish a national consortium to assess how dosage and timing of exposure to neighborhood socioeconomic disadvantage across the life course impacts brain function, structure, neuropathology, and the risk for Alzheimer's disease. This new, national consortium spans leading academic institutions across the United States and involves some of the brightest minds in neuroscience, genetics, sociology, and clinical intervention. The goal is for this to be the first of many large interdisciplinary mechanistic health disparities NIH grants facilitated by CHDR.

Additionally, CHDR is now the home of the Neighborhood Atlas, a nationally recognized

data-democratization tool that enables anyone to perform customized mapping or download data on precise geometrics of neighborhood socioeconomic contextual disadvantage for the full United States. Such metrics provide a key step in social exposome assessment, and the Atlas platform has been heralded by the NIH as a model for open science.

The Neighborhood Atlas has deep Wisconsin roots, as it has been developed, curated, disseminated, and updated by an SMPH team led by Dr Kind. The Neighborhood Atlas' data have been accessed nearly 500,000 times, and the data are being used for research, health, and policy applications throughout the nation. For example, Atlas metrics are being applied for active mitigation of disparities in COVID-19 therapy and vaccine prioritization across a number of US states; leveraged as a resource-targeting tool across many large health systems; and used as a cornerstone for health policy decision-making in Maryland. Simultaneously, these same Atlas metrics have been utilized by thousands of researchers to link neighborhood disadvantage exposure to epigenetic expression, premature aging, and a diverse array of morbidity and mortality outcomes spanning the fields of cardiovascular disease, cancer, brain health, diabetes, pediatric mental health, addictions, and more.

This next stage in the evolution of health disparities research offers new hope for real-world solutions. It is a research area that is expanding with purpose. We welcome CHDR as a key resource to facilitate cross-disciplinary advancement and to bring together as many brilliant minds as possible, with a shared vision of eliminating health disparities. It is a unifying cause that needs us all.

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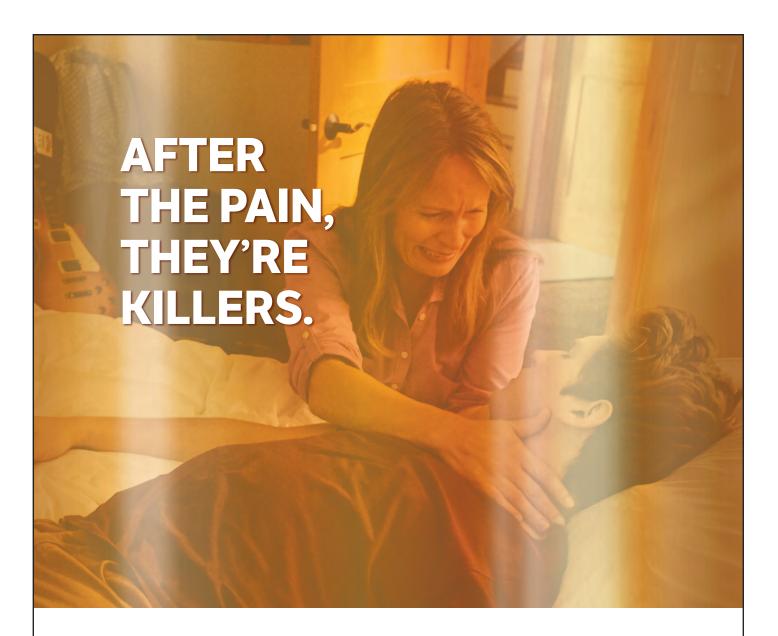




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