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# June is Men's Health Month



SPECIAL SECTION

## REFLECTIONS *on* MEN'S HEALTH

GUEST EDITOR: MARK R. PAULOS, MD

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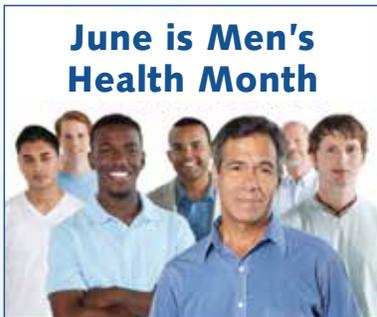
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Mark R. Paulos, MD

### Reflections on Men's Health

MARK R. PAULOS, MD  
GUEST EDITOR



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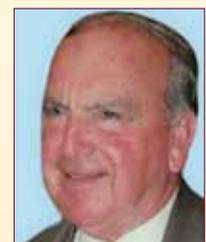
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## The Evolution of Men's Health

MARK R. PAULOS, MD

In recognition of June as national Men's Health Month, the current issue of the *Rhode Island Medical Journal* (RIMJ) focuses on this young and evolving discipline in the field of medicine. The discipline has its roots in Rhode Island at the Men's Health Center at The Miriam Hospital, the first of its kind multidisciplinary center founded by **MARTIN M. MINER, MD**, in 2008.

The term "men's health" is used interchangeably in medicine, media and advertising, which makes its definition a challenge. From a healthcare perspective, it implies urologists treating male-specific disorders like erectile dysfunction or prostate cancer in a clinic or traditional office setting. Outside of the office, the term assumes a less academic and more commercial meaning. An internet search of men's health reveals a proliferation of websites for fitness and grooming products and direct-to-consumer (DTC) platforms selling anti-aging elixirs and male-enhancement products. The line between healthcare and consumerism is becoming increasingly blurred, and whether the academic and online identities of men's health are complementary or in competition remains to be seen.

### Necessity of a gender-based approach

The striking health disparities between men and women provide a compelling argument for why a gender-based approach to healthcare for men is necessary. Life expectancy for males in the United States is 4.8 years less than that for females,<sup>1</sup> and men die at higher rates than women from 9 of the top 10 leading causes of death. In addition, men have higher lifetime risks for heart disease, cancer, diabetes and HIV/AIDS,<sup>2</sup> and are disproportionately affected by substance abuse and homelessness.<sup>3</sup>

Men's mental health is the focus of increasing attention as well, largely based on the disproportionate impact of mental health issues like suicide and substance abuse. Men commit suicide at a rate nearly four times higher than women, yet men are half as likely to use mental health services.<sup>4</sup> When they experience depression they are more likely to "act out" and engage in dangerous risk taking and alcohol and substance abuse.<sup>5</sup> Traditional screening tools for depression do not capture these symptoms, and mental health disorders in men may be significantly underdiagnosed.

Men in underserved populations are affected by unique challenges resulting from the combined effects of race,

ethnicity and gender-based discrimination.<sup>6</sup> Obstacles to socioeconomic status, safety and education drive these disparities, and a mistrust of the healthcare system perpetuates the problem. The result is a disproportionate burden of chronic disease in Black and Hispanic men. African American men are affected by violence and incarceration at alarming rates, and young African American men are 53 times more likely to be murdered than their White counterparts.<sup>7</sup>

### Action steps needed on academic, federal level

Despite the poor health outcomes that men face, academic medicine has been slow to embrace men's health as a discipline. Most institutions offering services under the umbrella of men's health do so within the department of urology and provide a narrow range of services for problems like low testosterone and erectile dysfunction. A survey of the top 50 hospitals for urology in the U.S. News and World Report rankings revealed that only 16 of the top 50 programs offered some form of a men's health center, while 49 out of 50 offered a women's health center. Of the 16 centers offering some form of men's health, only four provided primary care services like treatment for cardiovascular disease, diabetes, musculoskeletal injuries or preventive care.<sup>8</sup> Research is lacking, and there are only six journals indexed in MEDLINE dedicated to men's health as compared to 62 journals dedicated to women's health. A PubMed search of papers and abstracts from 1970 to 2018 showed that the term "men's health" has been used 1,555 times, whereas the term "women's health" has been used 14,501 times.<sup>3</sup> A coordinated public health policy to address these disparities is absent. There are currently zero federal dollars dedicated to funding men's health, and a federally funded office of men's health does not currently exist.

### Alternatives: online platforms, telemedicine

The advent of interactive websites and telemedicine has made access to health information increasingly convenient. Men now have alternatives to the traditional office setting and can access information about embarrassing male-specific issues like erectile dysfunction, Peyronie's disease and infertility from the comfort of their own homes. Studies confirm that only a small fraction of men suffering from sexual dysfunction seek help from a doctor,<sup>9</sup> and a recent survey that was part of Cleveland Clinic's MENTion It campaign

demonstrated that 40% of men preferred to talk about a sexual health problem with a physician online or by phone because they were “too embarrassed” to discuss them in person.<sup>10</sup> The widespread availability of sexual health information online has helped to normalize a discussion about a sensitive subject like erectile dysfunction, and it provides a unique opportunity to educate men about the link between erectile dysfunction and cardiovascular risk. Younger men who go online to search topics related to sexual function, fertility and contraception can be introduced to information about the importance of paternal health and the need for preconception care for the male parent. Young men drop out of the healthcare system at an alarming rate after their high school years, and keeping them engaged in a conversation about their health and wellness is a potential step in the right direction.

The internet has been a particularly successful medium for combating the mental health crisis that men are facing. Organizations like HeadsUpGuys have reached millions of men around the world and provided guidance and hope to men suffering from depression or contemplating suicide.<sup>11</sup> The National Black Men's Health Network and The Confess Project have leveraged the far reach of the internet to extend healthcare from the office into the community and promote programs that address the unmet mental health needs of minority men. As a result of this outreach, men in underserved communities are now able to start a conversation about their mental health in a comfortable and trusted environment.

However, online platforms are unregulated, and the spread of misinformation is also very real. DTC sales of testosterone, anti-aging and male-enhancement products via online platforms bypass the physician's office entirely. They run the risk of directing men away from important health screenings and preventive care. A recent study of internet traffic to six major DTC prescribing websites offering erectile dysfunction evaluation and treatment showed that the number of unique, quarterly visitors increased from 655,733 in the 4th quarter 2017 to over 11 million in the 4th quarter 2019.<sup>12</sup> Demand for this type of transactional care is eye-popping and presents a significant challenge to our healthcare system.

### Going forward

For the discipline of men's health to evolve to meet the healthcare needs of men, it will require partnerships and cooperation within medicine and beyond the four walls of the office. A coordinated plan to promote men's health must be supported by academic medicine, and leaders in the field must agree to share responsibility for this movement with no single specialty having ownership. Brick and mortar men's health centers have the potential to act as medical homes delivering basic primary care services and linking men with specialty care and research. Such centers gain

credibility from associations with medical schools and large healthcare systems. Valuable lessons can be learned about men's preferences for non-traditional modes of delivery by the success of online men's health platforms, and finding creative ways to improve access and reach men in the communities where they live and work will be essential to the success of the field.

### Contributions

The authors featured in this issue have made important contributions to the field of men's health and are working to shape its future. **MARTIN M. MINER, MD**, is Clinical Professor of Family Medicine and Urology at The Alpert Medical School of Brown University and, as noted, founder of the Men's Health Center at The Miriam Hospital. He and co-authors describe the evolution of men's health as an academic discipline and outline the need for a dedicated curriculum to train clinicians in this field. **MYLES SPAR, MD, MPH**, is a leader in the field of Integrative Men's Health and former National Medical Director for Vault Health, a successful virtual health platform delivering men's health services. Drs. Spar and Miner discuss the successful expansion of healthcare for men to online platforms and the potential for these platforms to assume a larger role in preventive care. **YUL D. EJNES, MD**, is Clinical Professor of Medicine at The Alpert Medical School of Brown University, Chair of the Board of Directors for the American Board of Internal Medicine and Chair-Emeritus of the ACP Board of Regents. He offers a unique perspective on the disintermediation of primary care providers in the age of transactional medicine. **JOHN S. OGDONICZUK, PhD**, is Professor and Director of the University of British Columbia Psychotherapy program and founder of HeadsUpGuys, an eHealth resource for men with depression. He and colleagues describe how this digital platform was developed to normalize mental health seeking behavior for men. **DAVID P. GUO, MD**, completed his training in urology at Stanford University and fellowship in Male Reproductive Medicine and Surgery at Brown University. He provides a review of the factors affecting male fertility and introduces the concept of using preconception care as an opportunity to keep younger men engaged in their own health and wellness.

Collectively, it is our hope that the above contributions inform our colleagues and raise awareness of the specific healthcare needs of men, and the evolving discipline rooted in our home state.

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#### Author

Mark R. Paulos, MD, Clinical Assistant Professor of Medicine and Urology, The Alpert Medical School of Brown University; Co-Director of The Miriam Hospital Men's Health Center, Providence, RI.

#### Correspondence

[Mark\\_paulos@brown.edu](mailto:Mark_paulos@brown.edu)

# Men's Health Centers: An Emerging Paradigm of Sexual Function and Cardiometabolic Risk Reduction

MARTIN M. MINER, MD; MARK PAULOS, MD; VINCENT HARISARAN, MD

## INTRODUCTION: WHY MEN'S HEALTH?

Gender-based medicine, specifically recognizing the differences in the health of men and women, drew significant attention in the 1990s with regard toward addressing disparities. The National Institutes of Health's (NIH) Office of Research on Women's Health was established in 1990, and in 1994 the U.S. Food and Drug Administration (FDA) created an Office of Women's Health, resulting in a dramatic increase in the quantity and quality of research devoted to examining numerous aspects of women's health, rendering women's health in the mainstream today.<sup>1</sup> While decades of research have yielded important findings about health disparities and disease burden in men, such knowledge has not resulted in the benefits expected. Men are still less likely than women to seek medical care and are nearly one-half as likely as women to pursue preventive health visits or undergo evidence-based screening tests.<sup>2</sup> Recent data indicate that 68.6% of men aged 20 years and older are overweight,<sup>3</sup> and male life expectancy trailed that of women by nearly five years in 2014 (76.4 years for men and 81.2 years for women) in the United States (U.S.) and globally.<sup>4</sup>

Men's health as a concept and discipline is in a historic and germinal state compared with women's health. Most clinicians and the public consider men's health to be a field concerned only with diseases of the prostate and sexual function. Men's health has recently become a hot topic in these specific areas with billions of dollars spent on remedies for prostate health, improved urinary flow, enhanced erections, and, by comparison, a much smaller amount directed at overall improved preventive health.<sup>5</sup> Ex-athletes tout the wonders of testosterone supplements for aging men, and the radio announces the availability of low-intensity shock-wave therapy as non-invasive therapies for ED at a cost of \$6,000–\$8,000 for a treatment cycle. Yet, outside of this publicity, the serious gender-health disparities that

continue to exist are not addressed.

Adult men aged 18 to 65 do not use or react to healthcare services in the same way as women,<sup>6</sup> and are less likely to attend preventive healthcare visits.<sup>7</sup> Men are also less likely to follow medical regimens, and are less likely to achieve control with long-term therapeutic treatments for chronic diseases, including hypertension, diabetes mellitus, and atherosclerotic heart disease.<sup>8,9</sup> Men are more likely to be

motivated to visit the doctor for diseases that specifically affect men most, such as baldness, sports injuries, or erectile dysfunction (ED). Acknowledging this disparity, The Commonwealth Fund recommended that increased efforts should be made that address the special needs of men as well as their attitudes toward healthcare.<sup>10</sup>

The presentation of a man to the clinician's office with a sexual health complaint should present an opportunity for a more complete evaluation, most notably with the complaint of erectile dysfunction. In a landmark article published in December 2005, Thompson<sup>11</sup> and others confirmed what had been long believed: that ED is a sentinel marker and risk factor for future cardiovascular events. After adjustment, incident ED occurring in the 4,300 men without ED at study entry enrolled in the Prostate Cancer Prevention Trial (PCPT) was associated with a hazard ratio of 1.25 for subsequent cardiovascular events during the nine-year study follow-up (1994–2003). For men with either incident or prevalent ED, the hazard ratio was 1.45. Thus, men with ED are at risk for developing cardiac events over the next 10 years, with ED as strong a risk factor as current smoking or premature family history of cardiac disease. Never before had the association of ED or a male sexual dysfunction been so strongly linked as a harbinger of cardiovascular clinical events in men. Therefore, in the early 2000s, we proposed the following as a means to begin to address gender-based health disparity:

- 1) Establishment of men's health centers linking medicine and urologic care through cardiometabolic health excellence;
- 2) The formation of a men's health curriculum.

While we have partially succeeded in the first goal, we have not yet completed the latter to be formally incorporated into the medical school curriculum.

## WHO IS THE MEN'S HEALTH DOCTOR: PCP VS. PCP MEN'S HEALTH SUBSPECIALIST VS. UROLOGIST?

With the advent of the Patient Protection and Affordable Care Act (commonly shortened to the Affordable Care Act, or ACA) in March 2010, millions of men ages 18 through 45 years who previously did not have access to healthcare entered the health insurance marketplace. The current

decade has also seen a mathematical challenge in graduating an adequate number of healthcare providers who practice primary and preventive care. Most primary care residency programs do not have a codified curriculum for men's health, provide limited exposure to multidisciplinary men's health with a dedicated focus on social determinants, or have no formal training at all in male healthcare needs.

A dedicated men's health curriculum is long overdue. Such a curriculum would begin with a deep understanding of the social determinants of men's health, why men do or don't seek healthcare, and most importantly, how they view and address their acute and chronic health conditions. Teaching men's health should not be solely focused on urologic or cardiovascular conditions, but should focus on the interaction between the two, and the implications for morbidity and mortality. Common conditions that are often overlooked in men's health include the impact and burden of mental health, gastrointestinal, rheumatologic, and renal diseases. More men than ever are considering complementary and alternative solutions toward addressing healthcare issues. Healthcare providers need to be adequately trained to care for men who have sex with men, transgendered patients, and complex geriatric men. The future should see fellowships based upon such curricular platforms to train men's health specialists.

While urologists are typically thought of as *men's doctors* as obstetrician-gynecologists are considered *women's doctors*, the issue remains who is to shoulder this responsibility in the decades to come, regardless of reform? Will it be a shared care approach, including clear communication between urologists and primary care clinicians, and vice-versa, or do we need to enhance this relationship or specialty? Do we need to create separate "Centers of Excellence" for Men's Health as we have done for women's health? Do we need to establish Men's Health Fellowships for non-urologists dealing more with the issues of "medical urology" yet including psychiatry, endocrinology, lipidology, cardiology and sleep medicine?

The appeal of an integrated Men's Health Center may be through initiation of a single, highly personal medical or urological problem, often sexual dysfunction, with the skillset and knowledge that this sexual dysfunction bridges two or more distinct fields of medicine: urology, cardiology, endocrinology, and psychiatry. Perhaps this is a patient complaint that normally was managed in the urological field and now is broadened to discern all the components that impact that man's quality of life, what has come to be known as cardiometabolic health.

Our clinician-patient interactions in the Miriam's Men's Health Center are not replicated in the world of volume primary care, and we are the first to acknowledge the time taken for evaluation, summation, and developing a plan of action may not be an ideal business model. Seeing 18–22 consultative patients daily and experiencing time constraints does not generate a wealth of practice income. Urologists

thus work alongside medicine clinicians and generate more procedural revenue. Indeed, our focus is often as much "lifestyle coach" as it is cardiometabolic medicine.

Which system is better: PCP or men's health specialist? This is yet to be known in terms of clinical outcomes. Intuitively, we feel that this combination of urologist-andrologist/internal medicine-family physician/psychologist-sex therapist schema is most unusual and offers a unique opportunity to enhance gender-specific care. Disparities among multicultural differences in Men's Health, as it exists in a socioeconomic means and disease prevalence among various multiethnic groups, are beyond the scope of this manuscript.

### CARDIOMETABOLIC MEN'S HEALTH AND MALE SEXUAL EVALUATION

Erectile dysfunction (ED) is defined as the inability to reach or maintain an erection sufficient for satisfactory sexual performance. The fact that ED often coexists with hypertension, hyperlipidemia, and diabetes provides support for a vasculogenic etiology of ED as impaired endothelial function.<sup>12</sup> Beyond its association with vascular risk factors, vasculogenic ED has been recently recognized as a predictor of future cardiovascular events, most strikingly in men in their fifth and sixth decades.<sup>13,14</sup> Consequently, the identification of vasculogenic ED in the younger-middle aged man has a potentially significant prognostic importance.

Cardiovascular disease (CVD) is a leading cause of death in men, with as many as one in three adult males in the U.S. having some form.<sup>15–18</sup> Half of the men who die suddenly of coronary heart disease have no previous symptoms of CVD. Between 70% and 89% of sudden cardiac events occur in men.<sup>19,20</sup> Because of the common risk factors and pathophysiologic processes, men with CVD are more likely to have ED and vice versa.<sup>21–25</sup> ED severity has been correlated with atherosclerotic coronary disease, and the presence of ED has been independently associated with CVD events.<sup>26,27</sup> Perhaps more importantly, it has been found that ED symptoms precede clinically-evident CVD by as long as two to five years, making the diagnosis of ED especially useful as a marker of probable subclinical CVD.<sup>27</sup>

ED can be categorized as organic (vasculogenic) or psychogenic or mixed. In general, primary vasculogenic ED is characterized by a gradual onset. Erectile rigidity may be weakened, duration may be shortened, or both. These changes are evident under most or all circumstances, including the morning erection, nocturnal erection, or sexually stimulated erection. The most common type of organic ED is vasculogenic ED. Situational ED, such as that occurring with a partner but not with morning erections or masturbatory behavior, is usually considered largely psychogenic in origin.<sup>27,28</sup>

The relationship between ED and cardiovascular risk has been observed with predominantly vasculogenic ED,

therefore this discussion of ED as a CVD risk factor is predicated on an initial diagnosis of vasculogenic ED.<sup>27</sup> Men with vasculogenic ED will benefit from a rigorous cardiovascular evaluation, while those with psychogenic ED may benefit from psychosexual intervention. While often ED presents as a mixture of both vasculogenic and psychogenic etiology, when one determines that the ED is predominantly vasculogenic, it is thought to be related to impaired blood inflow/outflow, which may be modified by atherosclerotic burden or other factors affecting endothelial and smooth muscle function which prevent appropriate vasodilation during sexual stimulation.<sup>28</sup> Of course, this is seen especially in comorbid disease states with increased inflammatory markers and reduced testosterone levels.<sup>29-31</sup> Many of the risk factors for vasculogenic erectile dysfunction are shared risk factors for cardiovascular disease, including age, abdominal obesity, smoking, and the metabolic syndrome.<sup>32,33</sup> Therefore, the presence of these risk factors in men with ED should give providers with clues to the possibility of otherwise silent CVD.

Development of ED has been found to have similar or greater predictive value for future cardiovascular events when compared with traditional CVD risk factors like family history of myocardial infarction, smoking, and hyperlipidemia.<sup>32</sup> Araujo et al found that while ED was a strong predictor of CVD (hazard ratio 1.42, 95 % confidence interval 1.05 to 1.90), it did not improve upon traditional Framingham risk calculations.<sup>33</sup> Other studies have suggested that ED may have greater prognostic significance in younger men. Results from the Olmstead County Study showed that ED was more predictive of coronary artery disease in men aged 40–49 years when compared to older men.<sup>14</sup> Another study found that the incidence of cardiovascular events in men less than 40 years old with ED was more than seven times higher than a reference group.<sup>34</sup> Riedner et al performed a case–controlled study of 242 men referred for elective coronary angiography.<sup>35</sup> Coronary artery disease (CAD) and ED were associated in patients younger than 60 years (ED in 68.8 % of patients with CAD vs. 46.7 % of patients without CAD,  $P = 0.009$ ) and were independent of cardiovascular risk factors, testosterone, and C-reactive protein. Severity of CAD was higher in patients younger than 60 years with ED.<sup>35</sup> In contrast, Riedner did not find an association between ED and probability of CAD in men  $\geq 60$  years. Summarily, studies have focused on ED as a particularly significant harbinger of CVD in two populations: men <60 years of age and those with diabetes.<sup>36</sup> These studies suggest that ED is an early marker of generalized CVD and supports the need for cardiovascular workup in younger men and diabetic men with vasculogenic erectile dysfunction.<sup>36</sup>

We believe that the 2019 American College of Cardiology (ACC)/American Heart Association (AHA) ASCVD risk assessment guidelines, which recommend use of a risk score calculator, are an appropriate starting point for risk stratification.<sup>37</sup> However, because of the reliance on a small

number of traditional risk factors and the strong reliance of age in the risk estimates, we propose more advanced testing for all younger men (aged 40–60) with vasculogenic ED as these patients normally do not score as high risk with the ACC/AHA risk estimator and therefore likely have significant unaccounted for CVD risk.<sup>38</sup>

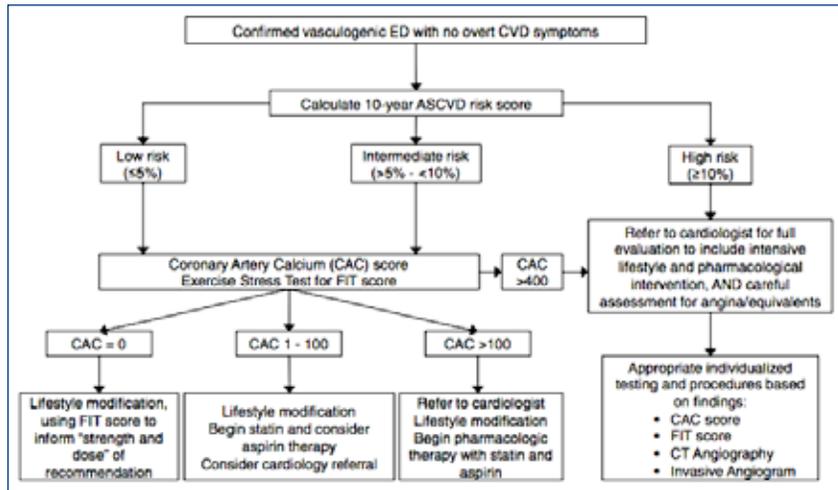
## RECOMMENDATIONS FOR EVALUATION AND MANAGEMENT OF CARDIOVASCULAR RISK IN MEN WITH ED

We recommend evaluation of fasting plasma glucose, A1c, serum creatinine (estimated glomerular filtration rate) and albumin: creatinine ratio (or urine for microalbumin) and lipids. In addition, the presence or absence of metabolic syndrome is used to further characterize cardiovascular risk.<sup>39</sup> We also recommend measurement of total testosterone levels, particularly for patients who have failed a trial of phosphodiesterase type 5 inhibitors.<sup>40</sup> Based on consensus opinion, we recommend considering testosterone repletion for men with total testosterone <10.4 nmol/L (300 ng/dL) who are symptomatic (decreased libido, decreased spontaneous erections, low energy, increased sleepiness, or reduced muscle bulk and strength).<sup>40-43</sup> We do not recommend testosterone repletion for total testosterone >12 nmol/L (>350 ng/dL).<sup>43</sup> In cases of ED where there is no clear etiology, the treating primary care physician should refer the patient to a urologist or sexual medicine specialist for more experienced evaluation with possible additional diagnostic testing (i.e., penile Doppler ultrasound; nocturnal tumescence testing). In a routine setting, this additional testing is not indicated if one does an adequate history to determine the presence of vasculogenic ED.<sup>44</sup>

For men 40 to 60 years-old with suspected vasculogenic ED and no overt CVD symptoms, we recommend initial risk stratification with the ACC/AHA 2019 10-year risk score for atherosclerotic CVD (ASCVD), which estimates the 10-year risk for myocardial infarction and stroke as well as lifetime risk up to age 59 years.<sup>56</sup> This risk calculator incorporates age, sex, total and high-density lipoprotein cholesterol, smoking, systolic blood pressure, and use of antihypertensive medications and history of diabetes.<sup>39</sup> The ACC/AHA guideline on the assessment of cardiovascular risk mentions ED with the following disclaimer: “The following variables were given consideration as risk predictors but their contribution awaits further consideration at a later time: BMI, waist circumference, lipoprotein (a), left bundle branch block, sleep apnea, ED, systemic lupus erythematosus, rheumatoid arthritis and physical activity.”<sup>37</sup>

It is important to identify men whose cardiovascular risk may not be captured in current risk scores, and this may be accomplished using the presence or absence of the metabolic syndrome.<sup>44</sup> (Figure 1) Since studies have shown that treatment of sleep apnea can lead to improved

**Figure 1.** Evaluation and management of cardiovascular risk in men with vasculogenic erectile dysfunction but no known cardiovascular disease recommended for the primary care physician and urologist. Symptomatic men are presumed to have cardiovascular disease and are therefore at high risk for cardiovascular disease events. A thorough history, physical exam (including measures of visceral adiposity), assessment of erectile dysfunction severity and duration, and evaluation of fasting plasma glucose, resting electrocardiogram, serum creatinine (estimated glomerular filtration rate) and albumin:creatinine ratio, and presence or absence of the metabolic syndrome and obstructive sleep apnea may be used to further characterize cardiovascular risk.



Based on Same R, Miner M, Blaha M, Feldman D, Billups K. Erectile dysfunction: An Early Sign of Cardiovascular Disease. *Curr Cardiovasc Risk Rep.* 2015; 9:49-57.

outcomes in both ED and CVD, we recommend evaluation for sleep apnea and other chronic sleep disorders in patients diagnosed with ED.<sup>45-48</sup>

After the initial assessment outlined above, the physician will be able to recommend a number of lifestyle changes (i.e., diet, exercise, smoking cessation, improved sleep habits) which will contribute to reduction in both cardiovascular risk and ED. Additionally, the screening may help identify specific cardiovascular risk factors which require treatment (i.e., diabetes, hypertension, hyperlipidemia, obstructive sleep apnea).<sup>49-50</sup> Men who appear to be at high risk for cardiovascular events based on suggestive symptoms (i.e., chest pain, exertional shortness of breath, decreasing exercise tolerance) or ASCVD score >10% should be referred to a cardiologist. We suggest that all other men with vasculogenic ED and no overt cardiovascular disease symptoms undergo further noninvasive evaluation using coronary artery calcium scoring as the primary diagnostic test to detect subclinical atherosclerosis for the purpose of advanced risk stratification.<sup>39</sup> Exercise stress testing with calculation of the FIT Treadmill Score may also have appropriate roles in the evaluation of men with vasculogenic ED.<sup>51</sup> Interventions to control specific cardiovascular risk factors (e.g., hypertension, diabetes, hyperlipidemia, obstructive sleep apnea, obesity) may also be appropriate. Interestingly, perhaps the future treatment of metabolic syndrome in both sexes may include the use of

a novel medicine initially developed to treat type 2 diabetes. The use of a GLP-1 receptor agonist (semaglutide SQ once weekly) has recently been approved for non-diabetic obese individuals and may have a significant impact on weight loss and reduction of poor cardiac and renal outcomes and improved longevity.<sup>52</sup> The ability of a men's health center to now treat metabolic syndrome in a pharmacologic fashion is a potential "gamechanger".

### CT CALCIUM SCORES (CAC)

Coronary artery calcium (CAC) scoring has been prospectively validated as a predictor of cardiovascular disease, although studies of its use in a population of men with ED is limited.<sup>53</sup> A study by Jackson and Padley compared results of exercise treadmill testing and CAC scoring in men aged 39 to 69 with ED and no cardiac symptoms.<sup>54</sup> The study found that 9 of 11 men who had elevated coronary artery calcium scores had subclinical, non-flow-limiting coronary artery disease that would not have been detected by exercise stress testing. More recently, in a comparison of the ability of six risk markers (CACs, CIMT, ABI, brachial flow-mediated

dilation, high-sensitivity C-reactive protein [hsCRP], and family history of coronary heart disease) to improve prediction of incident coronary heart disease/CVD in FRS intermediate-risk patients (10-year risk, >5% and <20%) enrolled in the Multi-Ethnic Study of Atherosclerosis, CAC scores provided superior improvements in risk estimation versus the other risk markers.<sup>55</sup> The Dallas Heart study demonstrated the value of CAC in risk reclassification in a younger population (Mean age 44.4 ±9 years).<sup>56</sup> It is this younger population with high lifetime risk but lower 10-year risk that has the most to gain by effective ASCVD risk reclassification.

Of all the markers studied, coronary artery calcium scoring was the most useful for estimating risk, and its sensitivity and specificity far exceeded the other tests in the new version of the Expert Consensus Statement from the Society of Cardiovascular Computed Tomography (2017).<sup>53</sup> In these expert consensus recommendations (not guidelines) to perform CAC testing, the concepts broadened include shared decision-making in asymptomatic individuals without ASCVD who are 40–75 years in the 5–20% 10-year ASCVD risk group.<sup>53</sup>

ED is a common problem in aging males and may serve as a useful clinical hook that will get them into the clinician's office. Given the emerging evidence that ED is an independent risk factor for cardiovascular disease, men who present to physician offices with ED complaints provide an opportunity for cardiovascular risk mitigation that would

otherwise go unrecognized. Indeed, a recent study published in the *Journal of Sexual Medicine* showed that screening for CVD in men presenting with ED would result in a 20% decrease in cardiovascular events (1.1 million cardiovascular events) saving \$21.3 billion over 20 years.<sup>57</sup> We suggest that an updated and modified algorithm for CVD risk assessment could play an important role in identification and treatment of CVD in younger men (ages 40 to 60 years old) with vasculogenic ED and risk mitigation.

## THE NEED FOR AND THE COMPONENTS OF A MEN'S HEALTH CURRICULUM

We have yet to format a men's health curriculum. Men's health should be categorized into four general categories: 1) conditions that are unique to men (e.g., prostate cancer, prostate disease, erectile dysfunction); 2) diseases or illnesses that are more prevalent in men compared to women (e.g., cardiovascular disease, stroke, renal disease); 3) health issues for which risk factors and adverse outcomes are different in men (e.g., obesity); and 4) health issues for which different interventions to achieve improvements in health and well-being at the individual or population level are required for men (e.g., access to care).

A men's health curriculum is desperately needed, as the curricular and educational paradigms of medical school and residency education are often lacking in adequately preparing future clinicians for caring for men across the life cycle. Males and females present in approximately equal proportions to healthcare providers from birth through age 18 years, yet, as noted previously, men significantly lag behind women in presentation for health maintenance examinations, management of chronic health conditions, and mental health services.

An ideal men's health curriculum should commence with an introduction to men and their challenge of seeking help and healthcare services and must be rooted in the deep understanding of the impact of masculinity factors on healthcare engagement and outcomes. Hegemonic masculinity is the idealized cultural standard that sets the ideal of "how to be a man" and sets the standards by which men are judged in society. As various psychosocial stressors directly and indirectly contribute to high rates of unhealthy behaviors, chronic disease diagnoses, and premature mortality among men, these factors help to explain men's self-representation and internalization of notions of masculine social norms that drive or avoid the receipt of appropriate healthcare services. Understanding poor health status and literacy in men includes considering how masculinity and gendered social determinants of health (e.g., social norms and expectations of biological males at a certain age and setting) shape men's lives and experiences through their economic and environmental factors.

Once a foundation in the social determinants of men's

health can be established, a men's health curriculum can then explore the challenges of providing preventive services to men. This represents a very complex, time-intensive, and longitudinal effort toward providing evidence-based provisions of interval care. Every effort should be made to encourage routine interval wellness visits for boys and men throughout the life cycle.

A multidisciplinary approach to men's health can be taught from an organ-system based paradigm, focusing on risk stratification, appropriate pharmacotherapy and nutrition, and exercise. Men are at increased predisposition of cardiovascular, gastrointestinal, renal, and other major categories of diseases and should receive significant attention from an epidemiological standpoint. Urologic conditions will be the nucleus of a men's health curriculum, but with a deep understanding of integration across other organ systems especially with relation to cardiovascular and endocrine disorders. These include testosterone deficiency and cardiometabolic syndrome.

Special populations of men also deserve attention in a broad-based men's health curriculum. Education should include caring for men who have sex with men, incarcerated men, men with significant mental health concerns, athletes, male executives, veterans, immigrants, and transgendered patients. Each population has unique needs, social determinants, biases, and outcomes. Teaching of a men's health curriculum for these and other populations should be comprised of primary care providers, urologists, advanced practice providers, mental health providers and social workers, medical experts across all specialty fields, and allied health professionals.

## CONCLUSION

We live in a time of great stress upon the medical system and healthcare providers. The adaptation of the patient-centered medical home model, as well as increasing scrutiny of testing and outcomes, all add to our burden of clinical management of our male patients. A Men's Health Center and concentration can allow those symptoms men see as vital to a healthy life (e.g. sexual function) and propel them into a softer landing for a greater preventative focus and risk-factor analysis. This effort requires an astute urologist who acknowledges and seeks evaluation of appropriate medical comorbidities coupled with a productive partnership with primary care clinicians, or focused within the context of a Men's Health Center established to address these needs.

We live in an age of women's health, family health, and pediatric health. It is vital that we understand the factors and determinants of improving men's health and lessening the gender gap regarding both disease morbidity and mortality. Building a Men's Health Center should be viewed as a viable business enterprise. Patients expect efficient, cost-effective and ultimately improved care. Men's health is family health.

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### Authors

Martin M. Miner, MD, Founder, The Men's Health Center, The Miriam Hospital, Providence, RI; Clinical Professor of Family Medicine and Urology, Dept. of Family Medicine and Urology, The Alpert Medical School of Brown University, Providence, RI.

Mark R. Paulos, MD, Clinical Assistant Professor of Medicine and Urology, The Alpert Medical School of Brown University; Co-Director of The Miriam Hospital Men's Health Center, Providence, RI.

Vincent Harisaran, MD, The Miriam Hospital, Providence, RI; Clinical Assistant Professor of Urology, The Alpert Medical School of Brown University, Providence, RI.

### Disclosures

Dr. Martin Miner consults for Antares and Acerus Pharmaceuticals, companies that produce testosterone products. He is regional medical director for Vault Health, a telemedicine company and staff physician for the Men's Health Center at the Miriam Hospital.

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### Correspondence

[Martin\\_Miner@Brown.edu](mailto:Martin_Miner@Brown.edu)

## ED & Cardiometabolic Risk Stratification: Can This Be Done on an Asynchronous Platform?

MYLES SPAR, MD, MPH; MARTIN M. MINER, MD

### INTRODUCTION

Prior to and during the COVID-19 pandemic, a growing number of patients are utilizing direct-to-consumer (DTC) Internet-based prescription and pharmacy platforms that offer asynchronous digital consultation for the diagnosis and treatment of erectile dysfunction (ED). This process is open to scrutiny in terms of quality of care, as these visits do not incorporate an evaluation of risk for comorbid disease states associated with ED.

It is noteworthy that ED is highly prevalent and increasingly recognized in younger men.<sup>1</sup> It is also undertreated, with <25% of patients with sexual dysfunction seeking care, in contrast to 56% of couples in a study of infertility seeking professional help.<sup>2</sup> Perhaps this may be related to the stigma associated with ED which is not present with infertility. Thus, there is a need for more discrete and convenient options for therapy, especially for younger men who are more reticent to seek out the care they need. However, easily accessible treatments through many such asynchronous digital consultations miss the opportunity to offer greater health benefits to such men seeking such treatment.

ED in younger men may be associated with early, preventable, yet undiagnosed medical comorbidities including hypertension, hyperlipidemia, diabetes or metabolic syndrome, psychological disorders, medication-induced sexual dysfunction, hypogonadism and sleep disorders. Specifically, regarding the possible missed opportunity to identify cardiovascular disease risk factors among such men, one of the co-authors wrote an editorial for the Mayo Proceedings upon publication of the seminal Inman Olmsted County Study involving 1,402 men. It found that ED in young men was a statistically significant predictor of future cardiovascular (CV) events compared to men without ED.<sup>3</sup> Miner wrote, "The importance of this study cannot be overstated. Although ED had little relationship to the impact on the development of incident cardiac events in men 70 years and older, it was associated with a nearly 50-fold increase in the 10-year incidence in men 49 years and younger. This raises the possibility of a "window of curability" in which progression of cardiac disease might be slowed or halted by medical intervention. Younger men with ED could provide ideal populations for future studies of CV risk prevention."<sup>4</sup>

Men with ED delay or often bypass a visit to a physician or clinician for a variety of reasons, real or imagined. Some

have expressed concern that a physician might dismiss their complaints or fail to offer medical therapy, while others find it difficult to discuss sexual health issues due to privacy concerns or feelings of embarrassment associated with sexual dysfunctions.<sup>5</sup> Thus, the utilization of more anonymous asynchronous care is an appealing way to get help for sexual function issues. Access to care also remains a major deterrent to in-person care, with potential access to the urologic specialty a challenge, with an anticipated 50% manpower shortage of urologists by 2025.<sup>6</sup> Is the experience of DTC sites to become the norm for men seeking ED therapies?

Even prior to the COVID-19 pandemic, a study by Wackerbarth examining marketing analytics noted an increase in the number of quarterly visitors to six popular DTC websites for ED between Q4 2017 and Q4 2019.<sup>7</sup> Then the pandemic catapulted telemedicine to the forefront of healthcare delivery. In 2021, a single academic center study observed an increase in telemedicine visits for primary sexual concerns (including ED, hypogonadism and infertility). Sexual medicine visits made up a larger overall share of their practice, with these visits involving younger patients than outpatients seen the year prior to the pandemic.<sup>8</sup> The paradigm shift of telemedicine appears semi-permanent in the disciplines of Men's Health and sexual medicine. Therefore, we must safely proceed with telemedicine. The key question in our minds becomes, "How do we ensure quality of care of these visits?" We are improving access via telemedicine. Now we must not miss these younger men presenting with sexual dysfunction who are at risk for significant morbidity and perhaps mortality. How are these men with ED and increased CVD risk fully identified?

### ED AS THE CANARY IN THE COAL MINE

While ease of access to treatment through telemedicine for ED and other sexual conditions is beneficial in terms of improving access to needed care among younger men, there is legitimate concern that asynchronous platforms selling PDE-5 inhibitors in this manner may miss opportunities for needed screening for comorbid conditions that are especially prevalent in men with ED at a younger age.<sup>9</sup> In fact, such care *may* operate in conflict with the American Urological Association (AUA) guidelines on ED which support a focal physical examination.<sup>10</sup> We concur that cost is always a

concern, yet the fear of missing a vital comorbidity or opportunity to improve preventative care remains a critical issue. As clinical leaders for Vault Health, an asynchronous health-care company initially founded to support men's health, we have been tasked with this challenge to offer standard-of-care medicine in men's health and preventative medicine in the sphere of cardiometabolic health for men and women, while meeting consumer needs, expectations, convenience and addressing the cause of the dysfunctions.

A recent Pro/Con "Fertile Battles" in a Fertility and Sterility discussion on "Online" and "at-home" versus traditional models of health care: *enhancing access or impeding optimal therapeutics?* highlights some of these issues in a most provocative fashion.<sup>11</sup> Dr. Alexis Melnick of Weil Cornell Medicine reports, "ED has been shown across several studies to be a proxy of overall health and a sentinel marker for CVD, diabetes mellitus, and metabolic syndrome, particularly in men under 40 years-old – the demographic most likely to use DTC services."<sup>11</sup>

Dr. Melnick goes on to point out that a "direct-to-consumer approach to sexual and reproductive health allows patients to circumvent their general medical care." She notes that a 2019 report from Accenture found that only 55% of generation Z patients have a primary care physician, in contrast to 84% for prior generations.<sup>12</sup> "The belief is that while online health platforms clearly state they are not a substitute for a primary care physician, by allowing for a quick fix they discourage a visit to the doctor in which a discussion of the chief complaint will be followed by a thorough health history, a physical examination, and a conversation about preventative care. It is often a problem-focused visit that leads to the establishment of a long-term doctor-patient relationship. The asynchronous approach may therefore cause more harm than good, both within the domains it is aiming to treat and to the overall health of its consumers."<sup>11</sup>

While such concerns are well-founded, the truth is that PCPs have minimal availability or time to address the sexual dysfunction and fertility concerns of their patients. They are overburdened with the management of chronic disease and mental health disorders exacerbated by the pandemic. The increasing number of PCPs retiring or resigning, and the shortage of primary care providers, is well documented. Between this and the demand for more anonymous and accessible care, there is a role for more expeditious treatment for common sexual conditions such as ED without the need to include an in-person visit with a primary care provider.

However, currently the solution being utilized through asynchronous care involves PDE-5 meds being prescribed with little knowledge that ED is a potential marker of CVD. Patients are not advised how best to utilize the medications, let alone receive cardiometabolic evaluations for their possible sub-clinical coronary disease. There is a way to offer both – ease of access to needed treatments along with appropriate evaluation for potential increased risk of dangerous CVD events.

## EXAMPLES OF CASE STUDIES

Some examples of typical patient use cases may help to exemplify the type of patient with ED who has an intermediate risk of a future cardiac event, the assessment of which may be missed if he goes straight to an online asynchronous care provider of ED medications without any further evaluation of his risks.

### Case 1

Robert is a 46-year-old African American man with mildly high cholesterol of 237 mg/dL (LDL of 152 and HDL of 38). His last blood pressure check revealed a value of 140/94 mm Hg. He was told to monitor it and follow up with a primary care provider, but he never did. Without treatment for elevated cholesterol or hypertension, his 10-year atherosclerotic cardiovascular disease (ASCVD) risk of a cardiac event is moderate at 5.8%. With blood pressure treatment, his risk falls to 4.3%. With blood pressure and statin therapy, Robert's risk would be reduced farther to 3.2%. The opportunity for such treatment is lost if these issues aren't addressed during his quest for ED treatment. The 10-year risk of ASCVD is estimated using the ACC/AHA 2019 10-year risk score for atherosclerotic CVD (ASCVD) Risk Estimator Plus algorithm available online.<sup>13</sup>

### Case 2

Max is a 44-year-old Caucasian American man with normal blood pressure of 128/74 but with a BMI of 29. He doesn't know his cholesterol. According to the Framingham risk calculator, his 10-year risk for a cardiac event is 7.3%. With most current asynchronous approaches to PDE-5i treatment, this elevated risk would go unaddressed.

### Case 3

Sam is a 48-year-old Asian American man with blood pressure of 135/82 mm HG and undiagnosed metabolic syndrome because he has not had a physical exam in over three years. When last checked his total cholesterol was 228 mg/dL (HDL of 34). Even though he has never smoked, his risk by the ACC ASCVD Risk Estimator Plus is 5.8%; however, the risk estimator does not take into account his metabolic syndrome, which confers a two- to threefold increase in risk of cardiovascular disease.<sup>14</sup>

## FUTURE DIRECTIONS

What if we could modify the present model to include the access and convenience offered by the DTC virtual care sites but broaden screening to encompass the cause of the ED and address the obesity and metabolic syndrome that often give rise to the sexual dysfunction? How might this be achieved?

We believe that if three basic guidelines are followed, then the pathology associated with ED can be discovered even when using telehealth approaches. We have sought to include these evaluations in men presenting for ED and/or testosterone deficiency at Vault Health.

## Evaluations

The evaluations include:

- A waist circumference measured at the level of the umbilicus (if the WC is >40 inches the likelihood of metabolic syndrome is significant)
- BP measurement done by a brachial cuff sent to the patient (Target BP should generally be <130/80 mm Hg)
- Adults who are 40–75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year ASCVD risk estimation and have a clinician-patient risk discussion before starting on pharmacological therapy. Such a discussion would include the consideration of referral for indicated treatment such as antihypertensive therapy or hyperlipidemia treatment with a statin. In addition, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals and foster discussions of lifestyle recommendations to attenuate risk.<sup>15</sup>

## CONCLUSION

The evaluation and treatment of ED should come under the cardiometabolic evaluation of ASCVD risk prevention given the associated increased risk of cardiovascular disease among men with ED. The asynchronous DTC format as presently constructed on many platforms may miss vital comorbidities in men presently targeted, especially those less than 50 years of age. They are missed not because of the lack of examination, but due to the lack of awareness of a need for a cardiometabolic platform and assessment of risk. If answers to the above three tenets suggest a higher need of personalized evaluation, then this should be done in conjunction with cardiometabolic risk stratification.

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## Authors

- Myles Spar, MD, MPH, Performance Medicine, New York City; Assistant Professor of Integrative Medicine, Andrew Weil Center for Integrative Medicine, University of Arizona School of Medicine.
- Martin M. Miner, MD, Founder, Men's Health Center, The Miriam Hospital, Providence, RI; Clinical Professor of Family Medicine and Urology, Dept. of Family Medicine and Urology, The Warren Alpert Medical School of Brown University, Providence, RI.

## Disclosures

Martin M. Miner, MD, holds a medical leadership position in Vault Health, an asynchronous healthcare company initially founded to support men's health. Myles Spar, MD, is former medical director of Vault.

## Correspondence

[Martin\\_Miner@Brown.edu](mailto:Martin_Miner@Brown.edu)

## Perspective: The Paradox of Men's Health

YUL D. EJNES, MD

Men's health is a booming business. Global sales of testosterone replacement therapy (TRT) were estimated at \$1.6 billion in 2018.<sup>1</sup> The figures for erectile dysfunction (ED) drugs were significantly higher, at approximately \$4.8 billion in sales worldwide in 2017.<sup>2</sup> By comparison, global sales of acetaminophen were estimated at \$9.4 billion in 2021.<sup>3</sup> It even appears that sales were helped by COVID-19; there was a 67% increase in PDE-5 inhibitor prescriptions in the United States between February 2020 and December 2020.<sup>4</sup>

A significant portion of these transactions occurs outside the traditional relationship between a patient and a primary care physician. Some of the care is delivered in other conventional settings, such as subspecialty offices or academic men's health centers, but not always with the involvement of the primary care physician. Online providers comprise a growing source of TRT and ED treatment.<sup>5</sup> Even when care is delivered in the primary care office, it is often driven by marketing beyond the office.

One would expect a primary care physician in practice for over 30 years to be concerned and strongly object to what is happening in men's health. However, while it worries me, I also see it as an opportunity to reflect on it within the bigger context of changes in how we deliver care, how people access medical information, and the evolving preferences of American society.

Disintermediation, medicalization, consumerization, and democratization of technology and knowledge – what some refer to as the “participatory web”<sup>6</sup> – have changed the dynamic between patients and physicians.

Defined as “cutting out the middleperson,” disintermediation challenges the physician's historic role in filtering and distilling knowledge about diseases, diagnostics, and treatments for patients. Before the Internet, there was direct-to-consumer (DTC) advertising, perhaps the first salvo to displace physicians from their role as “the” source of information for patients.<sup>7</sup>

With the explosion of DTC advertising, relatively minor common conditions became major threats to the health of the population. In some instances, this process of medicalization introduced catchy names – “ED” and “Low-T,” among them.<sup>8</sup> A lost erection following a double work shift, a few beers, and the distraction of a crying baby in the next room became a medical problem in need of a drug. Decreases in hormone production related to normal aging were reframed

as abnormalities that needed to be detected and corrected.

The business model didn't stop at creating a product and a demand for that product. New ways of delivering the treatment or test were developed, aided by the widening availability of online access. While most of us became telemedicine users recently because of the pandemic, industry was years ahead of the profession in utilizing technology to connect willing patients with willing providers.

Coinciding with these market forces, healthcare delivery became increasingly transactional and less relational.<sup>9</sup> Preceded by the spread of urgent care centers in the 1970s,<sup>10</sup> the emergence of retail clinics brought the disintermediation and fragmentation to new physical locations, meeting the needs of patients who did not have physicians or patients who had physicians but could not get in to see them.

Some might attribute the growth of retail clinics (some of which promote themselves as “men's health” centers) and online options to the difficulty of getting an appointment with one's regular doctor, but it's more than that. It also meets a need created by everchanging preferences. A growing number of people favor the convenience (and cost, in some cases) of transactional care over the whole patient orientation and longitudinal features of relational care. Moreover, in settings where traditional relationships with a primary care physician exist, patients may self-refer to other specialists, sometimes without the knowledge of the primary.

Many in primary care believe that if we expand availability, increase access options, and market ourselves better, this will all go away. As helpful as that may be, it may not go far enough. Ask yourself why you don't have a personal banker or don't go to the local bookstore as often as you used to and use an ATM or shop online at Amazon instead.

Keeping all of the above in mind, the question of whether men's health care outside the traditional model is a good thing or a bad thing has to be asked with qualifiers: for whom – the patient, physicians, others – and through which lens – a business lens or a patient care lens?

Online, specialty-based, and non-traditional sources of men's health care offer some advantages. For men who don't have a primary care physician, they offer access. Even for men who have a medical home, the alternatives may be more convenient, less expensive, and, for those who are embarrassed by their problem, more comfortable. When science conflicts with consumerism – for example, a man

for whom hormone replacement is not indicated based on a proper medical evaluation but still is convinced that he has “Low-T” – it serves as a path to getting what one thinks they need based on marketing or their own research.<sup>11</sup> This would seem to be all good from the consumer perspective.

The primary care viewpoint is less straightforward. Fragmentation of care is anathema to the core principles of primary care.<sup>12</sup> However, even though we complain about fragmentation, we've played a role in it as well, with the division of inpatient and outpatient care and gaps in after-hours access for our patients. Ironically, while fragmentation often raises barriers to patients' getting care, in the case of men's health, it may lower them.

Fragmentation has implications at the macro level on cost and resource utilization, and at the individual patient level, it introduces risk. Information sharing that would help avoid redundant testing or drug interactions usually doesn't occur when a patient seeks care from an online provider or outside clinic. The treating physician or provider does not have access to the patient's full medical record and must rely on information provided by the patient to identify features that would affect the diagnosis or choice of treatment.

There are potential harms when receiving care outside the practice, especially from a source that is separated from the usual referral network or community. Did the prescriber get a complete history to ensure that there were no alternate diagnoses or treatments or contraindications to specific drugs? Were there missed diagnoses or misdiagnoses?

For instance, if the erectile dysfunction is a sign of marital discord, undiagnosed sleep apnea, or vascular disease, will the patient get appropriate counseling, workup, and referral by the dot.com provider, or a prescription for a PDE-5 inhibitor regardless? If a patient is getting androgen therapy, is the prescriber monitoring for adverse effects with regular follow-up and appropriate lab monitoring?

Additionally, as physicians are held more accountable for quality and cost of care, treatment received outside of the practice poses new challenges. Not only are we ethically responsible for keeping patients healthy and safe, but also we're on the financial hook for what they do, much of which we can't control.

There are bureaucratic and administrative hassles that come with the outsourcing of men's health care. Patients who need refills and can't access their subspecialist or online provider may approach the primary care physician, who lacks access to the outside record to inform the refill, or even worse, the prior authorization process that might be required for some of the drugs. When there are adverse reactions or things do not go smoothly, guess who often ends up getting the call?

Are biases and conflicts of interest at play? Two old sayings come to mind: Maslow's – “If the only tool you have is a hammer, you tend to see every problem as a nail,” and the uncredited – “When you go to Midas, you get a muffler.”

How many men who go to outside providers or a website for an ED medication or TRT walk away with a treatment, compared to those who are treated by their primary care physician or referred to an academic center of excellence? Does the heavy marketing of TRT contribute to overtesting, overdiagnosis, and overtreatment? A 2017 review suggested that it does.<sup>11</sup>

What are the financial relationships between the provider, lab, and pharmacy in the outside practices? A 2015 review of testosterone replacement websites reported that a small minority disclosed financial conflicts and only 27% described side effects, while 95% promoted the benefits of treatment.<sup>13</sup>

That is not to say that physicians in traditional practice settings are free of dualities, but there's a difference between doing something to help patients that might also be profitable and doing something that is profitable that might also help patients.

We should also ask if all of this exacerbates health inequities, especially given the reliance on technology that may not be accessible to all and the “cash or credit” nature of many of the providers of men's health care.

The explosion of options for treatment of ED and testosterone deficiency are symptoms of a broader dysfunction in the healthcare system. Like it or not, some of our patients are “voting with their feet,” or in the case of online care, with their fingers. Rather than fight the inevitable, as primary care physicians we must find ways to respect our patients' preferences while minimizing the dangers of their seeking care outside our offices. It is the patient-centered thing to do.

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#### Author

Yul D. Ejnes, MD, MACP, Clinical Associate Professor of Medicine, The Alpert Medical School of Brown University; Chair, Board of Directors, American Board of Internal Medicine; Chair-Emeritus, ACP Board of Regents.

#### Correspondence

Yul\_Ejnes@brown.edu

# HeadsUpGuys: An E-Mental Health Resource for Men with Depression

JOHN S. OGRODNICZUK, PhD; JOSHUA BEHARRY, BSc; JOHN L. OLIFFE, PhD

## INTRODUCTION

Often referred to as a “silent crisis”, the persistently high rate of male suicide – one of the leading causes of death for men under the age of 50 – is beginning to gain much-needed attention.<sup>1</sup> Yet, despite this, there remains uncertainty about how suicide among men should be tackled. One of the strongest risk factors for suicide is depression,<sup>2</sup> positioning it as a likely upstream target for male suicide-prevention strategies. However, evidence points to men's reluctance to seek professional help for mental-health concerns, including depression.<sup>3</sup>

Psychological help-seeking has long been understood as transgressing prevailing masculine ideals, including strength, self-reliance, and stoicism.<sup>3,4</sup> Concerns about stigma associated with being known to need mental health care services also stand as a significant barrier to ‘in person’ help-seeking for men who experience depression.<sup>5</sup> Considering the profound social and economic burden of untreated depression in men and globally high male suicide rates, there is an urgent need to develop resources tailored more specifically to men, and responsive to their needs, as a means to better engage them in their own mental health and with professional services when needed.<sup>6-8</sup>

Rapid growth in the area of eHealth represents a new frontier for delivering tailored interventions to men.<sup>9,10</sup> Research has reported that young men in particular have a strong preference for web-based health information and interventions.<sup>11,12</sup> Various eHealth programs tailored to men have been developed to address prostate cancer, smoking cessation, prenatal health education, weight loss, sexual health, fathering, and health behaviours.<sup>13-19</sup> However, there has been little development of eHealth programs specifically oriented to men with depression, despite eHealth interventions for depression showing promise.<sup>20-23</sup> Attending to this gap, Cheng and colleagues advocate for further development of targeted eHealth initiatives proactively aimed at men to advance their mental health management and engagement with health services.<sup>24,25</sup>

## HEADSUPGUYS: A MEN'S DEPRESSION E-MENTAL HEALTH RESOURCE

Building on the promise of eHealth resources for providing men anonymity in accessing information about depression, a team of researchers, clinicians, and mental health

advocates developed the HeadsUpGuys website (headsupguys.org).<sup>26</sup> Following a comprehensive development process that involved environmental scans, surveys, focus groups, and individual interviews of men with lived experience of depression and suicidality, this free online resource was launched in June 2015, offering men information, practical tips, and guidance for managing and recovering from depression. The resource provides a male-friendly medium through which to start the help-seeking process. It was designed to appeal to men's desire for independence, autonomy, and inclination for self-sufficiency, while also building in messaging to norm and affirm men's connections to peer and/or professional help. By building a ladder approach (i.e., moving from self-sufficiency to engaging with others for help) that normalizes help-seeking, HeadsUpGuys worked to bridge men's tendency to self-manage their mental health<sup>27</sup> with augmenting and/or directing to more formal care resources. The language used on the site is purposefully commonplace, rather than technical/medically-oriented, in order to make the material on the site accessible and digestible to a wide range of visitors, and positions effective self-management and help-seeking as manly strengths and normative values.

## FEATURES OF HEADSUPGUYS

The HeadsUpGuys website is organized into four main sections: 1) Depression in Men; 2) Take Action; 3) Articles; and 4) For Friends and Family. The ‘Depression in Men’ section contains information about depression and suicide, including potential risk factors and triggers, as well as common misconceptions about depression among men (e.g., depression is a sign of personal weakness). It also includes a self-check screening tool for depression, with directives for action when the user is provided with the screening score results. The HeadsUpGuys Self Check (**Box 1**) is a web-based interactive version of the Patient Health Questionnaire-9 (PHQ-9),<sup>28</sup> a validated self-report measure of depressive symptomatology representing the nine DSM-5 criteria for major depressive disorder.<sup>29</sup> The PHQ-9 has been used extensively across diverse research and clinical contexts. Another important feature of the ‘Depression in Men’ section is the HeadsUpGuys Stress Test, a proprietary tool developed specifically for the website (**Box 2**). The purpose of the Stress Test is to get visitors to reflect on diverse aspects

**Box 1. HeadsUpGuys Self Check**

Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Little interest or pleasure in doing things	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Trouble falling or staying asleep, or sleeping too much	0	1	2	3
Feeling tired or having little energy	0	1	2	3
Poor appetite or overeating	0	1	2	3
Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

**Box 2. HeadsUpGuys Stress Test**

List of stressors included in the Stress Test:

Personal illness or injury	Difficulties at work
Illness or injury of close family member	Difficulties at school
Loss of social status	Separation or divorce
Difficulties with alcohol, tobacco, cannabis or other substance use	Issues with sexual performance
Retirement	Death of a pet
Loneliness	Death of a spouse
Lack of purpose or meaning in life	Death of a loved one (family member, close friend)
Loss of employment	Being bullied or cyberbullied
Financial strain	Relationship problems with spouse/romantic partner
Move to a new neighbourhood	Birth of a child/adoption of a new child
	Other

**Stress Test item ratings:**

Over what period of has this stressor been affecting you? [duration]  
 Week    Month    Several Months    Year    Multiple Years

How intense is the stress caused by this issue? [intensity]  
 Minimally stressful    1    2    3    4    5    Extremely stressful

How well are you able to manage this stress? [manageability]  
 Not managing at all    1    2    3    4    5    Managing very well

of their lives that may be contributing to their depression or may be impacted by their depression. The Stress Test covers 20 different stressors for which users rate the intensity of the stressor, duration of the stressor, and perceived capacity to manage the stressor. Directives for action are provided to users along with their Stress Test scores.

The 'Take Action' section of the site provides visitors with practical tips for self-management, focusing on the topics of sleep, stress management, social life, physical activity, food, and sex and relationships. Also included is clear messaging about engaging the help of others to "build your team" that can support one's recovery from depression. To help guide men's engagement with support resources, the 'Take Action' section includes advice on how to reach out to others, including friends, family, and health professionals; information about health and crisis lines that men can reach out to for help; who to contact if a crisis (i.e., heightened suicide risk) arises; and information about professional services, including psychotherapy, medications, and inpatient services. A recent addition to the 'Take Action' section is the HeadsUpGuys Therapist Directory, which includes listings to therapists in the United States, Canada, the United Kingdom, Australia, and Ireland, and provides a mechanism for visitors to the site to connect with professional support.

The 'Articles' section, as the names implies, is where visitors to the site can find articles on a wide variety of topics related to depression and suicide. The articles are brief, informative, often directive, and as much as possible, attempt to leave the reader with actionable 'next steps'. Examples of such articles are: "How to reframe negative thoughts", "Managing depression with the help of meditation", and "How journaling can help combat depression". In addition to such 'tip' articles, the section also includes a large number of real story blogs and videos from men who share their journeys of struggling with and recovering from depression. The real story blogs and videos also are geared toward providing the reader/viewer with practical guidance around strategies for recovering from depression and living well. Also included in the 'Articles' section is a repository of campaign articles, pieces that focus on topics around which HeadsUpGuys' three yearly campaigns are shaped.

The final section of the site, 'For Friends and Family', speaks to those who are providing support to a man who is dealing with depression. Recognizing that these supporters play a crucial role in a man's recovery from depression, the section provides guidance around how to a) have an initial conversation to share one's concerns, b) provide ongoing support, c) manage suicide risk, and d) take care of oneself while in a supporting role.

HeadsUpGuys also makes use of various social media platforms (Facebook, Twitter, Instagram, and LinkedIn), as well as hosting a YouTube channel, to encourage user engagement.

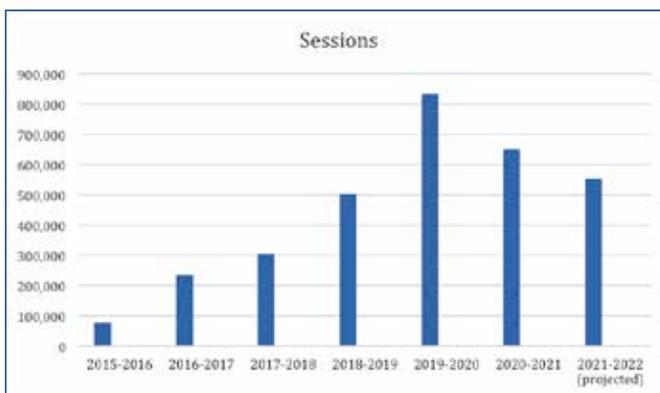
## USER ENGAGEMENT

Since launching in June 2015, HeadsUpGuys has had a total of 2,629,988 users (as of March 16, 2022), amounting to 3,079,576 sessions (i.e., website visits) and 5,210,800 pageviews (Figure 1). Figure 2 illustrates the change in number of sessions since launch, revealing a progressive increase in site traffic; however, the clear increasing trajectory was interrupted by the COVID-19 pandemic. Organic traffic accounts for the highest proportion (49.95%;  $n = 1,538,326$ ) of all website sessions. Users of the HeadsUpGuys website come from many places across the world, but three countries (United States, United Kingdom, Canada) account for over two-thirds (69.20%;  $n = 2,131,186$  visitors) of the website traffic. The United States alone provides just over a quarter (27.22%;  $n = 838,383$  visitors) of traffic to the site.

Figure 1. HeadsUpGuys overview presented in Google Analytics



Figure 2. Sessions by year



The top pages by page views are listed in Table 1. The Self Check page receives the most page views (17.90% of all page views;  $n = 932,929$ ). The second most viewed page (14.80%;  $n = 770,982$ ) is the home page. Among the top 10 pages, three are articles (Five Steps to Overcoming Suicidal Thoughts; Marijuana and Depression; I Never Wanted to Die, I Only Wanted to End My Pain). Table 2 presents the top 10 queries from Google searches (November 20, 2020–March 16, 2022; the longest period of time that Google makes search data available) that brings users to the website. Three of the top 10 queries relate to suicidality. Among these, the query “my boyfriend is suicidal” had the highest search position (3.82) and the highest click through rate (29.41%).

A total of 397,566 Self Checks have been completed. Currently, the Self Check receives an average of 162 submissions per day. Table 3 presents the distribution of Self Check scores according to the PHQ-9 scoring instructions developed by Kroenke and colleagues,<sup>28</sup> revealing that 78.7% ( $n = 312,772$ ) of Self Check completions scored above the threshold for moderate depression. For item 9 (the suicidality item), 58.0% of Self Check completers ( $n = 230,458$ ) scored above 0, indicating at least some suicidal ideation, with 17.7% ( $n = 70,338$ ) indicating suicidal ideation nearly every day.

The Stress Test, a feature added in February 2019, was completed 71,597 times. Since the launch of the Stress Test, it has received an average of 67 submissions per day. Figure 3 reports the five most frequently endorsed stressors by visitors who completed the Stress Test, revealing that lack of purpose or meaning in life and loneliness as the two stressors that were endorsed by more than half the Stress Test completers.

## CONCLUSION

Considering men's low uptake of in-person mental health services and the increased risk of suicide among men with untreated depression, it is imperative to establish alternate avenues of engagement, especially for those men who might be isolated from other sources of support in their daily lives.<sup>20</sup> Despite the growth of eHealth programs to serve men, there has been minimal focus on developing eHealth programs specifically for men with depression. HeadsUpGuys was developed to help fill this gap.

A review of HeadsUpGuys' engagement metrics reveals a high and rising volume of users and global reach. Organic search traffic accounted for half of all website sessions. The most obvious benefit of organic search traffic is a cost advantage, in that there are no direct acquisition costs for these visitors. The high organic search traffic also testifies to the growing credibility of HeadsUpGuys as a reliable mental health resource.

With regard to the Self Check, besides providing users with a score and prompts for action, it was also used as an

**Table 1.** Top 10 pages by pageviews

	Page	Pageviews <sup>a</sup>	Unique Pageviews <sup>b</sup>	Avg. Time on Page <sup>c</sup>	Entrances <sup>d</sup>	Bounce Rate <sup>e</sup>	Exit % <sup>f</sup>
1.	Self Check	932,929	809,792	0:02:49	590,219	68.10%	62.19%
2.	Homepage	770,982	641,194	0:01:11	619,543	48.79%	50.74%
3.	Five Steps to Overcoming Suicidal Thoughts	337,324	313,830	0:03:16	300,048	84.86%	83.99%
4.	Depression in Men: Symptoms	307,830	274,850	0:02:06	142,374	73.28%	55.49%
5.	Marijuana and Depression	170,779	162,586	0:05:14	160,888	89.47%	92.21%
6.	Stress Test	161,278	137,680	0:04:16	17,396	74.97%	51.93%
7.	Depression in Men	155,052	128,019	0:01:10	62,102	49.36%	36.07%
8.	Practical Tips	148,372	107,195	0:00:26	12,141	55.81%	17.91%
9.	22 Male Athletes Speaking Out About Depression	129,134	122,249	0:04:51	121,511	89.54%	90.59%
10.	"I never wanted to die, I only wanted to end my pain."	127,901	118,272	0:08:21	117,024	85.20%	90.44%

a Pageviews: Number of times a page from the website is loaded (or reloaded) in a user's browser (one user visiting a page multiple times, will result in multiple pageviews).

b Unique pageviews: Number of pageviews by unique users to the site (one user visiting the same page multiple times, will result in one unique pageview).

c Avg. Time on Page: The average amount of time a session lasts on a page, before the user switches to another page.

d Entrances: Number of times a user's session begins on a page.

e Bounce rate: The percentage of single-page sessions a page received (the percentage of visits to the site, where a user leaves from the same page they entered on, without visiting another page, or triggering an event such as a form submission).

f Exit %: The percentage of users who left the website from a page (the last page visited by a user, before they leave the website).

**Table 2.** Google search traffic: Top queries ranked by clicks

Query	Impressions <sup>a</sup>	Clicks <sup>b</sup>	Click through rate <sup>c</sup>	Position <sup>d</sup>
heads up guys	9695	71.15%	1.09	9695
heads up guys	8958	71.14%	1.09	8958
how to stop suicidal thoughts	51398	4.77%	9.18	51398
my boyfriend is suicidal	4985	29.41%	3.82	4985
how to overcome suicidal thoughts	7542	12.60%	6.71	7542
how to improve social life	3966	22.87%	1.54	3966
how to have a social life	4250	20.92%	1.09	4250
how to improve your social life	3598	24.54%	1.65	3598
brryan jackson	13934	6.18%	4.93	13934
social life	158713	0.52%	9.52	158713

a Impressions: Number of times any URL from the site appears in Google Search results, viewed by a user (not including from paid ads).

b Clicks: Number of clicks on a URL from the site, appearing on Google Search results page (not including from paid ads).

c Click through rate: The proportion of clicks received per impressions.

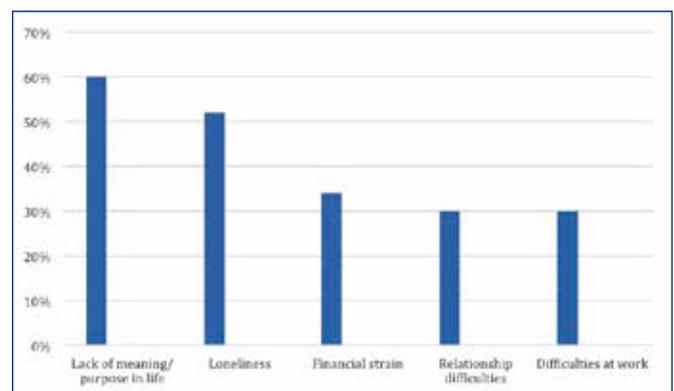
d Position: The average ranking of the website's URLs for the search terms (with 1 being the first website listed at the top search results).

**Table 3.** Distribution of Self Check (PHQ-9) scores\* (n = 397,566)

Self Check score	N	Percentage
0	1,938	0.5%
1–4 Minimal depression	17,634	4.4%
5–9 Mild depression	65,222	16.4%
10–14 Moderate depression	98,264	24.7%
15–19 Moderately severe depression	108,072	27.2%
20–27 Severe depression	106,436	26.8%

\* According to PHQ-9 scoring instructions (Kroenke et al., 2001).

**Figure 3.** Most frequently endorsed stressors from Stress Test (n = 71,597)



opportunity to inform visitors of the symptoms of depression and, in this way, help improve their mental health literacy around depression, further contributing to the usefulness of this particular website feature. Of the nearly 400,000 Self Check completions, almost 80% scored above the threshold for moderate depression, providing strong evidence that the site was drawing in those from its intended audience (i.e., men experiencing depression). Additionally, more than half of the Self Check completers endorsed at least some suicidal ideation, which resonates with the findings of suicide-related pages being among the most visited on the site and with suicidality featuring prominently in the organic search traffic. Though the Stress Test was a relatively new feature of the site, findings indicated good engagement. The Stress Test results are also revealing, with lack of purpose or meaning in life and loneliness emerging as significant stressors for more than half of the men who complete it.

That there are no commercial interests underpinning HeadsUpGuys reinforces the attraction of authentic conversations to catalyze men's informed self-management. This is especially important in the context of men's mental health in which self-reliance preferences can be satiated by encouraging men to consider, choose, and build upon a variety of health-advancing strategies. The success of HeadsUpGuys may help rewrite (and perhaps overwrite) the long-standing tropes regarding men's reticence for seeking mental health care in pointing to robust growth and engagement. Retelling this narrative in and of itself norms men's eHealth help-seeking to proactively reconsider where and how men engage mental health resources.<sup>30</sup>

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### Authors

John S. Ogrodniczuk, PhD, Department of Psychiatry, University of British Columbia; Founder of HeadsUpGuys.  
 Joshua Beharry, BSc, Department of Psychiatry, University of British Columbia.  
 John L. Oliffe, PhD, School of Nursing, University of British Columbia; Department of Nursing, University of Melbourne.

### Disclosures

None

### Correspondence

John S. Ogrodniczuk, PhD  
 420-5950 University Boulevard  
 Vancouver, British Columbia, V6T 1Z3  
[john.ogrodniczuk@ubc.ca](mailto:john.ogrodniczuk@ubc.ca)

# Preconception Considerations for Male Fertility

DAVID P. GUO, MD

## INTRODUCTION

Preconception counseling has traditionally been considered the domain of the female partner. However, it is commonly held among fertility specialists that 50% of couples experiencing infertility have a male contribution. For this reason, there is growing interest in the involvement of men in preconception counseling. In fact, the U.S. Centers for Disease Control (CDC) has published recommendations for pre-conception care of men.<sup>1</sup>

The primary purpose of preconception counseling is to improve the chances of pregnancy. Furthermore, preconception care for men can further improve family planning outcomes, enhance the reproductive health of women, and help men prepare for fatherhood.<sup>2</sup> Moreover, this represents an opportunity for disease prevention and general health promotion for reproductive-aged males, a demographic that has historically underutilized health care (**Box 1**).

### Box 1. Potential Benefits of Preconception Care for Men

- Increased chances of pregnancy
- Improved family planning
- Enhanced female reproductive health
- Preparation for fatherhood
- Primary care disease prevention and health promotion

There is no current consensus on the ideal location and provider of preconception care for men. Primary care providers may screen for those interested in conception as part of their annual visit for reproductive-aged men.<sup>3</sup> Physicians and advanced practice providers at a Men's Health clinic may provide this counseling as a specific offering. Another opportunity for preconception counseling may be with the Reproductive Endocrinology and Infertility specialist or advanced provider during the female partner's visit at a fertility center. The patient may also be referred to a general urologist or a fellowship-trained reproductive urologist, who has received advanced training in these topics.

Preconception counseling for male fertility should occur at least three months before planned conception. This three-month window takes into the account that new sperm is produced approximately every 42–76 days,<sup>4</sup> and assumes that damaged sperm can be replaced within three months

of mitigated exposures. Furthermore, a sufficient time interval may be needed to improve upon habitual behaviors and pursue long-lasting lifestyle changes. It should be noted that while semen parameters are often interpreted as an indication of male fertility, it is by no means a direct proxy for fertility. A more direct outcome for fertility would be confirmed pregnancies and live births, but this data can be difficult to collect and be subjected to numerous confounding elements.

There are a multitude of popular claims circulating around male infertility, ranging from the type of undergarments that men wear to the food they eat and the activities they engage in. Some of this advice does seem logical and may not have much downside. However, many of these claims are supported by very limited data. In an effort to organize the clinical content of preconception care, Frey and colleagues have previously posited a model framework to approach preconception counseling according to three components: risk assessment, health promotion, and clinical interventions.<sup>2,5</sup> In this report, we will review the literature supporting preconception considerations for male fertility according to this framework (**Box 2**).

### Box 2. Components of Preconception Counseling

- Risk Assessment
- Health Promotion
- Clinical Interventions

## RISK ASSESSMENT

The first step in preconception counseling is the assessment of risks that may affect fertility. Men should review pertinent elements of their medical history: sexually transmitted infections (STIs), chronic disease, medications, and family history of congenital disease or infertility. Men should also consider the implications of their age, as well as their partner, prior to attempting to conceive (**Box 3**).

Because STIs can affect both their partner and offspring, men should consider their risk for sexually transmitted infections, and potentially request a screening test. Screening should be conducted for chlamydia, gonorrhea, syphilis, human immunodeficiency virus (HIV), and hepatitis B and C. Urethral discharge and dysuria may be signs of chlamydia

**Box 3. Risk Assessment**

<p>Screen for sexually transmitted infections</p> <p>Manage chronic disease</p> <p>Review medications</p> <p>Review family history of congenital disease or infertility</p> <p>Consider paternal and maternal age</p>
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and gonorrhea, but some men may be asymptomatic, which underscores the importance of screening. Chlamydia and gonorrhea may affect both male and female fertility by causing scarring in the reproductive tracts; for example, pelvic inflammatory disease may result in female tubal infertility. Syphilis may cause epididymitis, and later stages of syphilis may affect nerve and erectile function. Furthermore, it can cause spontaneous abortion or infection of the newborn. HIV and hepatitis should be screened due to the significant potential impact on the partner and offspring. Additionally, these may impact male fertility potential by impairing semen parameters or affecting sexual function.<sup>6,7</sup>

Men should review their own medical history and chronic illnesses and make sure they are managed to the best of their ability. This may require further guidance of their primary care provider or appropriate specialist. Chronic illnesses such as hypertension and diabetes have been linked to male infertility.<sup>8</sup> For instance, diabetes can affect fertility at multiple levels. Diabetes may result in erectile dysfunction and retrograde ejaculation, and it may directly affect semen quality.<sup>9,10</sup> It may even raise the risk of diabetes in the offspring through epigenetic pathways.<sup>11</sup> Other medical conditions that may predispose men toward infertility include genitourinary conditions (e.g. varicocele, cryptorchidism), surgeries or injuries, infections and malignancies, as well as treatment with prior chemotherapy or radiation therapy. These men may seek reproductive screening with semen analysis earlier, possibly even before attempted conception. Men who have received chemotherapy, or received radiation to the pelvic region, should wait at least 12 months prior to attempted conception due to the risk of genetic alterations to the sperm.<sup>12,13</sup>

Men should review their current medications and make sure these are medically necessary to continue, as these may have an impact on fertility. Medications may influence fertility directly via gonadotoxic effect or indirectly by affecting the central hormonal axis or sexual function. Exogenous testosterone supplementation is well known to suppress the hypogonadal-pituitary-gonadal hormonal axis and decrease or completely shut down sperm production. Other commonly used medications that may affect reproduction include finasteride (for male pattern baldness), antihypertensives, and psychiatric medications such as selective serotonin reuptake inhibitors (SSRIs).<sup>14</sup> For example, SSRIs used to treat anxiety and depression have been associated

with delayed ejaculation, which may disrupt the conception process. While certain medications, such as chemotherapeutic agents, are commonly known to exert a direct effect of spermatogenesis, other medications may not have such a clear connection. Providers may consider using a commercial database, such as Reprotox<sup>®</sup>, that enumerates possible toxic side effects of common medications.

Patients who have family history of infertility or congenital diseases may consider earlier evaluation by a reproductive specialist. Congenital diseases such as cystic fibrosis or sickle cell anemia may have an impact on reproduction function, as well as potential impacts for the offspring. For example, men who are carriers for the mutated cystic fibrosis gene may have congenital absence of the vas deferens and are unable to produce sperm in the ejaculated semen. In addition, if the partner is also a carrier, there could be severe consequences for the offspring. Therefore, genetic counseling is commonly recommended prior to conception. Men whose father had difficulty conceiving may also have a chromosomal or Y-chromosome microdeletion abnormality.

The decreasing fertility potential associated with advanced female age is well known. There is a more gradual decline in male fertility. A systematic review examined the association between advancing paternal age and several semen parameters, and demonstrated small age-dependent declines in motility, morphology, volume, but not in sperm concentration.<sup>15</sup> Given the sheer number of sperm production, paternity may be advanced even into the senior years. Aside from the impact on conception, paternal age may influence the characteristics of offspring. Several studies have demonstrated an association between advanced paternal age and psychological illness in the offspring, including schizophrenia and attention-deficit hyperactivity disorder.<sup>16,17</sup>

In addition to considering their own age, men should consider the impact of their partner's age, and to understand the basics of ovulatory timing. Men should be counseled that advanced maternal age is associated with greater difficulty in conceiving, as well as higher impact on medical illnesses on offspring. Female fertility peaks in the mid- to late-20s and then begins to decline,<sup>18</sup> with women above age 35 considered to be of advanced maternal age. Ability to conceive is determined not only by egg quantity, but quality – which is age-related. To optimize chances of conception, we advise couples to attempt conception every other day in the ovulatory window, as sperm may survive in the female vaginal tract for several days.<sup>19</sup> This cadence may reduce male sexual performance anxiety related to “performing on command.” In summary, men should be counseled that there is a “window of fertility” for women and the concept of timing with ovulation. In addition, knowledge regarding the impact of female age may affect family planning – possibly planning to have children earlier, or to consider alternative options for family building (e.g., egg donor, adoption).

## HEALTH PROMOTION

A number of lifestyle exposures, behaviors and habits may potentially affect male fertility, and these should be highlighted during the preconception counseling. Obesity and exposure to tobacco, marijuana or alcohol in excess can disrupt fertility, as can the use of opioids and anabolic steroids. Fertility may be affected by certain toxic substances associated with specific industries and hobbies, such as manufacturing and agriculture (**Box 4**).

### Box 4. Health Promotion

Obesity
"Unhealthy" diet
Alcohol excess
Tobacco
Marijuana
Testosterone/anabolic steroids
Chronic opioid use
Industrial and agricultural toxins

The rate of obesity has increased significantly in the United States. The U.S. obesity prevalence was 30.5% from 1999–2000 and had reached 42.4% as of 2017–2018.<sup>20</sup> Retrospective studies have demonstrated lower sperm concentrations and rates of oligospermia in men with elevated BMI.<sup>21</sup> For instance, one meta-analysis showed that overweight men (BMI 25–29) were 11% and obese men (BMI > 30) were 42% more likely to have low sperm counts than men with normal BMI.<sup>22</sup> Multiple hypotheses have been posited to explain the connection between obesity and lower sperm count. These include disruption of the HPG axis, elevated scrotal temperature due to fat accumulation around the genitals, or even direct effects on spermatogenesis. While it is unclear whether obesity is a cause or a correlation with male infertility, a small, single-center randomized, control trial showed improvements in sperm quality in obese men who were enrolled in a 16-week exercise program.<sup>23</sup>

Several studies have examined specific diets that may affect male infertility. While the quality of evidence is low, observational studies have suggested that dietary patterns that are good for cardiovascular health may be beneficial for male fertility as well. A 2017 systematic review of observational studies associated diets rich in items such as seafood, poultry, whole grains, vegetables and fruits and low-fat dairy with higher quality semen parameters compared to diets rich in processed and sugar-sweetened foods and full-fat dairy.<sup>24</sup> Whether these sorts of diets represent correlation or causation is not clear. However, due to the benefit to the general health of the male in addition to the potential fertility benefit, it is advisable for the provider to recommend adherence to a "healthier" diet favoring seafood, poultry, nuts, whole grains, fruits, and vegetables.<sup>25,26</sup>

Caffeine consumption does not have a strong correlation with semen parameters. A meta-analysis comprising 19,967 subjects did not demonstrate a consistent effect from caffeine from coffee, tea or cocoa drinks.<sup>27</sup> There was a possible association with DNA damage and aneuploidy, but without observable clinical effect.

While moderate alcohol use does not appear to affect male fertility, heavy alcohol use may affect male fertility at multiple levels. A multi-national cross-sectional study of 8,344 healthy men, in which the median weekly intake was eight drinks, in Europe and the US showed no correlation between alcohol use and semen variables.<sup>28</sup> However, additional studies have associated variable semen abnormalities with heavy alcohol use.<sup>29–31</sup> Heavy alcohol use may result in liver dysfunction, disrupt the hypothalamic-pituitary-gonadal hormonal axis, and directly affect testicular function.<sup>32</sup>

A large collection of retrospective data likewise draws a connection between smoking and male infertility. Specifically, smoking tobacco has been associated with a small negative impact on sperm concentration, motility, and morphology, but the quality of evidence is low.<sup>33–37</sup> For example, one cross-sectional study demonstrated a 19% lower sperm concentration in heavy smokers (defined in this study as >20 cigarettes/day) compared to non-smokers.<sup>34</sup> Observational studies also suggest that marijuana use may negatively impact semen parameters such as concentration, motility and morphology, but the data is of limited quality.<sup>38</sup> For instance, a Danish study of 1,215 healthy young men showed that regular marijuana smoking (more than once weekly) was associated with 28% lower sperm concentration.<sup>39</sup>

Chronic opioid use may result affect male fertility by altering the hormonal axis. Chronic opioid use is familiar cause of hypogonadism.<sup>40</sup> Not only can this affect sexual function, but it has been linked to decreased semen parameters.<sup>41</sup> Current use of testosterone-replacement therapy or anabolic steroids, are known to disrupt the hypothalamic-pituitary-gonadal axis and inhibit spermatogenesis.<sup>42</sup> The time to recovery after testosterone replacement was noted to be 67% at six months and 90% at 12 months after cessation in one study.<sup>43</sup> There is not strong evidence suggesting permanent infertility, though the timing of recovery may be variable.

Exposures to heavy metals (lead, cadmium) and pesticides should be queried. Lead is well recognized as being toxic to gonadal tissue, and may come from lead-based paints, piping, water and industrial sources. Men who work in manufacturing fields may come into contact with heavy metals. Agricultural workers may be exposed to pesticides such as DBCP, DDT, as well as organophosphates, which can impact spermatogenesis. Therefore, screening for type of work and workplace environment, especially in the manufacturing and agriculture, may help men protect themselves from potential exposures.<sup>13</sup>

Studies in the laboratory have demonstrated that increased heat can impair spermatogenesis. Starting from this premise,

researchers have hypothesized that a variety of factors that may increase testicular temperature may also impair spermatogenesis.<sup>44</sup> This includes hot tub use, laptop usage, type of underwear, and types of activities (such as cycling),<sup>45-49</sup> while some studies have pointed toward a correlation, these have been retrospective and have low quality, without the ability to account for confounding variables. In summary, while these studies should not dissuade men from wearing their favorite underwear or sports activities, men who are struggling to conceive may consider these behavior changes with low downside.

## CLINICAL INTERVENTIONS

Pre-natal vitamins, particularly with folic acid, are routinely recommended for women who are planning to conceive. Similarly, vitamins, and particularly antioxidants, have been commonly recommended for male partners who are planning to conceive. The prevailing theory was that antioxidants would reduce the reactive oxygen species and associated free radicals that could be detrimental to DNA in sperm. Indeed, branded “male fertility supplements” containing such antioxidants such as vitamin C, vitamin E, selenium, have been marketed to men who are attempting to conceive. Traditionally, antioxidants have been widely offered to men to improve semen parameters in men for whom targeted medical and surgical therapies are not indicated. This practice was based on limited studies; a 2019 Cochrane review did show a modest improvement of clinical pregnancy rates, but also highlighted the low quality of evidence.<sup>50</sup>

In 2020, the Males, Antioxidants, and Infertility (MOXI) trial, a double-blinded, multi-institutional, randomized controlled trial that was adequately powered with 144 men demonstrated no improvement in sperm parameters or clinical pregnancy for a combination antioxidant pill containing vitamin E, selenium, N-acetylcysteine, and carnitine.<sup>51</sup> While the aforementioned supplements are unlikely to be of benefit, the use of Coenzyme Q10, which was not tested in the MOXI trial, has been associated with improvement in semen parameters in a small prior study.<sup>52</sup> While the benefit is far from clear, the risk of substantial harm has also not been widely proven (**Table 1**).

**Table 1.** Clinical Intervention: Antioxidants

Unlikely Benefit*	Possible Benefit**
Vitamin C	Coenzyme Q10
Selenium	
N-Acetylcysteine	
L-Carnitine	
Zinc	

\*Based on high quality data<sup>1</sup>

\*\*Based on low quality data<sup>2</sup>

## CONCLUSION

Preconception counseling for men can be a valuable initial step in the journey to fatherhood. This should occur at least three months prior to planned conception, and should include a risk assessment and discussion of health promotion and possible interventions. The risk assessment should involve an STI screen and review of the patient's medical and family history, as well as take into account paternal age. Health promotion should highlight the potential negative impact of lifestyle choices and exposures, including obesity, excessive alcohol, tobacco and marijuana use, and ongoing use of testosterone or anabolic steroids. While laboratory research has demonstrated the negative impact of increased heat on sperm production, the real-world implications for the type of undergarments worn, sauna and hot tub use, and cycling is less clear. Furthermore, antioxidants have traditionally been considered a helpful intervention, but more recent high-quality data does not show reliable improvement with most antioxidants tested. In summary, preconception counseling for the male partner can optimize a couple's chances for pregnancy, as well as improve a man's personal health.

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#### Author

David P. Guo, MD, Affiliate Assistant Professor,  
Department of Urology, Stanford University.

#### Disclosures

None

#### Correspondence

David.Guo@kp.org

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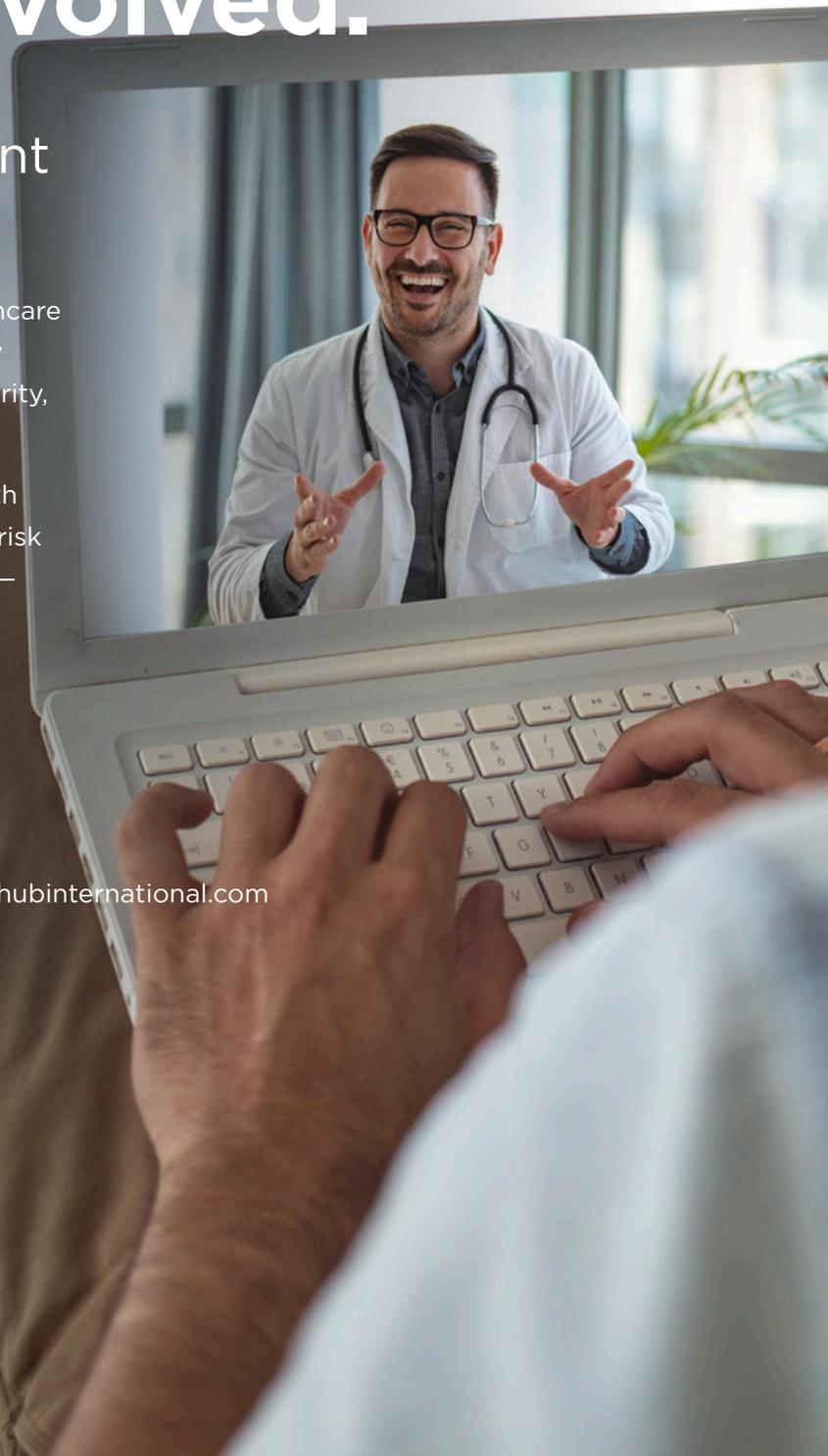
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# Lung Findings in a Patient with a History of Nicotine Vaping and Cannabis Smoking

WINSTON McCORMICK, BS; YIGIT BAYKARA, MD; AYESHA SIDDIQUE, MD; LANCE VAN TRUONG, DO;  
MEL CORBETT, MB, BCh, BAO; SEAN M. HACKING, MB, BCh, BAO

## ABSTRACT

We report a collection of lung findings in a patient with a remote history of cigarette smoking, but now engaged in heavy nicotine vaping with daily edible and combustible cannabis use. Computed tomography (CT) imaging demonstrated numerous, small, and bilateral nodules with ground-glass appearance. The largest nodule is demonstrated in the right upper lung lobe. Clinically the differential diagnosis at this time included hypersensitivity pneumonitis and sarcoidosis. Atypical infection, particularly of a fungal etiology, and metastatic malignancy were also considered. Initial pathology of the right lung needle biopsy revealed alveolar septal thickening with associated atypical pneumocyte proliferation, suggestive of atypical adenomatous hyperplasia (AAH). Subsequently the patient underwent wedge resection of the right upper, middle and lower lobes. Pathology examination revealed pulmonary Langerhans cell histiocytosis (PLCH) in the upper and lower lobes, with CD1a staining highlighting the aggregates of Langerhans cells. Vascular changes were also present including intimal thickening of muscular pulmonary arteries, consistent with pulmonary hypertensive changes. Background lung parenchyma demonstrated respiratory bronchiolitis, smoking-related interstitial fibrosis, an organizing thrombus in muscular artery and associated pneumocyte hyperplasia.

**KEYWORDS:** lung findings, Langerhans cell histiocytosis, nicotine vaping, cannabis smoking

## INTRODUCTION

Smoking has long been understood to be associated with findings of lung injury, chronic obstructive pulmonary disease (COPD) as well as malignancy. Today the proportion of female COPD patients with a history of smoking is 72.8%, while in males it has been found to be 92.7%.<sup>1</sup> It is estimated that cigarette smoking can explain around 90% of lung cancers in men, and 70 to 80% in women.<sup>2</sup>

In recent years, smoking cigarettes has fallen out of public favor in exchange for smoking cannabis, as well as vaping both nicotine and cannabis. The health effects of vaping are largely unknown, but vaping can cause vaping-related lung injury.<sup>3</sup> The data pertaining to the physical health effects of long-term cannabis use is also limited.<sup>4</sup>

Regrading vaping, a six-case cluster has been reported from the University of Utah,<sup>5</sup> and image changes have been demonstrated in a range of cases<sup>6</sup> by the University of California. The Centers for Disease Control and Prevention (CDC) now refers to this syndrome as e-cigarette, or vaping, product use-associated lung injury (EVALI).<sup>3</sup> However, despite the accumulation of data demonstrating both the clinical and imaging features of vaping-associated lung injury, the pathology can be relatively non-specific and is still poorly understood. Butt et al.<sup>7</sup> have postulated that histologic changes in vaping-associated lung injury represent airway-centered chemical pneumonitis, secondary to one or more inhaled toxic substances, instead of an exogenous lipid pneumonia.

Cannabis or marijuana refers to the dried flowers and leaves of the plant *Cannabis sativa L* which contains  $\delta$ -9-tetrahydrocannabinol (THC) and cannabidiol (CBD).<sup>8</sup> Today, marijuana is categorized as a hallucinogen and considered to be controlled Schedule 1 substance with no currently accepted medical usage. Clinically, the effects of cannabis could vary depending on different formulations, as well as in both the method and intensity of use, such as combustion vs vaping.

Cases of pulmonary Langerhans cell histiocytosis (PLCH) have long been understood to occur in the setting of cigarette smoking, and they predominantly affect young adult smokers.<sup>9</sup> Any potential relationships to vaporized nicotine and cannabis oil, as well as combustible cannabis are not as well understood. One case report<sup>10</sup> documents PLCH in a 36-year-old male with minimal cigarette smoking and daily marijuana use while another<sup>11</sup> documented PLCH in a 19-year-old man who smoked half a pack of cigarettes and seven marijuana joints per day. A UK-wide cohort of 106 patients with PLCH demonstrated that 25% of patients were current smokers, 71.7% ex-smokers, and 6% reported smoking cannabis.<sup>12</sup>

Herein, we present lung findings from a patient with chronic nicotine vaping and cannabis smoking who had a remote history of cigarette smoking. Current trends include a shift away from smoking tobacco, and with the growing legalization of marijuana, vaporization of both marijuana and nicotine is on the rise. Examining lung findings from patients with a history of both cannabis and electronic vaping could be important for defining the risk of potential lung injury for the world population at large.

## CASE REPORT

A 44-year-old female presented to the Rhode Island Hospital Emergency Department (ED) for left chest wall pain that radiated to her back and was rated as a 10/10 in pain intensity. Her past medical history was significant for hyperlipidemia and fibromyalgia. She had had a cholecystectomy and a tubal ligation after two spontaneous vaginal deliveries. The patient had a remote history of cigarette smoking, but now engaged in heavy, everyday nicotine vaping, with both daily edible and combustible marijuana use. Complete metabolic panel and complete blood count in the ED were unremarkable. Troponin, hepatic function tests, and lipase levels were within normal limits. The patient left against medical advice before a complete work-up could be pursued.

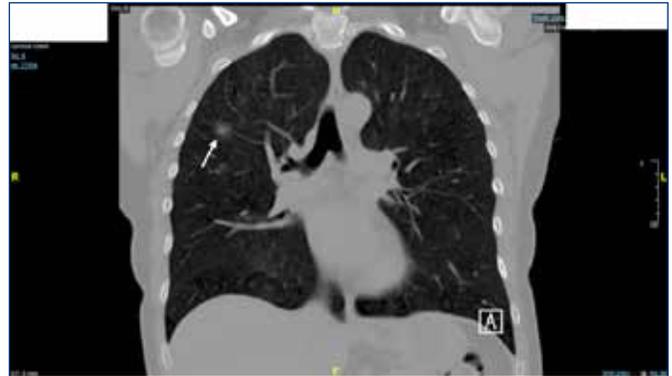
Her out-patient primary care physician ordered a chest computed tomography (CT) scan which revealed exostosis on the sixth rib of the left hemithorax and an incidental, small, right-sided ground-glass nodule in the right upper lobe. Pulmonary function tests (PFT) were obtained and were unremarkable. The decision was made to re-assess the lung nodule in three months due to lack of pulmonary symptoms at that time.

Repeat chest CT demonstrated a marked enlargement of the primary lung nodule compared with the previous CT scan, measuring up to 2.2 cm with a 4 mm central solid component (**Figure 1**). Numerous bilateral smaller ground-glass nodules that are more prominent in the upper lobes were also apparent (**Figure 2**). There was no evidence of cysts. The decision was made to pursue CT-guided biopsy of the primary nodule one month after this result. Additional chest CTs were obtained immediately after the biopsy and one month after the biopsy. The chest CT obtained immediately after the lung biopsy revealed interval increase in size of the upper lobe lesions. Differential diagnosis at this time included hypersensitivity pneumonitis and sarcoidosis. Atypical infection, particularly of a fungal etiology, and metastatic malignancy were also considered. CT one month after the biopsy revealed increased solid components within the numerous lesions, raising concern for Wegner's vasculitis. Findings were inconsistent with vaping-related lung injury.

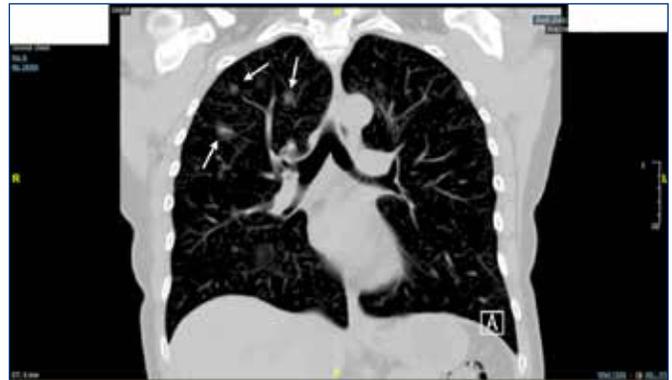
Initial pathology of the right lung needle biopsy revealed alveolar septal thickening with associated atypical pneumocyte proliferation (**Figure 3**), suggestive of atypical adenomatous hyperplasia (AAH). Clinical and radiological correlation was recommended by the consultant anatomical pathologist at the time of biopsy diagnosis.

QuantiFERON gold TB test was negative, and antineutrophil cytoplasmic antibody (ANCA) and angiotensin converting enzyme (ACE) levels were within normal limits. Rheumatoid factor (RF) was undetectable, and the erythrocyte sedimentation rate (ESR) was not elevated. The decision was made to pursue wedge resection of the right upper, middle and lower lobes.

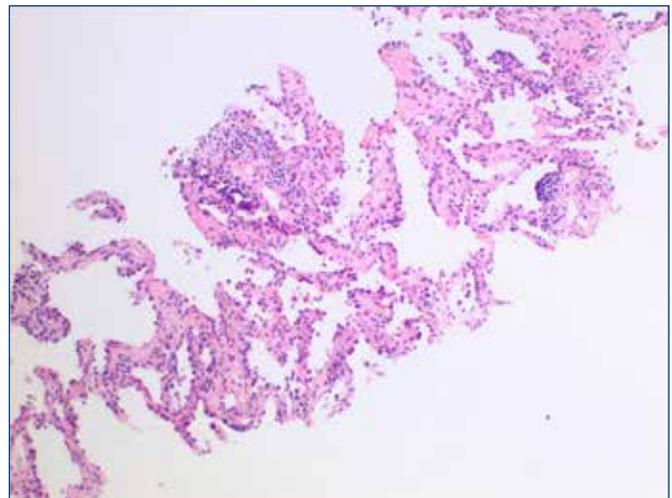
**Figure 1.** CT findings demonstrating the largest nodule (white arrow) with ground-glass appearance is seen in the right upper lobe on non-contrast CT is indicated in the coronal plane.



**Figure 2.** CT findings demonstrating the numerous, small, and bilateral nodules (white arrows) with ground-glass appearance on non-contrast CT is indicated in the coronal plane.



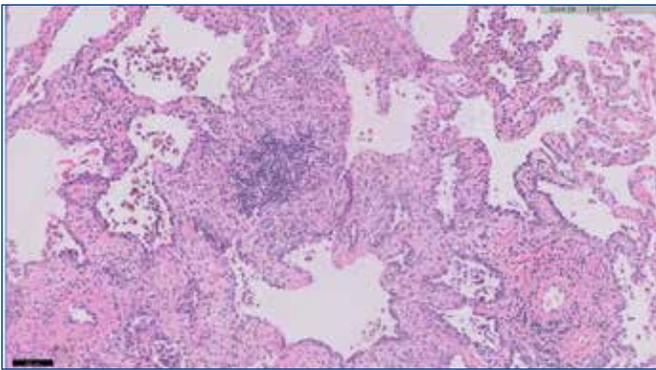
**Figure 3.** Initial pathology of the right lung needle biopsy revealed alveolar septal thickening with associated atypical pneumocyte proliferation, suggestive of atypical adenomatous hyperplasia (10x).



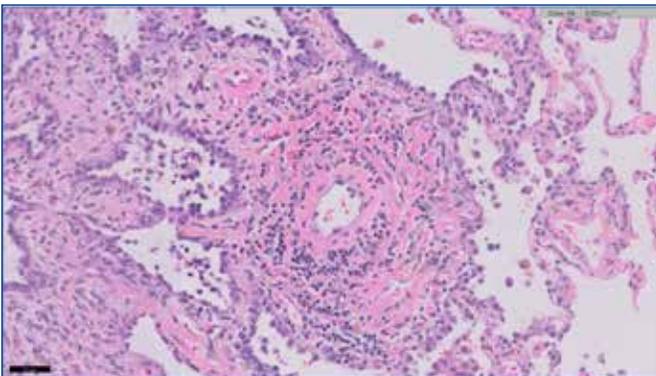
Pathology examination of the right upper lobe revealed a tan-white spongy nodule measuring 0.5 x 0.4 x 0.3 cm which lies 1 mm from the inked resection margin. Histologic evaluation revealed stellate-shaped areas found mostly in the periphery of the lungs containing sparse cellular proliferations (**Figure 4**). Higher power microscopic evaluation demonstrated proliferation of small, spindled Langerhans cells admixed with abundant eosinophils (**Figure 5**). CD1a stain highlights the aggregates of Langerhans cells (**Figure 6**). Vascular changes were also present including intimal

thickening of muscular pulmonary arteries, consistent with pulmonary hypertensive changes. Background lung parenchyma demonstrated respiratory bronchiolitis, smoking-related interstitial fibrosis and an organizing thrombus in muscular artery found in the right middle lobe wedge resection. Associated pneumocyte hyperplasia was also noted. Repeat chest CT seven months after surgery revealed no residual disease.

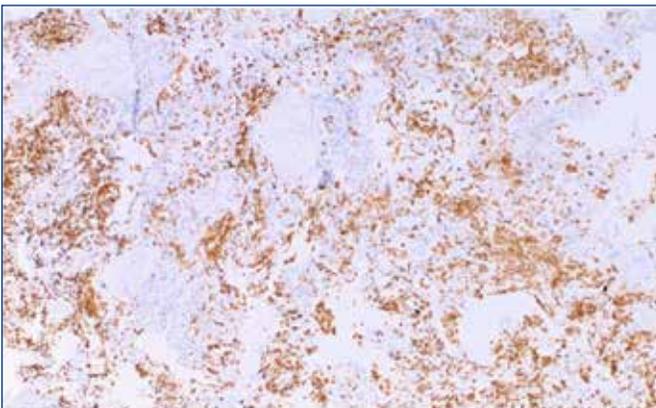
**Figure 4.** Pulmonary Langerhans cell histiocytosis (LCH) in the upper and lower lobes (10x).



**Figure 5.** Prominent eosinophilic inflammation (20x).



**Figure 6.** CD1a stain highlighting the aggregates of Langerhans cells (4x).



## DISCUSSION

Langerhans cell histiocytosis (LCH) represents a clonal proliferation of Langerhans cells, tissue-resident macrophages found primarily in the epidermis and papillary dermis that also function as antigen-presenting cells.<sup>13</sup> In LCH, tumor cells are often found prominently disseminated, particularly to lymph nodes and the skin. Langerhans cells are characterized by Birbeck granules which stain positive for CD1a, S100, and Langerin.<sup>13,14</sup> Contrary to what was previously believed, LCH is now understood to be a clonal process with mutations including BRAF c.1799T>A (p.Val600Glu).<sup>13</sup>

LCH is a class of neoplasm that contains a wide spectrum of clinical presentations.<sup>13,14</sup> It is predominantly a disease of the pediatric population and may be self-limiting.<sup>13-15</sup> The self-limiting forms are associated with particularly good prognoses.<sup>14</sup> Typical disease features include eosinophilic granulomas secondary to lytic bone lesions, most commonly in the skull and long bones, exophthalmos, polyuria, and the Letterer-Siwe disease: a fulminant clinical syndrome which includes hepatosplenomegaly, lymphadenopathy, skin rash, and pancytopenia.<sup>13, 15</sup> Furthermore, LCH can present in nearly any organ except the kidney, and it may present as single- or multi-organ disease.<sup>9,13,16</sup>

One manifestation of LCH is PLCH, which occurs typically in cigarette smokers aged between 20–40 years.<sup>9,17</sup> The correlation between cigarette smoking and PLCH is so strong that the disease has been called a smoking-related illness.<sup>17,18</sup> Indeed, PLCH is the most common LCH in adults,<sup>19</sup> and the most common presenting symptoms include cough and dyspnea on exertion, yet one-third of patients may be asymptomatic.<sup>16,17,19</sup> Pulmonary function testing often reveals a decreased diffusion capacity of carbon monoxide, reduced vital capacity, normal or increased residual volume, and preserved total lung capacity, however it is often normal in early disease.<sup>9, 18,19</sup>

PLCH remains a rare and poorly understood disease of active young-adult cigarette smokers whose exact etiology is unknown. Our patient's presentation was typical, in that she was asymptomatic and was incidentally identified as having a single ground-glass nodule that rapidly advanced to involve the bilateral lungs. Indeed, the chest imaging is often abnormal and can be the first clue toward pathology.<sup>16</sup> Nonetheless, she was outside the typical age-range for PLCH, and her smoking history was remote. So strong is the

link between active cigarette smoking and PLCH that cessation of smoking can lead to remission of PLCH.<sup>17,19</sup> Given this patient's remote cigarette smoking history and the fact that PLCH is often rapidly progressing, as her case was, it is unlikely that cigarette smoking played a role in her disease.<sup>9</sup>

By contrast, this patient presented with active nicotine vaping and marijuana smoking. Her presentation suggests that inflammation due to heated smoke, nicotine itself, or some compound in smoked marijuana may be the underlying culprit in the pathogenesis of PLCH. The current molecular understanding suggests a *BRAF* or *MAPK* mutation is responsible for PLCH and that it is therefore monoclonal.<sup>9,13,15,18</sup> Inflammation could be a driving factor involved in PLCH pathogenesis. Most recently, mice models have shown that *BRAF*-V600E mutations increase dendritic cell responsiveness to stimuli, including chemokines, while mutant cells accumulate in the lungs of cigarette smoking-exposed mice is due to both increased cellular viability and enhanced recruitment.<sup>20</sup>

This patient underwent multilobe right lung wedge resections which revealed PLCH. Current treatments rely on cigarette smoking cessation followed by observation.<sup>15,18</sup> If PLCH does not resolve, corticosteroids, systemic chemotherapy such as cladribine, with some consideration given to *BRAF* or *MEK* inhibitors, is used.<sup>15,16,19</sup> Our patient did not receive systemic chemotherapy and continued to vape nicotine and smoke marijuana. Lung transplant is pursued in some patients with refractory disease or in those with limited life expectancy.<sup>9,16</sup>

Many of the findings in the lungs were non-specific. These included vascular changes including intimal thickening of muscular pulmonary arteries, consistent with pulmonary hypertensive changes, with background lung parenchyma demonstrating respiratory bronchiolitis, smoking related interstitial fibrosis, an organizing thrombus in muscular artery and associated pneumocyte hyperplasia.

The vascular changes consistent with pulmonary hypertensive could possibly be a consequence of smoking cannabis and tobacco, as well as vaping nicotine. Tobacco smoking has been found to be significantly more common in patients with pulmonary arterial hypertension compared to control subjects.<sup>21</sup> However, the correlation of nicotine vaping and cannabis smoking to pulmonary hypertension is still obscure. Additionally, pulmonary hypertension can occur in the setting of PLCH due to vascular dysfunction.<sup>22</sup> Further suggesting the findings of pulmonary hypertension in this patient could be multifactorial in etiology.

Respiratory bronchiolitis is commonly found in smokers, but has also been reported in patients using electronic nicotine delivery systems.<sup>23</sup> The findings of an organizing thrombus could be secondary to vaping, as studies have demonstrated even short-term exposure to the JUUL e-cigarettes increases the risk of thrombotic events by modulating platelet function, such as aggregation and secretion.<sup>24</sup>

Pneumonocyte hyperplasia is extremely non-specific and can represent any response or injury to respiratory epithelium.

Despite the history of electronic nicotine vaping, findings consistent with a diagnosis of vaping-related lung injury including acute fibrinous pneumonitis, diffuse alveolar damage, or organizing pneumonia accompanied by bronchiolitis were not seen.<sup>7</sup> It is worth mentioning that even though no histologic findings are necessarily specific for EVALI, foamy macrophages and pneumocyte vacuolization can be useful diagnostic clues in an appropriate clinical context.<sup>7</sup>

Much remains to be understood about both vaping lung injuries and the long-term effects of cannabis smoking.<sup>4</sup> One case report details the presence of vanishing lung syndrome in a patient who vaped nicotine and smoked cannabis, but other deleterious physical effects of simultaneously using both substances, particularly PLCH, have not been documented.<sup>25</sup> This patient's presentation suggests that PLCH should be considered in any patient who vapes nicotine, smokes cannabis, or both, and who presents with rapidly progressing lung nodules. It also suggests wedge resection could be considered for any patient who fails initial conservative therapy.

Although cigarette smoking has rapidly declined in popularity, nicotine vaping and cannabis smoking, long seen as safe options, are exploding in popularity. Much remains to be understood about the long-term effects of both electronic vaping and cannabis smoking on the lungs.

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## Authors

Winston McCormick, BS, Warren Alpert Medical School of Brown University.

Yigit Baykara, MD, Department of Pathology and Laboratory Medicine, Rhode Island Hospital and Lifespan Medical Center, Warren Alpert Medical School of Brown University.

Ayesha Siddique, MD, Department of Pathology and Laboratory Medicine, Rhode Island Hospital and Lifespan Medical Center, Warren Alpert Medical School of Brown University.

Lance Van Truong, DO, Department of Pathology and Laboratory Medicine, Rhode Island Hospital and Lifespan Medical Center, Warren Alpert Medical School of Brown University.

Mel Corbett, MB, BCh, BAO, Department of Otolaryngology/Head and Neck Surgery, University Hospital Galway, National University of Ireland.

Sean M. Hacking, MB, BCh, BAO, Department of Pathology and Laboratory Medicine, Rhode Island Hospital and Lifespan Medical Center, Warren Alpert Medical School of Brown University.

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## Correspondence

Sean M. Hacking, MB, BCh, BAO  
Department of Pathology and Laboratory Medicine,  
Rhode Island Hospital and Lifespan Medical Center,  
593 Eddy St, APC 12, Providence, RI, 02903  
sean\_hacking@brown.edu

# Multisystem Inflammatory Syndrome in an Adolescent Following SARS-CoV-2 Exposure Despite Three Doses of a COVID-19 Vaccine

ANURAG RATAN GOEL, MD; OSAMA IBRAHIM, MD; SILVIA S. CHIANG, MD; ALI YALCINDAG, MD

## ABSTRACT

The multisystem inflammatory syndrome in children (MIS-C) is a known complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the pediatric population. Recent studies have demonstrated high efficacy of a two-dose vaccine series in preventing MIS-C among adolescents. To date, such studies have only included children exposed to SARS-CoV-2 prior to the emergence of the Omicron variant (B.1.1.529). We report a case of an adolescent who received three doses of a vaccine yet developed MIS-C following known exposure to SARS-CoV-2. Given the uncertainty in whether current vaccines offer as much protection against MIS-C due to the Omicron variant or any potential new variants as they have for older variants, pediatric providers should maintain a high index of suspicion for MIS-C regardless of vaccination status.

**KEYWORDS:** COVID-19, SARS-CoV-2, MIS-C, multisystem inflammatory syndrome in children, Omicron

## INTRODUCTION

The multisystem inflammatory syndrome in children (MIS-C) is a known complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the pediatric population. It is described as a systemic inflammatory response, often resembling classic or atypical Kawasaki Disease (KD), affecting two or more organ systems following a usually mild or asymptomatic infection with SARS-CoV-2.<sup>1-4</sup> MIS-C primarily affects children aged 5–11,<sup>5</sup> with great variation in severity, from a mild self-limited illness to significant cardiac dysfunction and shock requiring hemodynamic support in an intensive care unit.<sup>6</sup> Although no standardized treatment exists for MIS-C, patients are commonly treated with a combination of immune modulating agents, including intravenous immune globulin (IVIG), glucocorticoids, anti-cytokine agents, and anti-platelet and anti-coagulant medications.<sup>6</sup> The long-term sequelae of such a systemic inflammatory response remain unknown.

As of March 2022, the BNT162b2 (Pfizer-BioNTech) vaccine is the only approved vaccine against SARS-CoV-2 in the pediatric population, currently authorized under Emergency

Use Authorization (EUA) for children aged 5–15, and fully approved for adolescents at least 16 years old by the Food and Drug Administration (FDA).<sup>7,8</sup> Vaccinating children against SARS-CoV-2 decreases the risk of infection and hospitalization due to COVID-19.<sup>9,10</sup> Vaccination also reduces the risk of developing MIS-C following exposure. A recent report showed a 91% efficacy of a two-dose Pfizer-BioNTech vaccine series in preventing MIS-C amongst children aged 12–18.<sup>11</sup> Another study found the incidence of MIS-C in the United States was only one per million after receiving at least one dose of a COVID-19 vaccine,<sup>12,13</sup> a significant reduction from a previously reported incidence of 164–224 per million SARS-CoV-2 infections in children aged 11–20.<sup>14</sup>

While protection against COVID-19 infection and MIS-C have been studied during periods when SARS-CoV-2 B.1.1.7 (Alpha variant) and SARS-CoV-2 B.1.617.2 (Delta variant)<sup>5,15</sup> were dominant in the United States, neutralization rates of SARS-CoV-2 B.1.1.529 (Omicron variant)<sup>5</sup> in fully vaccinated children and adolescents are still emerging, with one case series demonstrating 38% positivity in fully vaccinated adolescents,<sup>16</sup> compared to <10% positivity for the Delta variant in similar populations,<sup>17-19</sup> and a 93% efficacy in preventing hospitalizations due to the Delta variant in this population.<sup>20</sup> To the best of our knowledge, there have been no published reports describing rates and characterizing cases of MIS-C during the Omicron variant period. Given the evidence for increased rates of Omicron variant infection compared to that of the Delta variant in fully vaccinated children, it is important to describe cases of MIS-C during the Omicron surge in both unvaccinated and vaccinated children as we learn more about this complex syndrome.

We report a case of an adolescent who received three doses of the BNT162b2 (Pfizer-BioNTech) vaccine yet developed MIS-C with features of atypical KD following known recent exposure to SARS-CoV-2.

## CASE PRESENTATION

The patient is a 16-year-old male with a past medical history of mild asthma who presented to the emergency department with six days of subjective fever, initially associated with diffuse myalgias, headaches, and fatigue. He developed limbal-sparing conjunctivitis, abdominal pain, nausea, post-prandial non-bloody nonbilious emesis, and anorexia.

He had erythema of the oral mucosa and tongue with prominence of the lingual papillae, commonly described as the “strawberry-tongue” phenomenon. He did not have erythema, edema, or desquamation of the distal extremities; a rash anywhere on the body; oropharyngeal erythema, edema or exudates; or cervical lymphadenopathy. He denied sore throat, cough, dyspnea, diarrhea, dysuria, urinary urgency or frequency, focal pain, or edema. He denied weight loss, night sweats, or chills. Polymerase chain reaction (PCR) tests of nasopharyngeal swabs for SARS-CoV-2, influenza-A, and influenza-B were negative prior to his presentation to the emergency department.

His parents were both symptomatic and his mother tested positive for SARS-CoV-2 by PCR 36 days prior to his symptom onset. The patient never experienced COVID-19 symptoms before or after this exposure and did not take a SARS-CoV-2 PCR test at that time. He was attending high school in person daily and was employed at a drugstore in the weeks preceding his presentation. Of note, the patient had completed a two-dose series of the BNT162b2 (Pfizer-BioNTech) vaccine approximately 34 weeks prior to presentation and 28 weeks prior to his mother’s positive PCR tests. In addition, he received a third booster dose of the vaccine two weeks after the known exposure, three weeks prior to symptom onset. He was otherwise up to date on his vaccinations.

After arriving at the emergency department, the patient became tachycardic and hypotensive, and his shock physiology resolved with three 1-liter boluses of normal saline. Initial laboratory workup at that time revealed leukocytosis with lymphopenia, elevated ESR, CRP, ferritin, d-dimer, fibrinogen, low serum sodium, normal BNP, and troponin (Table 1). Group-A streptococcus PCR of a throat swab was positive, and he was deemed to be an asymptomatic colonized individual. A nasopharyngeal swab PCR panel for 22 common upper respiratory viruses, including SARS-CoV-2, was negative. A blood culture showed no growth after five days.

A SARS-CoV-2 antibody panel was notable for: anti-N-protein IgG 4.67 (positive), anti-S-protein IgM 1.04 (positive), and anti-RBD IgG >25,000 AU/mL (positive). A CMV antibody panel was only notable for an IgG of 7.7, and EBV antibodies were negative. Point-of-care and formal echocardiograms did not reveal any effusion, decreased ejection fraction, right heart strain, or ectasia or aneurysm of the visualized coronary arteries. He had a normal electrocardiogram.

He was diagnosed with MIS-C and received 2g/kg IVIG once, methylprednisolone 30mg twice daily, and enoxaparin twice daily. Following initiation of therapy, he demonstrated clinical improvement with resolution of exam findings. He was discharged in good condition with a prednisone taper, low-dose aspirin, and a final diagnosis of MIS-C with atypical KD features in a fully vaccinated adolescent.

**Table 1.** Serum Laboratory Studies Demonstrating Multisystem Inflammation Before Treatment with Intravenous Immune Globulin and Methylprednisolone

Lab (Reference Range)	Pre-Treatment Value
Serum Sodium, mEq/L (135--145)	<b>131</b>
hs-Troponin I, ng/L (3–57)	<3
B-type Natriuretic Peptide, pg/mL (0–33.3)	28.0
Alanine Aminotransferase, IU/L (8–36)	<b>60</b>
Serum Albumin, g/dL (3.1–4.8)	<b>3.0</b>
Ferritin, ng/mL (22–322)	<b>541</b>
D-Dimer Level, ng/mL (0–300)	<b>608</b>
Fibrinogen, mg/dL (150–480)	<b>820</b>
C-reactive Protein, mg/L (0–10.0)	<b>281.38</b>
Erythrocyte Sedimentation Rate, mm/h (0–15)	<b>106</b>
Serum Leukocytes, x10 <sup>9</sup> /L (3.5–11)	<b>19.2</b>
Absolute Lymphocyte Count, x10 <sup>9</sup> /L (1.0–4.0)	<b>0.5</b>
Absolute Neutrophil Count, x10 <sup>9</sup> /L (1.8–8.0)	<b>16.9</b>

Abnormal lab findings are in bold. Typical laboratory findings in MIS-C include: elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, B-type natriuretic protein (BNP), d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), neutrophilia, lymphopenia, and hypoalbuminemia.<sup>21</sup>

## DISCUSSION

This is a case of a 16-year-old male who had completed two doses of a SARS-CoV-2 vaccination series with a subsequent exposure to illness, followed by a third dose of the vaccine, who then presented with MIS-C that manifested as fluid-responsive hemodynamic instability, limb-sparing conjunctivitis, oropharyngeal erythema and edema, and gastrointestinal symptoms. To the best of our knowledge, this is the first known case of a fully vaccinated adolescent developing MIS-C in Rhode Island based on our review of the literature, chart review of records at Hasbro Children’s Hospital, the only tertiary care pediatric hospital in Rhode Island, and our correspondence with the Rhode Island Department of Health (RIDOH).

Our patient fulfilled the Centers for Disease Control and Prevention (CDC) diagnostic criteria for MIS-C given 1) fever, 2) inflammatory illness of multiple organ systems (in his case mucocutaneous and gastrointestinal), 3) typical laboratory abnormalities (Table 1),<sup>21</sup> and 4) recent infection demonstrated by serology.<sup>1</sup> He also fulfilled the World Health Organization’s (WHO) case definition for MIS-C.<sup>22</sup> His SARS-CoV-2 anti-N-protein IgG positivity confirmed exposure to natural SARS-CoV-2, as this is not an antibody generated in response to the mRNA vaccine.<sup>10</sup>

Both CDC and WHO criteria require alternative explanations be ruled out. While the adolescent also fulfilled well-accepted international criteria for atypical KD,<sup>23,24</sup> it is known that some patients who fulfill criteria for MIS-C will

also fulfill criteria for complete or atypical KD.<sup>2,4,25-28</sup> Upper respiratory infection, focal occult infection, bacteremia, CMV, and EBV were also ruled out. Although a Group-A streptococcus PCR of a throat swab was positive, it was clinically determined that this was likely due to colonization, and did not explain his presenting signs and symptoms.

This case demonstrates how SARS-CoV-2 exposure and asymptomatic breakthrough infection following a two-dose vaccination series in adolescents can still progress to MIS-C. The two-dose vaccine series was previously shown to be 91% effective in preventing MIS-C in children/adolescents aged 12–18. This was demonstrated in a case-control series of 283 patients admitted to 24 hospitals in the United States between July 1, 2021 and December 9, 2021.<sup>11</sup> Another study examined individuals aged 12–20 who had received at least one dose of a COVID-19 vaccine to identify potential cases of MIS-C by adjudicating cases reported to the MIS-C national surveillance system of the CDC, the Vaccine Adverse Event Reporting System, and CDC's Clinical Immunization Safety Assessment Project, between December 14, 2020 and August 31, 2021. The data demonstrated 21 cases of MIS-C amongst 21,335,331 individuals aged 12–20 who had received at least one dose of a vaccine – a case rate of 1 per one million patients.<sup>12,13</sup> Each study concluded there is a low risk of MIS-C among vaccinated children. The dominant variants in the United States during the study periods were SARS-CoV-2 B.1.1.7, the Alpha variant, and SARS-CoV-2 B.1.617.2, the Delta variant.<sup>5,15</sup> However, in weeks immediately following the end of both study periods, the predominant variant in the United States shifted away from Delta and became SARS-CoV-2 B.1.1.529, the Omicron variant.<sup>5</sup>

Similarly, 47% of COVID-19 positive tests that underwent whole genome sequencing during the week ending December 25, 2021 in Rhode Island resulted as the Omicron variant.<sup>29</sup> The following week, 83% of sequenced tests resulted as the Omicron variant.<sup>29</sup> While we cannot confirm the patient was infected with the Omicron variant, the timing of his MIS-C presentation and known exposure suggest the possibility that his MIS-C was due to an Omicron variant infection. According to the RIDOH, between 100,000–100,500 children/adolescents aged 5–18 in Rhode Island have received at least one dose of a COVID-19 vaccine.<sup>30</sup> Given the recent literature demonstrating vaccination does not confer as much protection against the Omicron variant as it does against the Delta variant,<sup>16-20,31</sup> future studies are needed to determine if the incidence of MIS-C in children exposed to the Omicron variant is higher than the previously reported incidence of 1 per million individuals.<sup>12,13</sup>

One alternative, but less likely explanation, is that this case of MIS-C is an adverse effect of the vaccination series. There have been isolated case reports of MIS in children (MIS-C) and adults (MIS-A) following one or two doses of an mRNA vaccine.<sup>32-36</sup> Each of these cases followed vaccination

with no known subsequent exposure, meeting the exposure requirement of CDC and WHO case definitions<sup>1,22</sup> due to positive IgG serology. Studies have shown anti-spike-protein antibody titers and neutralizing activity to be similar between children with or without MIS-C, with increased avidity associated with decreased severity of MIS-C.<sup>37,38</sup> In addition, each of these previously reported cases occurred within one week of a vaccine dose, whereas our patient's third dose was given three weeks prior to symptom onset. Our patient had a known exposure approximately five weeks prior to the onset of symptoms. The timeline, known exposure, and anti-N-protein IgG positivity make vaccine adverse effect a less likely etiology of his MIS-C, and there is no evidence in the literature to date that suggests vaccination plays a role in the pathogenesis of MIS-C.<sup>12,13</sup>

These data suggest an ongoing need to study MIS-C prevention strategies, treatment regimens, and its sequelae in the children. These findings are of particular interest to healthcare providers in Rhode Island, the leading state in total COVID-19 cases per million residents,<sup>39</sup> and the leading state in COVID-19 cases per 100,000 children.<sup>40</sup> Records from Hasbro Children's Hospital indicate 51 children were admitted with MIS-C between May 2020 and March 2022.

Importantly, as this window of susceptibility to MIS-C following SARS-CoV-2 infection due to the Omicron-variant peak remains open in the coming weeks to months, pediatricians should recognize that vaccine efficacy in preventing MIS-C was studied prior to emergence of the Omicron variant, and that it remains unclear whether a two- or three-dose series confers as much protection against this variant as reported for previous variants. Despite recent reports that MIS-C may be rare among vaccinated adolescents,<sup>11-13</sup> this case demonstrates it is critical that pediatric providers maintain a high index of suspicion for MIS-C, even in children who are fully vaccinated. Future work should focus on comparing neutralization rates and MIS-C incidence between vaccinated and unvaccinated children exposed to the Omicron variant, optimal timing of vaccination following diagnosis of MIS-C, and the dynamic utility of serological testing for diagnosis of MIS-C in vaccinated individuals.

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### Authors

- Anurag Ratan Goel, MD, Departments of Internal Medicine and Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI.
- Silvia S. Chiang, MD, Division of Pediatric Infectious Diseases, Department of Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI.
- Osama Ibrahim, MD, Division of Pediatric Infectious Diseases, Department of Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI.
- Ali Yalcindag, MD, Division of Pediatric Rheumatology, Department of Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI.

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### Correspondence

Ali Yalcindag, MD

Director, Division of Pediatric Rheumatology, Hasbro Children's Hospital

593 Eddy Street, Lower Level

Providence, RI 02903

401-444-6540

Fax 401-444-6543

[ali\\_yalcindag@brown.edu](mailto:ali_yalcindag@brown.edu)

# Delays in Presentation of New Onset Diabetes at the Start of the COVID-19 Pandemic

SABITHA SASIDHARAN PILLAI, MD; CAN CAO, BA; CASSANDRA J. DREES, MD; TZU-CHUN CHU, MPH; KATHERINE MASON, MD; LISA SWARTZ TOPOR, MD, MMSc

## ABSTRACT

**OBJECTIVE:** To compare the frequency, severity of presentation and initial presentations of new onset diabetes mellitus (DM) in youth in Rhode Island during the early phase of the COVID-19 pandemic compared to the same time frame in 2018 and 2019.

**METHODS:** A retrospective cohort study of youth treated for new onset DM at Hasbro Children's Hospital between March 1 and May 15, 2020, compared to those diagnosed in the same period in 2018 and 2019.

**RESULTS:** Fewer youth were diagnosed with new onset DM in Spring 2020 and the percentage of youth with DKA at time of DM diagnosis was higher in Spring 2020 compared to prior years ( $p=0.048$ ). Age, gender, and DKA complications did not differ by year.

**CONCLUSION:** Nearly 50% fewer youth were diagnosed with DM at the start of the COVID-19 pandemic compared to years prior, and those diagnosed with new onset DM in Spring 2020 were more likely to present with DKA. Delays in both initial health care evaluation and the recognition of DM symptoms may have contributed to the decline in overall DM diagnoses and the more severe presentations. Identification of DM symptoms is essential, especially during future surges of COVID-19 or other events that impact the healthcare system, to reduce the risk of DM complications including DKA.

**ABBREVIATIONS:** DKA: Diabetic ketoacidosis; DM: Diabetes mellitus

**KEYWORDS:** pediatrics, new onset diabetes, COVID-19, diabetic ketoacidosis

## INTRODUCTION

At the start of the COVID-19 pandemic, medical providers reported that adults with non-COVID-19 symptoms were delaying medical care for serious medical conditions.<sup>1,2</sup> Similarly, pediatricians reported delays in routine well-child visits and vaccinations,<sup>3</sup> as well as delays in the diagnosis of diabetes mellitus in youth.<sup>4-6</sup> Diabetic ketoacidosis (DKA) is a severe manifestation of prolonged insulin deficiency and is more likely to occur if the symptoms of diabetes mellitus

(DM) are unrecognized or if there is a delay in making the DM diagnosis after symptom onset.<sup>7</sup> In the United States, more than 30% of youth with newly diagnosed type 1 DM present with DKA each year,<sup>8</sup> while DKA is less common at the time of diagnosis with type 2 DM.

The start of the COVID-19 pandemic led to marked and sudden changes in the delivery of health care with many health care professionals (HCP) transitioning to telemedicine instead of in-person visits. Utilization of the health care system also decreased during the first months of the COVID-19 pandemic owing to a variety of factors including stay-at-home orders, closure of medical offices, concerns about crowded health care systems, and fears of contracting COVID-19.<sup>9-11,22</sup>

Emerging data collected during the COVID-19 pandemic reported an increase in the frequency of DKA in children presenting with new onset type 1 DM.<sup>9-22</sup> Given concerns about delays in care and rising rates of DKA, we sought to review local data about new onset DM in youth from Rhode Island's only pediatric hospital and intensive care unit. We hypothesized that during the initial wave of COVID-19 in the region, a higher proportion of youth with new onset DM in Rhode Island would present with DKA compared to the cohort presenting with new onset DM in prior years, similar to other hospitals.<sup>9-11,13-22</sup> We further hypothesized that during the initial wave of COVID-19, there would be a higher prevalence of both severe DKA ( $pH < 7.1$ ) and DKA with hyperosmolality due to longer duration of unrecognized symptoms. Finally, we hypothesized that patients would have a longer duration of symptoms before initial medical evaluation in 2020 compared to prior years.

## METHODS

### Participants

This was a retrospective cohort study of all youth with new onset DM diagnosed in inpatient or outpatient settings at Hasbro Children's Hospital, between March 1 and May 15, 2020, compared to those diagnosed in the same time period of 2018 and 2019. Inclusion criteria included subjects diagnosed with new onset diabetes (including Type 1 DM and Type 2 DM) during the time frame of the study. Subjects with a prior diagnosis of DM, with cystic fibrosis-related DM, and subjects with steroid-induced or medication-induced DM

were excluded. DKA and hyperosmolar hyperglycemic state (HHS) were defined in accordance with the International Society of Pediatric and Adolescent Diabetes (ISPAD) consensus guidelines.<sup>9</sup> DKA criteria included: 1) blood glucose  $\geq 200$  mg/dL (11 mmol/L), 2) pH  $\leq 7.3$  or bicarbonate  $\leq 15$  mEq/L (15 mmol/L), and 3) ketonuria and/or elevated serum beta-hydroxybutyrate. DKA was classified as mild (pH 7.2 to  $< 7.3$ ), moderate (pH 7.1 to  $< 7.2$ ) and severe (pH, 7.1).<sup>23</sup> HHS criteria included: 1) osmolality  $\geq 320$  mOsm/kg (measured when available, and otherwise calculated [2(serum sodium mEq/L) + (blood urea nitrogen mg/dL)/2.8 + (glucose mg/dL)/18]), 2) blood glucose  $\geq 600$  mg/dL (33.1 mmol/L), and 3) absence of acidosis (pH  $> 7.3$  without large ketosis). Events with features of both DKA and HHS were categorized as a “mixed presentation,” and included: 1) osmolality  $\geq 320$  mOsm/kg, 2) initial blood sugar  $\geq 600$  mg/dl (33.1 mmol/L), 3) acidosis (pH  $\leq 7.3$ ), and 4) ketonuria and/or elevated serum beta-hydroxybutyrate.<sup>24</sup> This study was approved by the Institutional Review Board (IRB) of Lifespan Corporation.

We collected information from the electronic health record (EHR) about demographics, duration of hospitalization, laboratory values at hospital presentation, and clinical course. We also gathered information about DM symptoms and any medical care sought prior to hospitalization with DKA. Altered mental status (AMS) included a Glasgow coma scale  $\leq 13$ , confusion, memory loss, focal neurological deficits, loss-of-consciousness, or other descriptors indicating impaired mental status. Fatigue and somnolence were not considered AMS. We collected information on complications through review of hospital records. Complications included additional diagnoses occurring in relation to the DM diagnosis that were not part of the expected clinical course that resulted in lengthened stay, additional interventions, increased monitoring, or additional imaging. We collected information about duration of symptoms prior to health care evaluation, and duration between initial health care evaluation and diagnosis of DM. Acute kidney injury was diagnosed if the creatinine value was more than 1.5 times the expected baseline creatinine level using the Schwartz estimating equation.<sup>25</sup>

### Statistical Methods

For descriptive analyses, we presented means with standard deviations for continuous variables, and frequencies with percentages for categorical variables. The Chi-squared tests were performed to evaluate frequencies of demographics and diagnoses across three consecutive study periods, and Fisher’s exact test was used when some cell counts were less than 5. The mean differences in age at diagnosis and HbA1c were tested using analysis of variance (ANOVA). For all analyses, R Version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) was used, and a two-tailed p value of 0.05 was considered statistically significant.

## RESULTS

### Diabetes Presentations

More youth were diagnosed with DM in Spring 2018 and 2019 compared to 2020, and a significantly higher percentage of the youth with new onset DM presented with DKA in 2020 compared to prior years (Table 1). The age and gender distribution of the patients with new onset DM were similar across all years. Of those with DKA, the DKA severity was similar across different years. The frequency of DKA with hyperosmolality differed by year ( $p=0.046$ ). Though not statistically significant, there was a trend towards fewer patients seeking evaluation by primary or urgent care prior to DM diagnosis in 2020 compared to prior years (Table 2).

### DKA Complications

Youth with new onset DM and DKA commonly experienced complications, and frequency of complications did not vary by year (Table 2). Among patients with DKA, the distribution of patients with altered neurologic status or other neurological findings did not differ by year. Acute kidney injury and neurological complications were the most common complications.

**Table 1.** Characteristics of patients diagnosed with new onset diabetes

Year	2018	2019	2020	p-value
Number of patients	34	26	15	
Mean age at diagnosis, y (SD)	10.7 (4.33)	13.2 (3.42)	10.7 (5.06)	NS
Male (%)	20 (58.8)	14 (53.8)	9 (60.0)	NS
Mean HbA1c, % (SD)	8.61 (4.51)	12.7 (2.65)	9.67 (5.17)	NS
DKA at diagnosis, N (%)	8 (23.5)	9 (34.6)	9 (60.0)	0.048
DKA with hyperosmolality, N (%)	4 (50)	0	2 (22)	0.046

DKA: diabetic ketoacidosis, HbA1c: hemoglobin A1c

**Table 2.** Characteristics of youth with new onset diabetes who presented with DKA

Year	2018	2019	2020	p-value
Documentation of office/telehealth visit prior to DM diagnosis, N (%)	26 (76.5)	19 (76.0)	8 (53.3)	NS
Delay in diagnosis, N (%)	5 (14.7)	4 (16.0)	6 (40.0)	NS
Altered mental status, N (%)	4 (50)	4 (44.4)	5 (55.6)	NS
Acute kidney injury, N (%)	3 (37.5)	1 (11.1)	2 (22.2)	NS

DM: diabetes mellitus

## DISCUSSION

Our institution had close to a 50% reduction in new DM diagnoses in youth between March 1 and May 15, 2020, compared to the same periods in 2018 and 2019. Those with new onset DM during the initial wave of COVID-19 in Spring 2020 were more likely to present with DKA compared to those diagnosed in prior years (Table 1). We did not find differences in DKA severity by year, though did find that one-third of youth with new onset DM presented with severe DKA during Spring 2020. There were no differences in complications across years.

The time frame of our study was selected to correspond with the initial COVID-19 surge in Rhode Island and New England. Public schools in Rhode Island closed for in-person learning on March 16, 2020, a stay-at-home order was in effect from March 28 to May 8, 2020, and the reopening of the economy began on May 15, 2020. Our study, which included both Type 1 and Type 2 DM, found decreased DM diagnoses in youth during the first months of the COVID-19 pandemic, with a higher frequency of DKA at DM diagnosis compared to prior years (Table 1). This suggests that pediatric patients were not presenting for medical attention with typical mild symptoms of new onset DM including polyuria, polydipsia, and weight loss, and that they were brought to medical attention after prolonged and more serious symptoms of DKA such as nausea, vomiting, abdominal pain, tachypnea, and altered mental status. One multicenter study similarly reported that more than 60% of patients with new onset Type 1 DM presented with DKA at the outset of the COVID-19 pandemic.<sup>9</sup> Our findings were also consistent with studies from around the world that observed a higher DKA frequency in children with new onset Type 1 DM during the beginning of the COVID-19 pandemic.<sup>10-22</sup> One study from Italy reported a decrease in new diagnoses of Type 1 DM in March and April 2020 compared to the pre-pandemic period,<sup>13</sup> similar to our findings, while 3 studies reported an overall increase in the diagnosis of Type 1 DM during the start of the pandemic.<sup>10,12,26</sup> Other studies reported no significant difference between the pandemic and pre-pandemic periods.<sup>15-18</sup>

Delays in the diagnosis of new onset diabetes likely contributed to the increased frequency of DKA seen at the time of DM diagnosis in Spring 2020. At the outset of the COVID-19 pandemic public health measures were enacted to prevent the spread of COVID-19 which resulted in major societal changes, as people were instructed to remain at home due to fear of contracting the virus. Fear of exposure to COVID-19 infection may have contributed to decreased usage of in-person medical services and delays in seeking medical care. Children and adolescents had school vacation and transitioned to virtual school during Spring 2020, so teachers and school nurses were also no longer observers who could recognize changes in thirst and drinking patterns.

Though not statistically significant, we found that a

smaller proportion of patients sought medical care prior to diagnosis of DM in 2020 compared to prior years, and those who did were more likely to have utilized telemedicine to access the health care system. These virtual evaluations may have resulted in missed symptoms and underestimation of the severity of illness. Similar patterns in delays in DM diagnosis during the COVID-19 pandemic have been recognized by many other groups around the world.<sup>9-11,15,18,20,27,</sup>

<sup>28</sup> An electronic survey conducted by the British Pediatric Surveillance Unit in April 2020 among pediatric consultants reported that 32% of the consultants observed later presentations of many pediatric diseases, and the most reported late presentation was new diagnosis of Type 1 DM or DKA.<sup>29</sup>

Delays in the diagnosis of DM increase the risk of DKA, which can lead to increased need for hospitalization, prolonged hospitalization, and devastating acute complications. The long-term impact of DKA is also a concern, as a single episode of moderate or severe DKA in young children at the time of DM diagnosis has been associated with lower cognitive performance scores compared to those with none/mild DKA.<sup>30</sup> Youth who present with DKA also have increased healthcare costs in the 60 days after DM diagnosis compared to those without DKA.<sup>31</sup>

The diagnosis of DM can be particularly challenging, as many of the symptoms of diabetes, including weight loss, fatigue, polyuria, polydipsia, tachypnea, abdominal pain, and vomiting can be seen with viral infections or other common childhood illnesses, and many health care providers may have been more attuned to viral symptoms during the initial COVID-19 surge. Health care providers may have also been falsely reassured by reports of robust drinking and urination, especially when described via telemedicine and without a physical examination that could document weight loss, as these symptoms can be misinterpreted as indications of a well hydrated child.

Our study is limited by small sample size and the retrospective nature of data collection. However, as the only dedicated pediatric hospital and pediatric intensive care unit in Rhode Island, our institution serves the entire state and our catchment area remained stable during the period of this study. The changes in DM diagnoses and DKA frequency likely reflect true diagnoses in the region and are unlikely to be due to diagnoses made at other institutions.

## CONCLUSIONS

Early identification of diabetes symptoms such as polyuria and polydipsia allow health care providers to provide immediate referral to pediatric diabetes services and early initiation of treatment before the development of acute diabetes complications such as DKA. Delays in health care evaluation and in recognition of DM symptoms of diabetes by families and health care providers at the start of the COVID-19 pandemic were likely key factors that led to a decline in

overall DM diagnoses and an increase in frequency of DKA at the time of DM diagnosis.

Raising awareness about classic DM symptoms of polyuria, polydipsia, and weight loss for both the public and health care providers is vital as development of these symptoms require recognition and further evaluation. Pediatricians, family medicine doctors, and other providers could ask about thirst, urination patterns and weight loss, especially when engaging in telemedicine, as measured weight information is typically not available. Medical providers and larger health care systems can also reach out to patients to inform them that access is available, especially for sick visits, when the typical healthcare system is disrupted. Timely assessment and intervention can help in reducing the risk of DM complications including DKA during future surges of COVID-19 or other events that impact the healthcare system.

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### Authors

Sabitha Sasidharan Pillai, MD, Division of Pediatric Endocrinology, Hasbro Children's Hospital, Department of Pediatrics, Hasbro Children's Hospital, The Warren Alpert Medical School of Brown University, Rhode Island Hospital.

Can Cao, BA, The Warren Alpert Medical School of Brown University.

Cassandra J. Drees, MD, Department of Pediatrics, Hasbro Children's Hospital, The Warren Alpert Medical School of Brown University, Rhode Island Hospital.

Tzu-ChunChu, MPH, Center for Statistical Sciences, Brown University.

Katherine Mason, MD, Department of Pediatrics, Hasbro Children's Hospital, The Warren Alpert Medical School of Brown University, Rhode Island Hospital.

Lisa Swartz Topor, MD, MMSc, Division of Pediatric Endocrinology, Hasbro Children's Hospital, Department of Pediatrics, Hasbro Children's Hospital, The Warren Alpert Medical School of Brown University, Rhode Island Hospital.

### Disclosures

None

### Correspondence

Lisa Swartz Topor, MD, MMSc  
Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903  
401-444-5504

[lisa\\_swartz\\_topor@brown.edu](mailto:lisa_swartz_topor@brown.edu)

# Meeting Gynecologic Needs and Assuring Adherence to Screening Guidelines at a Student-Run Free Clinic for Uninsured, Low-Income Women

JOHANNA A. SUSKIN; KATHERINE BARRY; ELLA SATISH; MORGAN LEONARD; ANNE S. DE GROOT, MD

## ABSTRACT

**BACKGROUND:** Uninsured, low-income, Spanish-speaking patients face barriers to obtaining gynecologic care in the United States. Clínica Esperanza/Hope Clinic, a free clinic in Rhode Island, hosts a biweekly Women's Clinic (WC) established and run by local medical students.

**METHODS:** A retrospective chart review identified gynecologic services provided, needs met and adherence to screening guidelines at WC between June 2017 and May 2021.

**RESULTS:** During 80 clinics, 278 patients were seen. 362 encounters occurred, with 288 missed appointments. Women primarily attended WC for routine care (159, 43.9%) or abnormal uterine bleeding (41, 11.3%). Common services provided include gynecologic exams (302, 27.0%), Pap smears (221, 19.7%), and STI screening (166, 14.8%). Pap smear and mammography guidelines were adhered to during 92.3% and 94.1% of visits, respectively.

**CONCLUSIONS:** Accessible gynecologic care is a significant unmet need for uninsured, Spanish-speaking patients. These findings demonstrate the importance of gynecologic care at free clinics and warrant their expansion.

**KEYWORDS:** free clinic, gynecology, screening, uninsured

## INTRODUCTION

In recent years, disparities in healthcare access, quality, and outcomes in the US have moved to the forefront of public health and medical literature.<sup>1,2</sup> Reasons driving these inequities are multifactorial and incompletely understood, but individual and structural barriers play a role.<sup>3</sup> Structural inequities built into the healthcare system result in some patients experiencing advantages and others experiencing disadvantages in accessing and receiving care, based on their interacting identities and social determinants of health.

Lack of access to quality care is particularly common among patients seeking preventative gynecologic services, which can lead to disparities in outcomes and preventable poor outcomes for vulnerable populations. Patients without access to gynecologic primary care often forgo important, recommended cancer screenings and other preventative

Table 1. ACOG Screening Guidelines

Service	Age Group	Frequency
Pap smear	21–29	Every 3 years (cytology alone)
	30–65	Every 5 years (with HPV co-testing) OR every 3 years (cytology alone)
Mammogram	50–74 (with shared provider-patient decision making for ages 40–49)	Every 2 years

services. The breast and cervical cancer screening guidelines from the American College of Obstetricians and Gynecologists are included in **Table 1**.<sup>4,5</sup>

Clínica Esperanza/Hope Clinic (CEHC) is a non-profit free clinic which has provided medical care to uninsured Rhode Island residents since 2007. CEHC's serves a vulnerable, low-income Spanish-speaking population and its work and mission has been described previously.<sup>6–8</sup>

CEHC is open six days per week, offering both walk-in and scheduled visits in primary care and specialty clinics. Some of these clinics are organized by local medical and physician assistant students, which bring selected specialty clinics and resources to CEHC's patients. Among the most prominent of these specialty clinics is Women's Clinic (WC), established and run by medical students from The Warren Alpert Medical School of Brown University. Former medical students Natasha Kumar and Gabriele DuVernois founded WC in 2015 with the goal of providing quality gynecologic care to CEHC patients who otherwise lack access. Their publication on the establishment of this student-run and grant-funded "clinic within a clinic" illustrates how medical students can improve access to healthcare within an existing free clinic structure.<sup>9</sup>

CEHC WC offers a range of routine/preventive, infection-related, reproductive, and other services. Preventive services include gynecologic and breast exams, Pap smears, mammography referrals, and HPV vaccination; infection-related services include STI screening (gonorrhea/chlamydia testing, syphilis testing, and HIV testing), vaginitis screening, urinalysis and/or culture; contraceptive services include contraceptive counseling, IUD insertion and removal, OCP prescription, Depo-provera injection, infertility counseling, and urine pregnancy testing. Preliminary data from

2015–2017 regarding the gynecologic needs of this population and the WC team's ability to meet those needs was previously published.<sup>9</sup> This study aims to provide an update since the end of the prior study period and describe the accomplishments of CEHC WC through May 2021. Additionally, it seeks to assess the quality of care that CEHC WC patients receive by assessing adherence to screening guidelines.

## METHODS

The electronic medical record (EMR) database was queried to identify patients who received gynecologic care at WC appointments between June 2017 and May 2021. A chart review was performed to identify demographic data, including age and language, as well as clinical data. This included the primary reason for the visit, needs addressed during the visit, and tests performed or ordered. These findings were aggregated to determine rates of service utilization. This is the same eClinicalWorks EMR that was used for the chart review published in 2019, and records were not standardized between providers.<sup>9</sup>

Based on a patient's age and history of screenings, it was also determined if they were receiving guideline-adherent Pap smears and mammograms. Pap smears, which are performed in clinic, were considered up-to-date if a patient aged 21–29 had received a standard Pap (cytology only) in the past three years. Patients 30 or older were up-to-date if they had a Pap with high-risk HPV co-testing in the past 5 years.<sup>4</sup> Mammography was considered up-to-date if a patient over the age of 50 had received a referral to get their mammogram within the past two years.<sup>5</sup>

## RESULTS

As shown in **Table 2**, the mean age of 278 WC patients was 40.6 years. Most were Spanish-speaking (91.4%), with other primary languages including English (5.8%), Hindi, French, Quiche, Haitian Creole, or Cape Verdean (each <1%). All patients were uninsured at the time of visit, as is required to be eligible for WC. Eighty clinics took place, serving 278 unique patients (**Table 3**). In all, 650 encounters were scheduled with 362 completed. The patients who missed 288 encounters did not show without explanation (no-show, 161), canceled (74), or rescheduled (53). The missed encounter rate consistently decreased throughout the study, decreasing from 106 from June 2017 through May 2018 to 52 from June 2020 through May 2021, despite inconsistent scheduling of the clinic due to COVID-19.

CEHC WC offers consultation for gynecologic, breast, and urologic complaints (**Table 4**). Patients' reasons for attending visits included routine care (159), abnormal uterine bleeding (41), pelvic pain (34), vaginitis (28), contraception counseling (17), infertility (10), genital lesions (10), STI testing (5), and amenorrhea (2). These totals represent the primary reason for

**Table 2.** Demographics

Age, mean (sd)	40.6 (11.1)		
Primary Language, n (%)			
Spanish	254	91.4%	254 (91.4%)
English	16	5.8%	16 (5.8%)
Hindu	2	0.7%	2 (0.7%)
French	2	0.7%	2 (0.7%)
Quiche	2	0.7%	2 (0.7%)
Haitian Creole	1	0.4%	1 (0.4%)
Cape Verdean Creole	1	0.4%	1 (0.4%)

**Table 3.** Visit Characteristics

	Total	June 2017– May 2018	June 2018– May 2019	June 2019– May 2020*	June 2020– May 2021
Number of Clinics	80	24	23	14	19
Number of Scheduled Encounters	650	190	177	128	155
Number of Completed Encounters	362	84	102	73	103
Number of Missed Encounters	288	106	75	55	52
No show	161	62	41	36	22
Canceled	74	33	17	13	11
Rescheduled	53	11	17	6	19
Number of Patients Seen	278	75	88	69	91

the visit as stated by the patient; many women who came in for one need also had others addressed. For example, patients who came in for a routine visit often received incidental STI testing or contraception counseling. Breast complaints addressed include breast mass (5) and breast pain (3), and urologic complaints include dysuria/change in frequency/urgency (10) and incontinence (4). Follow-up appointments (34) addressed a range of topics; insufficient Pap smears were the most common reason for a repeat visit.

Routine tests, exams, and infection screening were among the most common services provided. Among the most frequently offered were gynecologic exams (302), STI screening tests including gonorrhea/chlamydia, syphilis, and/or HIV testing (166), breast exams (121), mammograms (87), and vaginitis screenings (71). Most patients received multiple services per visit. Referrals were also documented to services and clinics including urogynecology, gynecologic oncology, pregnancy care, and procedures like polyp removal, Nexplanon removal, colposcopy, and complex IUD removal, which could not be offered at CEHC WC.

**Table 4.** Women's Health Needs Met

	Total	June 2017– May 2018	June 2018– May 2019	June 2019– May 2020	June 2020– May 2021
<b>Gynecologic Complaints</b>					
Routine visit (including cancer screenings and/or exam)	159	23	46	43	47
Abnormal uterine bleeding	41	11	8	6	16
Pelvic pain	34	11	13	8	2
Vaginitis	28	9	11	4	4
Contraception counseling	17	4	5	2	6
Infertility	10	5	1	1	3
Amenorrhea	2	1	0	0	1
Genital lesion	10	3	2	2	3
STI testing	5	3	1	0	1
<b>Breast Complaints</b>					
Breast mass	5	2	0	0	3
Breast pain	3	1	1	1	0
<b>Urologic Complaints</b>					
Dysuria/change in frequency/urgency	10	6	1	1	2
Incontinence	4	1	2	0	1
<b>Other</b>					
Follow-up	34	4	11	5	14

Regarding Pap screening, ACOG guidelines were adhered to at 92.3% of visits and USPSTF mammogram guidelines were adhered to at 94.1% of visits. Reasons for non-adherence to the guidelines included patient requesting exam deferral (6) or inability to tolerate due to pain (2). In 16 instances, the reason for not performing a Pap was not documented. Reason for lack of adherence to mammography guidelines was not documented in any instance where it occurred.

Details on the number of health needs met and services provided are shown in **Table 4** and **Table 5**. While the quantity of routine visits increased over the four years of this study, the relative distribution of reasons for the visits remained largely stable. The types of services provided were also consistent over time except for IUD insertion/removal and Depo-provera shot, both of which were implemented during the fourth year of study. The quantity of referrals to outside clinics increased throughout the study.

## DISCUSSION

The number of medical-student run clinics has increased significantly in the US in recent years, with a growing

**Table 5.** Services Provided

	Total	June 2017– May 2018	June 2018– May 2019	June 2019– May 2020	June 2020– May 2021
<b>Routine Tests/Exams</b>					
Gynecologic exam	302	71	84	60	87
Pap smear	221	46	67	52	56
Breast exam	121	44	48	12	17
Mammogram	87	24	24	19	20
<b>Infection</b>					
STI screening	166	43	44	31	48
Gonorrhea/chlamydia testing	155	39	39	30	47
Syphilis testing	23	4	4	6	9
HIV testing	22	4	4	6	8
Vaginitis screening	71	24	19	12	16
Wet mount	23	9	5	1	8
Urinalysis and/or culture	22	6	3	6	7
<b>Reproduction</b>					
Contraceptive counseling	78	15	16	11	36
IUD	8	0	0	0	8
Insertion	2	0	0	0	2
Removal	5	0	0	0	5
Insertion + Removal	1	0	0	0	1
OCP prescription	28	7	7	6	8
Depo-Provera shot	4	0	0	0	4
Urine pregnancy testing	17	4	3	5	5
Infertility counseling/evaluation	20	9	3	3	5
<b>Other</b>					
HPV vaccine	11	1	5	5	0
Referrals to outside clinics	34	6	8	2	18

literature base endorsing this structure as an effective means of providing uninsured patient populations with long-term, quality healthcare. This clinic model is critically important for providing access to gynecologic care and corresponding specialized services that are harder to obtain than routine medical care.<sup>10,11</sup>

The demographics of patients attending CEHC WC are largely unchanged from those documented from 2015-2017 (Table 2), with a mean age of 40.6 and the vast majority of patients speaking Spanish.<sup>9</sup> The rate of missed encounters decreased since the prior study period, going from 50.7% to 44.3%, while the number of completed encounters per year remained consistent (Table 3).<sup>9</sup> It is important to note that the COVID-19 pandemic began during the June 2019-May 2020 year, during which time CEHC transitioned to telemedicine appointments for some clinic visits, in an effort to mitigate COVID risks. This ultimately led to a reduced number of services during the affected years. Surprisingly, no-show rates decreased during the COVID-19 pandemic. While telemedicine appointments were not offered to WC patients due to the nature of the specialty visit, it is possible that increased contact with patients before their appointments in the form of COVID contact and symptom screening may have served as an additional appointment reminder.

Despite the pandemic setting, the number of patients and services provided over the study period remained roughly stable from the prior study period. Improvements that were implemented since the publication of the prior study include the formalization of protocols for waitlist management, follow-ups, and specialty referrals.<sup>12</sup> Services that have been added to the clinic in the interim include IUD insertion and Depo-provera shot.

During this study period, routine care continued to be the most common reason for visits, underscoring the role of this clinic in providing preventive health care for WC patients (Table 4). The number of Pap smears per year increased from 41 in the prior study period to 55 in the most recent analysis (Table 5).<sup>9</sup> There was a large increase in the quantity of STI testing completed from the prior study (35 patients had gonorrhea/chlamydia testing over 2 years) to this study (155 gonorrhea/chlamydia tests, 23 syphilis tests, and 22 HIV tests were performed over four years). This contrast could be explained by increased offering of such tests by providers, and merits further exploration. In the future, screening efforts may be strengthened by offering STI screening to every patient, as part of WC protocol. These and other metrics described in this report also highlight the continued need for access to gyn care for uninsured women.

Various studies have documented disparities in access to cervical and breast cancer screening, identifying student-run free clinics as an effective means of increasing access.<sup>10,13,14</sup> Cervical cancer screening is among the most difficult to obtain, given the training required to perform these procedures. CEHC WC is the only clinic where many of its patients can receive preventive and routine gynecologic care; the 92.3% adherence rate to Pap smear guidelines is a testament to the high quality of care provided. Of note, Pap smear guidelines changed during the period studied. However, since the guidelines were relaxed during this time, this increased the number of patients who received

guideline-consistent care from their WC providers.<sup>4</sup>

The literature has consistently identified lower rates of mammography screening among uninsured patients as compared to those who are insured.<sup>13</sup> Thus, WC's 94.1% mammography adherence rate underscores the effectiveness of free clinics in substantially increasing access to such services. However, this rate is based on rates of appropriate orders being sent, which does not measure how many patients received mammograms and followed up on results. Future studies will gather this information.

Despite WC's increasing success in providing gynecologic care to patients who otherwise lack access, it is crucial to consider barriers that continue to preclude the receipt of such services. This primarily involves social determinants of health, including but not limited to access to transportation, cost, language barriers, and lack of education for this particular patient population.<sup>15</sup> CEHC and WC continue to combat these barriers and extend care, most recently in the context of the challenges imposed by the COVID-19 pandemic.

The retrospective nature of this study is an intrinsic limitation, as potential outcomes of interest to analyze were limited to those already present in patient charts. Another limitation is the fact that the clinic is comprised of multiple volunteer preceptors who have slightly different documentation styles, resulting in a lack of standardization of charting. However, this study provides valuable insight into the impact of free clinics such as WC on expanding gynecologic care. Findings build on prior research, underscoring the need for continued expansion of gynecologic health services to uninsured, low-income populations. Further research efforts should continue to identify and address the many barriers to obtaining gynecologic services, with the goal of improving access for the community and developing culturally specific interventions to combat them.

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### Authors

Johanna A. Suskin, The Warren Alpert Medical School of Brown University, Providence, RI.

Katherine Barry, The Warren Alpert Medical School of Brown University, Providence, RI.

Ella Satish, The Warren Alpert Medical School of Brown University, Providence, RI.

Morgan Leonard, Clínica Esperanza/Hope Clinic, Providence, RI.

Anne S. De Groot, MD, Clínica Esperanza/Hope Clinic, Providence, RI; EpiVax, Inc., Providence, RI.

### Correspondence

Anne S. De Groot, MD  
[annied@aplacetobehealthy](mailto:annied@aplacetobehealthy)

# Characterization of Shoulder Instability in Rhode Island: Incidence, Surgical Stabilization, and Recurrence

J. ALEX ALBRIGHT, BS; OZAIR MEGHANI, MS; NICHOLAS J. LEMME, MD; BRETT D. OWENS, MD

## ABSTRACT

**PURPOSE:** To characterize shoulder instability within the state of Rhode Island from 2011 to 2019.

**METHODS:** The Rhode Island All-Payer Claims Database (APCD) was used to identify all patients that make an insurance claim related to a shoulder instability event. All patients in the APCD with an ICD-9 code of 718.31, 718.32, or 831.00 through 831.19 or an ICD-10 code of S43.001 through S43.086 or M24.41 through M25.319 between January 1, 2011 and December 31, 2019 were selected. Chi-square analysis was used to compare age- and sex-delimited subgroups; multivariate logistic regression was used to assess for factors influencing rates of surgical intervention and recurrent instability; and Kaplan-Meier failure and log-rank analyses was used to analyze variation in the time to surgery and recurrence between age-delimited subgroups.

**RESULTS:** The incidence of overall shoulder instability (subluxations and dislocations) in Rhode Island was 62.20 instability events (95% CI, 60.61–63.78) per 100,000 person-years. The incidence of dislocations and subluxations were 49.46 injuries (95% CI, 48.05–50.88) and 12.73 injuries (95% CI, 12.02–13.45) per 100,000 person-years, respectively. Bivariate analysis demonstrated that male patients had significantly increased rates of surgical stabilization (6.36% vs. 2.80%) and recurrent instability (16.30% vs. 9.85%) compared to their female counterparts. However, after controlling for age at the primary instability event and the type and directionality of the instability, the difference in recurrence rates between males and females is no longer statistically significant ( $p = 0.326$ ). Contrary to sex, age maintained its significance with those patients aged 20 and younger and 21–40 years at significantly increased odds of surgical stabilization (3.12 and 1.99, respectively) and experiencing a recurrent instability event (3.96 and 2.77, respectively).

**CONCLUSION:** These data characterize the epidemiology of shoulder instability within the state of Rhode Island and demonstrate how increasing age at a primary instability event decreases the likelihood of both surgical stabilization and rates of recurrence.

**KEYWORDS:** shoulder instability, glenohumeral instability, epidemiology, recurrent instability, surgical stabilization

## INTRODUCTION

Due to the wide functional range of motion and lack of bony restraint, glenohumeral joint instability is common in the general U.S. population and reaches near endemic levels in young athletes.<sup>1–3</sup> Reported rates of the general population have ranged from 12 to 56 dislocations per 100,000 person-years, with rates reaching as high as 169 dislocations per 100,000 person-years among the United States Military.<sup>1,3,4</sup> Active individuals who experience a primary shoulder instability event are at significantly increased risk of subsequent instability due to the associated soft tissue and/or osseous injuries that occur at the time of the instability event and therefore, often require surgical stabilization to decrease the risk of recurrent instability.<sup>5–7</sup> In younger patients, these injuries often result in significant time loss from participation in athletics, while in older patients, they may limit their ability to exercise and complete their activities of daily living.<sup>8</sup> The long-term complications of glenohumeral instability are also significant as these patients are at increased risk for cumulative damage to the glenohumeral joint increasing the risk for future osteoarthritis.<sup>9–11</sup>

Rhode Island's All-Payer Claims Database (APCD) is part of the Rhode Island Department of Health's effort to identify healthcare quality and health outcome improvement opportunities. These data are gathered from health insurance payments made throughout the state, capturing health data for approximately 1.06 million patients.<sup>12</sup> The purpose of this study was to determine and characterize the incidence of shoulder instability and its management in the state of Rhode Island to help inform healthcare providers in the state to limit both short- and long-term complications of shoulder instability.

## METHODS

### Data Source

The Rhode Island All-Payer Claims Database (APCD) was used in this study. This database includes all healthcare insurance payment information for all people with health insurance living in Rhode Island. This information includes demographics and health status, medical services, emergency department visits, pharmacy claims, associated International Classification of Disease, Ninth and Tenth Revisions (ICD-9, ICD-10) and Current Procedural Terminology (CPT)

codes, as well as general demographic information on the rendering providers. This database does not include information on patients without health insurance and claims by small insurance companies with less than 3000 members. According to the Kaiser Family Foundation, 4.8% of Rhode Islanders were uninsured in 2018.<sup>13</sup> In aggregate, this database includes data on about 95% of Rhode Islanders that make a medical claim within the state of Rhode Island.

### Patient Selection

All patients in the APCD with an ICD-9 code of 718.31, 718.32 or 831.00 through 831.19 or an ICD-10 code of S43.001 through S43.086 or M24.41 through M25.319 were selected. These diagnosis codes represent all codes for shoulder dislocation or subluxation and recurrent instability events of the shoulder. Patients that presented between January 1, 2011 and December 31, 2019 were included in the study. All claims made with traditional Medicare Fee-For-Service (FFS) were excluded (14% of the state population) from the study as per the state's directive, but all Medicare Advantage recipients (40% of the Rhode Island Medicare beneficiaries) were included in the analysis.<sup>13</sup> Following all exclusions, this study included over 80% of Rhode Islanders that made a medical claim between January 1, 2011 and December 31, 2019.

### Statistical Analysis

Multivariate logistic regression was used to calculate odds ratios and 95% confidence intervals for all variables of interest and linear regression was used to assess trends in the incidence of shoulder instability. U.S. Census data was used to calculate at-risk person-years for both the greater Rhode Island population and the age and sex delimited subgroups. Kaplan-Meier failure and log-rank analyses were used to assess for significant differences between the rate of recurrence and surgical stabilization between subgroups. Thirteen patients underwent multiple surgical procedures over the study period and were treated as a single data point for surgical stabilization analysis.

## RESULTS

The query of the APCD yielded 5,930 patients who experienced a shoulder instability, event in Rhode Island between January 1, 2011 and December 31, 2019 and an associated 30,979 medical claims. This includes primary subluxation and dislocation, as well as recurrent instability. Of the 5,930 patients, 1,160 presented with recurrent instability following a primary dislocation or subluxation from before the study period, while the remaining 4,770 patients presented with primary shoulder instability (Table 1). Over 80% of these cases were dislocations (4,714) and just under 30% presented with anterior instability (64.8% had direction not specified in the database). The overall incidence rate of shoulder instability within Rhode Island during the study period was 62.20

**Table 1.** Characteristics of initial documented instability events within the state of Rhode Island from January 1, 2011 to December 31, 2011.

	Number of Cases	Proportion (95% CI)
<b>Type of Instability</b>		
Subluxation	1,214	20.47 (19.46–21.52)
Dislocation	4,716	79.53 (78.48–80.54)
<b>Directionality</b>		
Anterior	1,399	29.93 (28.64–31.26)
Posterior	147	3.15 (2.68–3.69)
Inferior	100	2.14 (1.76–2.60)
Not Specified	3,028	64.78 (63.40–66.14)
<b>Primary or Recurrent</b>		
Primary*	4,770	80.44 (79.41–81.43)
Recurrent	1,160	19.56 (18.57–20.59)
<b>Surgical Stabilization</b>		
Surgery	287	4.84 (4.32–5.42)
No Surgery	5,643	95.16 (94.58–95.68)

\*646 Patients experienced a recurrent instability event during the study period.

**Table 2.** Multivariate logistic regression analysis of independent factors that influence the likelihood of surgical stabilization and recurrent instability.

Variable	Surgery		Recurrent Instability	
	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Type of Instability</b>				
Subluxation	Reference	N/A	Reference	N/A
Dislocation	1.29 (0.74–2.25)	0.362	1.56 (1.15–2.10)	0.004
<b>Directionality</b>				
Anterior	3.67 (0.48–28.20)	0.211	0.98 (0.50–1.92)	0.959
Posterior	4.19 (0.50–35.32)	0.187	0.63 (0.28–1.42)	0.271
Inferior	Reference	N/A	Reference	N/A
Not Specified	1.90 (0.25–14.58)	0.537	0.62 (0.32–1.21)	0.165
<b>Primary or Recurrent</b>				
Primary	Reference	N/A	N/A	N/A
Recurrent*	6.61 (4.74–9.21)	< 0.001	N/A	N/A
<b>Sex</b>				
Male	1.49 (0.99–2.23)	0.055	1.11 (0.91–1.35)	0.326
Female	Reference	N/A	Reference	N/A
<b>Age</b>				
Under 21	3.12 (1.84–5.28)	< 0.001	3.96 (2.98–5.25)	< 0.001
21 to 40	1.99 (1.16–3.42)	0.012	2.77 (2.08–3.67)	< 0.001
41 to 60	Reference	N/A	Reference	N/A

\*Recurrent includes both patients who initially presented with a recurrent instability event and those who experienced a recurrent instability event following a primary instability event.

injuries (95% CI, 60.61–63.78) per 100,000 person-years. The incidence rates of dislocations and subluxations were 49.46 injuries (95% CI, 48.05–50.88) and 12.73 injuries (95% CI, 12.02–13.45) per 100,000 person-years, respectively (Table 2). Excluding all recurrent instability events, the incidence rate of primary instability (including subluxations and dislocation) was 50.03 injuries (95% CI, 48.61–51.45) per 100,000 person-years.

Male sex predominated with 3,394 (57.2%) of the total number of cases and the mean age was 44.16 ±23.9 years and ranged from 1 to 90 years. The incidence rate of shoulder instability in males was 73.13 (95% CI, 70.67–75.69) injuries per 100,000 person-years, compared to 51.83 (95% CI, 49.81–53.84) injuries per 100,000 person-years in females, yielding an incidence rate ratio of 1.41 (95% CI, 1.34–1.49). The peak incidence rate occurred in 2016 (75.9, 95% CI, 70.6–81.1), while the lowest incidence rate during the study period came in 2013 (51.3, 95% CI, 46.9–51.3). There was no significant change in the overall incidence of shoulder instability in Rhode Island during the study period (p = 0.058). The incidence of shoulder instability in males was also unchanged (p = 0.767), but the incidence of shoulder instability in females has significantly increased linearly (at a rate of 3.5 injuries per 100,000 person-years) across the study period (p = 0.012).

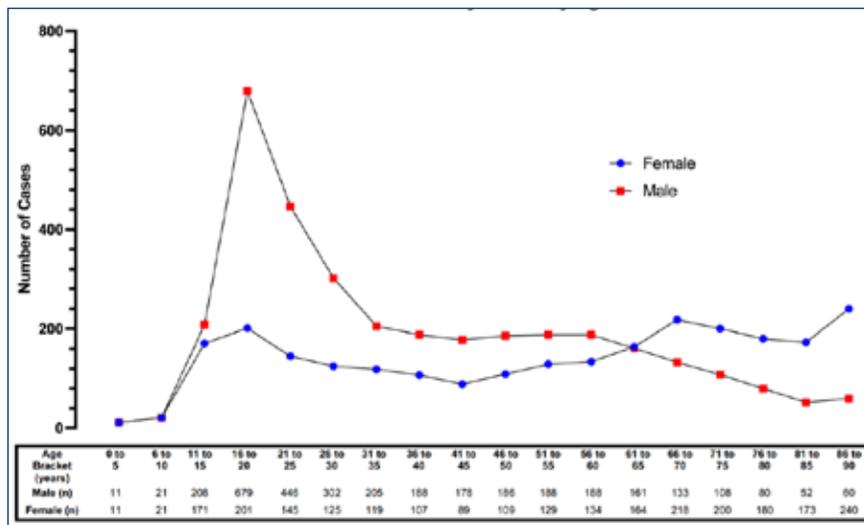
Just over 43% of the cases of shoulder instability occurred in patients aged 11 to 30 years. In males, 54.2% of the cases fell within this age bracket, compared to 30.0% in females (p < 0.001). The cases of shoulder instability gradually declined after the age of 60 in males, whereas in females, a second peak of cases occurred between the ages of 66 and 90 (Figure 1). The incidence of shoulder instability also differed significantly between age groups. The incidence rates within the

20 and younger, 21–40, and 41–60 age groups was 57.54 (95% CI, 54.44–60.64), 63.74 (95% CI, 60.65–66.83), and 48.81 (95% CI, 46.05–51.57), respectively (Table 2). Of note, the specific incidence rates for the 61–80 and 81 and older age group are not reported as their values likely underrepresent the true incidence as Medicare FFS recipients were excluded from the study.

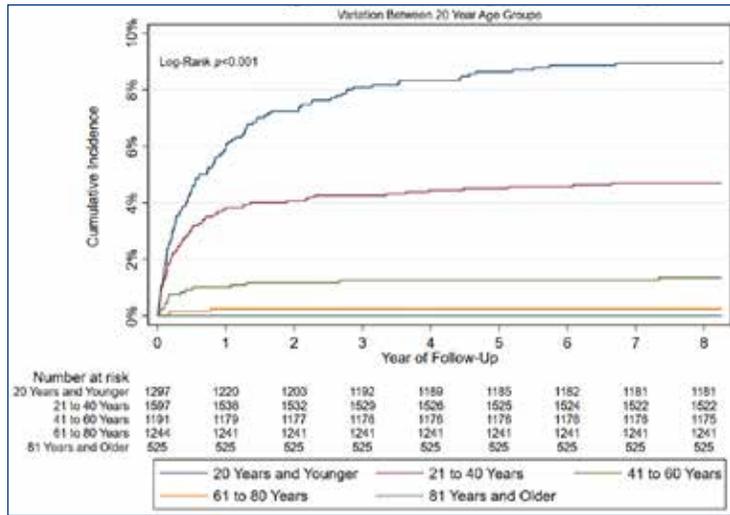
Of the 5,930 patients who experienced shoulder instability during the study period, 287 received surgical stabilization (4.84%, 95% CI, 4.32–5.42%). This percentage differed significantly depending on the sex of the patient. Males received surgical intervention at a rate of 6.36% (95% CI, 5.54–7.19%), compared to 2.80% in females (95% CI, 2.16–3.44) (p < 0.001). Of the 4,770 patients who presented with a primary instability event during the study period, 13.54% (95% CI, 12.60–14.54%) experienced recurrent instability. This rate also significantly differed depending on the sex of the patient. In males, 16.30% (95% CI, 14.91–17.69%) experienced recurrent instability, compared to 9.85% in females (95% CI, 8.56–11.15%) (p < 0.001). However, after using a multivariate logistic regression model to control for age, type of instability, and directionality of instability, the difference in likelihood of experiencing recurrent shoulder instability between males and females was no longer statistically significant (p=0.326). Recurrent instability was 6.61 times more likely to receive surgical stabilization compared to primary instability (p < 0.001) (Table 2). Patients in the 20 and younger and 21–40 years age groups were 3.12 (95% CI, 1.84–5.28) and 1.99 (95% CI, 1.16–3.42) times more likely to receive surgery than those aged 41–60 (p < 0.001 and p = 0.012, respectively). As for rates of recurrent instability, recurrence in those 20 years and younger or 21–40 years old were 3.96 (95% CI, 2.98–5.25) and 2.77 (95% CI, 2.08–3.67) times more likely compared to those aged 41–60 (p < 0.001 for both).

Kaplan-Meier failure analysis and log-rank testing further corroborated this finding with the youngest age group experiencing the highest percentage of both surgical stabilization (p < 0.001) and recurrent instability (p < 0.001) (Figures 2a and 2b). Table 3 shows the cumulative rates of surgical stabilization and recurrent instability at 30 days, 6 months, and 1 through 5 years after the initial presentation during the study period. At 1-year post-primary dislocation or subluxation, 5.9% of patients 20 years or younger received surgical stabilization to address their glenohumeral instability, compared to just 1.0% in patients aged 41 to 60 years. Similarly, 15.0% of patients 20 years or younger experienced

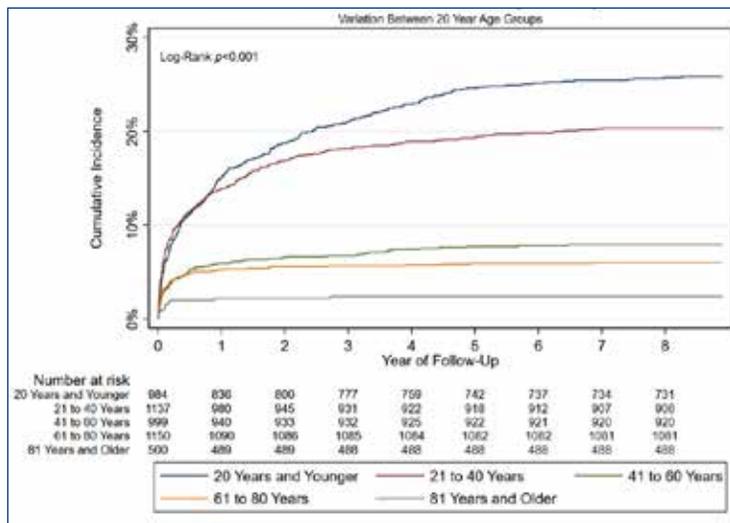
**Figure 1.** Age distribution of shoulder instability cases over five-year age brackets stratified by sex. This figure demonstrates the predominance of cases occurs in young adult males. After the age of 60, the number of cases in males begins to decrease, while the number of cases in females begins to peak for a second time.



**Figure 2a.** Kaplan-Meier Failure Analysis with log-rank analysis overlaid. The figure is depicting the cumulative percentage of surgical stabilization over time for each age-delimited subgroup.



**Figure 2b.** Kaplan-Meier Failure Analysis with log-rank analysis overlaid. The figure is depicting the cumulative percentage of recurrent dislocations following a primary instability event over time for each age-delimited subgroup.



recurrent instability within a year, compared to 5.9% of patients aged 41 to 60 years. Of note, those patients whose first claim within the APCD was either for surgical stabilization (76 patients) or recurrent instability (1,160 patients) were excluded from the Kaplan-Meier and log-rank analyses since their time to event was zero days.

**DISCUSSION**

Using the Rhode Island All-Payer Claims Database, we determined the incidence rate of shoulder instability within the state of Rhode Island to be 62.20 injuries (95% CI, 60.61–63.78) per 100,000 person-years, with the incidence of

**Table 3.** Cumulative surgical stabilization and recurrent instability rates using the Kaplan-Meier method over 20-year age groups.

Surgical Stabilization					
Time to Event	20 and Younger (%)	21 to 40 Years (%)	41 to 60 Years (%)	61 to 80 Years (%)	81 Years and Older (%)
30 days	1.3	1.2	0.3	0.0	0.0
6 months	4.5	3.1	0.9	0.2	0.0
1 year	5.9	3.8	1.0	0.2	0.0
2 years	7.2	4.1	1.2	0.2	0.0
3 years	8.1	4.3	1.3	0.2	0.0
4 years	8.3	4.4	1.3	0.2	0.0
5 years	8.6	4.5	1.3	0.2	0.0
Recurrent Instability					
Time to Event	20 and Younger (%)	21 to 40 Years (%)	41 to 60 Years (%)	61 to 80 Years (%)	81 Years and Older (%)
30 days	5.0	6.1	2.8	3.1	1.0
6 months	11.2	11.4	5.2	4.8	2.0
1 year	15.0	13.8	5.9	5.2	2.2
2 years	18.7	16.9	6.6	5.6	2.4
3 years	21.0	18.1	6.7	5.7	2.4
4 years	22.9	18.9	7.4	5.7	2.4
5 years	24.6	19.3	8.1	5.9	2.4

dislocations and subluxations at 49.46 injuries (95% CI, 48.05–50.88) and 12.73 injuries (95% CI, 12.02–13.45) per 100,000 person-years, respectively. The incidence of shoulder dislocations is on par with previously reported incidence rates for the general U.S. population. Zachilli and Owens reported an incidence rate of 23.9 dislocations per 100,000 person-years, with estimates in Canada (23.1 dislocations per 100,000 person-years), Denmark (12.3 dislocations per 100,000 person-years), Sweden (27.5 dislocations per 100,000 person-years), and Norway (56.3 dislocations per 100,000 person-years) also suggesting the burden of shoulder instability is significant.<sup>1,14-16</sup> To understand the near-endemic level of these injuries, this reported incidence of shoulder dislocations (49.46 injuries per 100,000 person-years) is greater than 9 times that of elbow dislocations (5.21 injuries per 100,000 person-years), although it still lags behind other common musculoskeletal injuries like ankle sprains (215 injuries per 100,000 person-years).<sup>17,18</sup> While shoulder dislocations may have a lesser burden on the general U.S. population compared to injuries like ankle sprains, in young, active populations and the military, the incidence of shoulder dislocations increases to 169 injuries per 100,000 person-years or greater.<sup>2,3</sup>

The present study reports an incidence rate of shoulder dislocations that is over double that previously reported within the general U.S. population. This may be the result of Zacchilli and Owens reporting the incidence of shoulder dislocations in the U.S. using emergency department gathered data.<sup>1</sup> The present study captures data from emergency departments within the state of Rhode Island as well as those patients who present directly to their primary care physician or a sports medicine specialist, likely capturing a greater proportion of the shoulder instability and increasing the incidence rate. However, like Zacchilli and Owens, this study was unable to capture athletes who presented to athletic trainers within their respective facilities, likely leading to an incidence rate that underrepresents the true burden of shoulder instability.<sup>1</sup> While the present study did include glenohumeral subluxations, these accounted for only 20.47% of all instability events, a previous study described subluxations accounting for 85% of all glenohumeral instability.<sup>19</sup> This suggests the vast majority of patients with shoulder subluxations are electing to not seek medical care, likely leading to a dramatically underdiagnosed number of subluxations.

Sex as a nonmodifiable risk factor for glenohumeral instability has long been described with much of the literature reporting significantly increased incidence among males when compared with females.<sup>5,9,20,21</sup> However, emerging data suggests when males and females participate in sports with similar risk exposure, the incidence of shoulder instability is also similar.<sup>9</sup> Peck *et al.* reported nearly identical rates of glenohumeral instability in male and female rugby athletes and Owens *et al.* reported the same among males and females participating in collegiate soccer, basketball, baseball/softball, and hockey.<sup>22,23</sup> This study initially demonstrates a significant difference between the incidence of shoulder instability among males and females (**Table 2**). The incidence of shoulder instability in males was 73.13 (95% CI, 70.67–75.69) injuries per 100,000 person-years, compared to 51.83 injuries (95% CI, 49.81–53.84) in females (IRR = 1.41, 95% CI, 1.34–1.49,  $p < 0.05$ ). On a pure percentage of recurrence basis, males experienced recurrent instability 65.5% more often than their female counterparts. However, when controlling for type of instability, directionality, and age at primary instability, sex as a risk factor of recurrent instability loses its significance. This information agrees with the emerging literature that suggests sex may not be as significant of a risk factor as once believed.

Of the 5,930 patients included in this study, 287 (4.84%) had surgical stabilization of the shoulder. This surgical stabilization rate is higher than that reported by Bokshan *et al.* (3.47%) who analyzed similar data within the state of Florida.<sup>24</sup> This is likely the result of the present study having a larger proportion of patients with recurrent instability, which is a higher risk population that often receives surgical intervention at increased rates compared to those

with primary instability. Males (6.36%) and females (2.80%) received surgical intervention at significant different rates. Olds *et al.* in a meta-analysis of risk factors for recurrent dislocation describe males having over a three-fold increase in risk of recurrent dislocation compared to females.<sup>25</sup> As research has shown that males and females of similar age and level of activity experience recurrent instability at similar rates, this discrepancy may be the result of surgeons being cautious with the young, male population. Since research regarding sex as a significant risk factor of recurrent instability has been inconsistent up to this point, surgeons are likely going to be more willing to perform surgery to limit the likelihood of recurrence in a population that has been shown in some research to be at increased risk.

Regarding recurrent instability, 1,806 of the 5,930 patients (30.46%) experienced a recurrent instability event during the study period. However, 1,160 of these patients initially presented during the study period with recurrent instability, while the remaining 646 patients initially presented with a primary instability event and subsequently redislocated during the study period. When considering the population who presented during the study period with primary instability, 13.54% experienced recurrent instability. Wasserstein *et al.* reported a pooled rate of recurrence after primary shoulder instability to be higher at 21% (range: 19% to 88%).<sup>26</sup> This may be the result of the Wasserstein study excluding those patients aged 12 years or younger and having an increased percentage of younger aged males, both of which would lead to higher reported rates of recurrence. Similar to the present study, Wasserstein *et al.* describe age at the time of primary glenohumeral instability as one of the most important prognostic factors for recurrent instability.<sup>26</sup> The current study found both age and initial dislocation (compared to subluxation) to be significant risk factors for recurrent instability, but unlike the Wasserstein study, sex was not a statistically significant risk factor.

Further analysis was done to compare rates and cumulative percentages of patients who received surgical stabilization and those who experienced recurrent instability dependent on age (**Figures 2a** and **2b**). This study demonstrates a significant difference in both the timing and cumulative percentage of surgical stabilization and recurrent instability among different 20-year age groups. The management of primary glenohumeral instability remains controversial as many physicians elect to reserve surgery for those patients who fail conservative management. However, studies of the young, athletic population have demonstrated a significant relative risk reduction in subsequent shoulder instability following arthroscopic stabilization.<sup>19,27,28</sup> This information corroborates the differences in surgical management and rates of recurrence between the younger and older populations. Younger, active patients are more likely to experience recurrent instability, making them better candidates for surgical stabilization, leading to increased rates of surgery in

the younger population. Furthermore, people over the age of 40 years are more likely to experience rotator cuff tears and will therefore undergo rotator cuff repair rather than labral repair. Labral repair is less frequently done within this population due to postoperative concerns, namely decreased satisfaction, stiffness, and reoperation.<sup>29</sup>

## LIMITATIONS

There are limitations to this study. Given the inherent nature of any database study, there is a possibility of missed shoulder instability events due to improper coding and no way of assessing the severity of the dislocation as this would impact the decision to manage a patient surgically rather than nonoperatively. Second, the underreporting of shoulder subluxations due to people not seeking medical care for these instability events likely led to a dramatic underestimate of the overall burden of shoulder instability within the state of Rhode Island. While the reported incidence of shoulder dislocation is more accurate, we recommend further research into the burden of shoulder subluxations within the state as there is likely a large population who has experienced such an event and not sought medical care. Third, as Rhode Island is a small state geographically, there is the chance patients crossed state borders to receive care, in which case these claims would not be captured in the Rhode Island APCD. It should also be noted that patients using Medicare FFS were excluded from the study as per the state's directive. The combination of these limitations likely led to an underestimate of the overall incidence of shoulder instability within Rhode Island but should have minimal influence on the analysis and comparisons made between types of instability, directionality, recurrence, and sex due to the sufficiently large and representative sample sizes. However, as some patients from adjacent states may have crossed into Rhode Island for treatment of their shoulder instability, this may have led to an overestimate of the incidence of shoulder instability. Despite these limitations, given the large number of cases over the nine-year study period, these data are likely reflectively of the general orthopaedic community nationwide. We were able to capture a large number of patients and complete a well-powered study to characterize the epidemiology and management of shoulder instability.

## CONCLUSION

The incidence of shoulder instability within the state of Rhode Island between January 1, 2011 and December 31, 2019 was calculated to be 62.20 injuries (95% CI, 60.61–63.78) per 100,000 person-years, with the incidence of shoulder dislocations specifically at 49.46 injuries (95% CI, 48.05–50.88). Using the Rhode Island APCD, this study characterized the epidemiology of shoulder instability and

demonstrated how increasing age decreases both the likelihood of receiving surgical stabilization and experiencing recurrent shoulder instability.

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## Authors

J. Alex Albright, BS, Warren Alpert Medical School of Brown University, Providence, RI.

Ozair Meghani, MS, Department of Orthopaedics, Warren Alpert Medical School of Brown University, Providence, RI.

Nicholas J. Lemme, MD, Department of Orthopaedics, Warren Alpert Medical School of Brown University, Providence, RI.

Brett D. Owens, MD, Department of Orthopaedics, Warren Alpert Medical School of Brown University, Providence, RI.

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## Correspondence

J. Alex Albright, BS

222 Richmond Avenue, Providence, RI

James\_albright@brown.edu

# Become a COVID-19 VACCINE PROVIDER!

Rhode Island State-supported vaccination sites will only be operating for a limited time, but COVID-19 vaccines and boosters are expected to become a part of annual care. To help ensure that COVID-19 vaccines continue to be widely available across the state, the Rhode Island Department of Health is asking primary care providers to enroll in the State-Supplied COVID-19 vaccine program.

Providers are best-suited to help patients make decisions about which COVID-19 vaccine to receive and when. Administration and storage have simplified since vaccines became available:

- Rhode Island is no longer supply-constrained.
- All COVID-19 vaccines can be stored in existing refrigeration units.
- Pfizer and Moderna vaccine vials can stay open for 12 hours (if refrigerated) after they have been punctured.
- COVID-19 vaccine can be co-administered in office with the flu vaccine as well as other routine vaccines.

Become a COVID-19 vaccine provider! To enroll in the State-supplied vaccine program visit [covid.ri.gov/vaxproviders](https://covid.ri.gov/vaxproviders)



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# Cervical Precancer Among Rhode Island Women, 2018-2019: A Quick Report after the Rhode Island Cancer Surveillance Regulation Change

JUNHIE OH, BDS, MPH; ERIC LAMY, BA

In 2017, the Rhode Island Cancer Registry (RICR) revised the “reportability” definition in its Regulations (Rhode Island Cancer Registry (216-RICR-10-10-2) – Rhode Island Department of State), and reinstated surveillance of cervical precancer for incident cases diagnosed in 2018 and forward. Cervical precancer reporting was discontinued in most of the U.S. central cancer registries since 1996, due to concerns over data collection and inconsistent disease classification resulting from changes to histopathologic terminology.<sup>1</sup> This report (1) summarizes Rhode Island women’s cervical precancerous lesions by age in 2018–2019, compared with invasive cancers, and (2) discusses importance of cervical precancer surveillance.

When women receive regular screening tests (Papanicolaou cytology and Human papillomavirus (HPV) testing) according to age-appropriate and risk-based recommendations, cervical cancer development is largely preventable.<sup>2</sup> Early detections of precancerous changes and carcinogenic HPV infection allow for early intervention, thereby halting the progression of precancerous lesions through effective follow-up and treatment.<sup>2,3</sup>

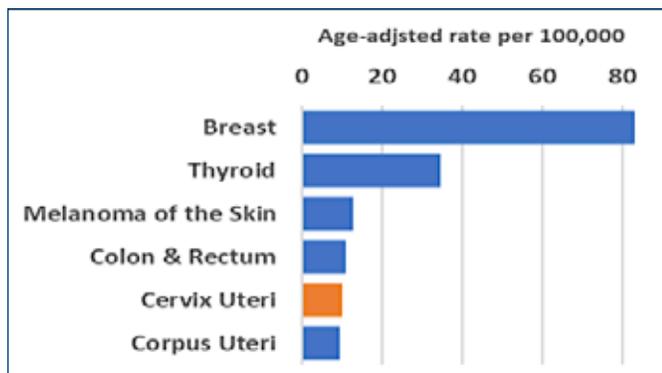
Since 1995 in Rhode Island, significant declines were observed in *invasive* cervical cancer diagnoses among women, attributed to the effective screening and successful

treatment of precancerous lesions.<sup>2</sup> However, cervical cancer is still one of the most commonly diagnosed malignancies among women aged 20–49, and the most common gynecologic cancer (**Figure 1**).

## METHODS

Using the RICR data, we obtained records of newly diagnosed precancerous lesions in the cervix – intraepithelial neoplasia grade 3 (CIN3), high-grade squamous epithelial lesion (HSIL), carcinoma in situ (CIS) and adenocarcinoma in situ (AIS) – International Classification of Disease for Oncology, 3rd edition (ICD-O-3) site/behavior/histology codes: C530-C539/2/8010, 8050, 8052, 8070-77, 8140 (WHO Classification of Tumours Online). These lesions are referred to collectively, in this report, as “precancer” or “precursor”. Cases diagnosed from January 1, 2018 through December 31, 2019 were limited to women aged 20 years and older, and compared with invasive cases (ICD-O-3 behavior code: 3) that were reported in the same study period. SEER\*Stat software v8.4.0 was used to summarize counts and age-adjusted rates (AAR per 100,000 women) to the 2000 US standard population (<http://www.seer.cancer.gov/seerstat/index.html>), using the RICR records extracted in December 2021. State population estimates for rate denominators were obtained from the National Cancer Institute Surveillance, Epidemiology, and End Results Program (NCI SEER. <http://seer.cancer.gov/popdata/download.html>).

**Figure 1.** Common Cancer Sites\* among Rhode Island Women Ages 20–49 Years, RICR 2015–2019

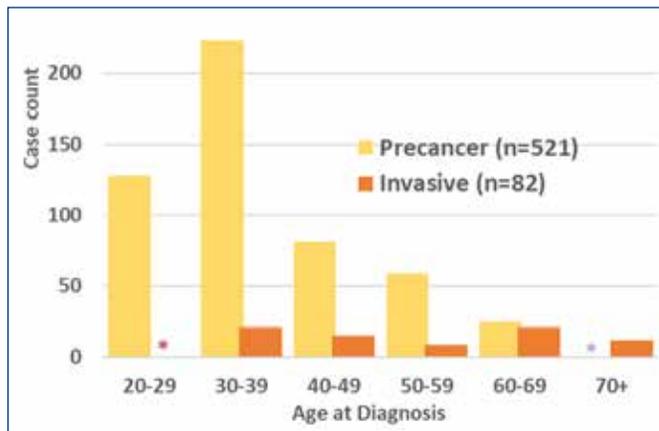


\* These six “common” cancer sites consist of approximately two-thirds of all newly diagnosed cancers, including invasive malignant cancers in all anatomic sites and in-situ urinary bladder cancer; Rate per 100,000 women adjusted to US Standard Population 2000 (19 age groups – Census P25-1130)  
 Data Source: Rhode Island Cancer Registry (as of December 2021)

## RESULTS

A total of 521 cervical precancerous lesions were reported in 2018 and 2019 (**Figure 2**). During the same period, 82 invasive cancers were newly diagnosed in Rhode Island women aged 20 and older. Overall incidence of precancerous lesions (by count) was sixfold higher than invasive cervical cancer. Women aged 30–39 had the highest burden of cervical precancers, accounting for 43% of the cases in 2018–2019 (n=223). As women’s age increases, precancer cases decrease. Invasive cancer diagnoses peaked in women aged 60–69 years.

**Figure 2.** Cervical Precancer and Invasive Cancer by Women's Age at Diagnosis ( $\geq 20$  Years), RICR 2018–2019



\* suppressed: statistics are not displayed when count of cases are fewer than 6.  
Data Source: Rhode Island Cancer Registry (as of December 2021)

## DISCUSSION

This is the *first* reporting of incidence of cervical precancerous lesions among Rhode Island women since revision of the RICR case reporting requirement in 2017. As comparable data was not collected prior to cases diagnosed in 2018, we could not study state-specific incidence changes and trend of cervical precancer over time. However, we could observe (1) a sixfold higher precancer incidence than invasive cancer in Rhode Island women, (2) the highest burden of cervical precancers among women in their age 30s, and (3) a lower precancer incidence in youngest cohort (ages 20–29 years) who were more likely to have received HPV vaccine during their adolescent period than women ages 30–39, given the study timeframe (2018–2019).

HPV vaccines effectively reduce the causal virus infections that can develop cervical cancer, as well as precancerous lesions.<sup>4</sup> In accordance with the Centers for Disease Control and Prevention (CDC)'s Advisory Committee on Immunization Practices (ACIP)' recommendations,<sup>5,6</sup> the Rhode Island Department of Health requires school children's vaccination against HPV for young females (since 2007), and young males (since 2011) (Immunization Information for Schools & Childcare Providers: Department of Health (ri.gov)).

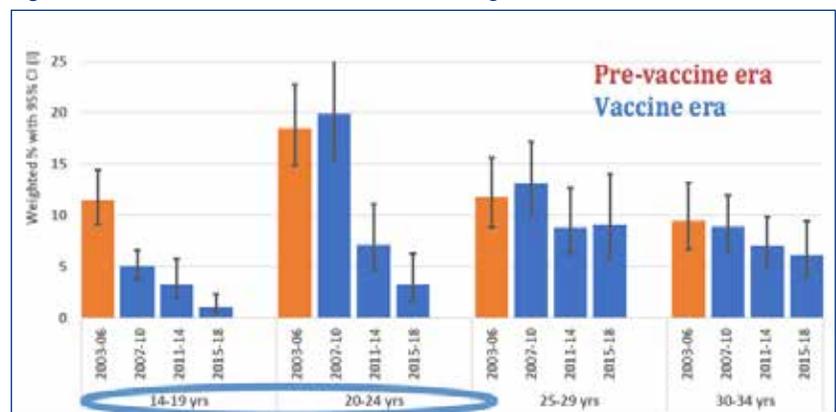
In the pre-vaccine era, HPV infection and precancer diagnosis among women in their 20s was known to be as high as, or even higher, than women in their ages 30s.<sup>7,8</sup> Through multiple population-based monitoring independently conducted in the U.S.,

early evidence of vaccine efficacy is strong and consistent; significant reductions of vaccine type-specific HPV infections (**Figure 3**), anogenital warts, CIN2+ (grade 2 or higher) diagnoses were reported, particularly among teens and young age women, who likely benefited from vaccine requirements in Rhode Island and nationwide, since 2007.<sup>8-10</sup> Similar results were *not* reported among older cohorts.

In monitoring the HPV vaccine effectiveness, cervical precursor (CIN3/CIS/AIS) surveillance is a practical tool, as it provides a relatively quick and intermediate population-based evidence. It would take decades to find effects on invasive cancer reduction, considering a slow cervical carcinogenic pathway that typically takes 20–30 years. Meanwhile, precancerous lesions can occur only 1–3 years after persistent cervical HPV infection and are much *more common* than invasive cancer, particularly in young women of reproductive ages.<sup>3</sup>

In addition to a lack of women's vaccine history, we were not able to collect the screening method by which precancer and cancer growth were diagnosed. Despite these limitations, population-based cervical precancer surveillance has the potential to provide important information to determine the burden of this preventable disease, to evaluate vaccine impacts on future precancer and invasive cancer diagnoses (intermediate and long-term endpoints), and to assist in the development of other cancer control activities. RICR plans to utilize data from state-based immunization registries and insurance claims to better understand precancer incidence in Rhode Island women associated with HPV vaccination, screening behavior, and risk factors.

**Figure 3.** Prevalence (%) of 4vHPV Infection\* among U.S. Females, NHANES 2013–2018



\* 4vHPV: HPV 6,11,16 or 18 (quadrivalent HPV vaccine target strains); collected by cervicovaginal swab. Vaccinated birth cohorts, in circle; CI=confidence interval. Recreated from Table 1. Rosenblum HG, Lewis RM, Gargano JW, Querec TD, Unger ER, Markowitz LE. Declines in Prevalence of Human Papillomavirus Vaccine-Type Infection Among Females after Introduction of Vaccine – United States, 2003–2018. *MMWR Morb Mortal Wkly Rep.* 2021;70: 415–420. Data Source: National Health and Nutritional Examination Survey (NHANES)

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We thank all dedicated Rhode Island cancer registrars in the central and local hospital registries for their quality cancer surveillance and reporting.

## Authors

Junhie Oh, BDS, MPH, is the Cancer Registry Administrator and the Senior Public Health Epidemiologist, Rhode Island Department of Health.

Eric Lamy, BA, is the Women's Cancer Screening Program Manager, Rhode Island Department of Health.

## Disclosure

The authors declare no conflict of interest.

## Correspondence

Junhie.Oh@health.ri.gov



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# The Long Haul: Pandemic Intensifies Youth Mental Health Crisis

WILLIAM D. BINDER, MD

Like many parents, our children were affected by the stressors associated with the pandemic. In early 2020 we were excited for the highs of girl's lacrosse and the final term of high school. Instead, my daughter wallowed in the lows associated with online education and diminished social interaction with peers. Our third-year college student returned home to a life he wasn't prepared to live. My wife and I continued to see patients in our respective fields, but as March faded into April, then May, and then the summer, we saw our children's adventurous spirits decay into pessimism and hopelessness.

Fortunately, my children have been resilient, and we have been lucky thus far. However, for many children and adolescents, the pandemic exacerbated a crisis a long time in the making. Prior to the pandemic, according to CDC data, about 20% of children were noted to have a mental health disorder, yet only 20% of these received care from a mental health provider.<sup>1</sup>

It is no surprise that waiting lists to see a therapist are long. Only about 4% of US psychologists are child and adolescent clinicians, and school psychologists are also in short supply. Disparities in care are evident as well. Students with marginal socioeconomic backgrounds often have lower rates of counselors and school psychologists in their systems.<sup>1</sup> The pandemic has been an accelerant. As Walters et al note in a special focus section in May on suicidal behavior in children and adolescents in the *Rhode Island Medical Journal* (RIMJ), psychiatric emergency department visits have risen about 25% since the start of the pandemic.<sup>2</sup> Adults have not been spared either. From January to June 2019, about 10% of adults reported symptoms of anxiety and depressive symptoms. By January 2021, up to 40% of adults had symptoms of anxiety and/or depression.<sup>3</sup>

While it may be convenient to cherry-pick data, the national trends correlate with personal experience. My wife, a pediatrician in the region, increasingly manages psychoactive medications for her growing panel of depressed and anxious patients. Patients with mental health needs routinely board for days in our emergency departments. Bed availability for patients requiring acute psychiatric care are in short supply in Rhode Island and in our region. During a recent trip to a hospital in western Massachusetts, I was stunned to learn that an adolescent had been in the

psychiatric wing of the emergency department for 40 days, as the health system looked for a scarce inpatient adolescent psychiatric bed. Worse yet, he had not been outside during this time – there was no staff to allow him to walk the hospital grounds or exercise.

In addition, substance abuse by adults and children, a chronic problem in Rhode Island, has only worsened. During a recent ED shift, over 50% of my patients were there due to either substance abuse or mental health issues, including both suicidal ideation and gestures. Recent articles in *The Providence Journal* and *The New York Times* underscore the local and national scale of our mental health crisis.<sup>4,5</sup>

Numerous variables, including social media's deleterious impact, increased screening and diagnosis, and changing behaviors such as decreased sleep and exercise, have all likely contributed to rising levels of anxiety and depression in adolescents. Yet, as the *Times* reported, the physical threat from the crisis has changed.<sup>5</sup> Among adolescents and young adults, suicide is the second most common cause of death in the US, with rates rising steadily since the turn of the century.<sup>6</sup> While overall rates of suicide declined in 2020, suicide increased in adolescent males and females nationwide.<sup>7</sup>

We are fortunate in Rhode Island to have strong training programs in clinical psychology and psychiatry, but it is apparent that the state needs to take a multifaceted approach to easing the crisis in mental health. In the short term, we need more inpatient beds, therapists, increased federal and state funding, and improved reimbursement from insurance companies to help alleviate this immediate problem. In the longer term, solutions are undoubtedly more complex. However, it is not a reach to suggest that our state needs to invest in schools with innovative programs in order to meet the intellectual, social/emotional, and physical needs of children as they grow and navigate adolescence. The May issue of RIMJ published a Declaration of Emergency prepared by The American Academy of Pediatrics, Rhode Island Chapter (RIAAP); the Rhode Island Council of Child and Adolescent Psychiatry (RICCAP), Hasbro Children's Hospital, and Bradley Hospital, which offers comprehensive action steps to address this crisis.<sup>8</sup> If we continue to merely react to this catastrophe, we will perpetuate a multigenerational calamity.

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## Author

William D. Binder, MD, Associate Professor of Emergency Medicine, The Warren Alpert Medical School of Brown University; Editor-in-Chief, *Rhode Island Medical Journal*.

## Correspondence

William\_binder@brown.edu

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## Working for You: RIMS advocacy activities

### May 2, Monday

American Medical Association (AMA) Advocacy update  
RIMS Board of Directors meeting:  
**Elizabeth Lange, MD**, President

### May 3, Tuesday

RIMS Physician Health Committee (PHC):  
**Herbert Rakatansky, MD**, Chair  
AMA Advocacy Resource Center in-person meeting in Chicago  
Senate Finance, Senate HHS, and House Finance RIMS-related bills heard in committee

### May 4, Wednesday

Protect our Healthcare coalition meeting  
House Finance RIMS-related bills heard in committee

### May 5, Thursday

Emergency Equality in Abortion Coverage Act (EACA) campaign planning call  
AMA Federation Health Equity Exchange  
Senate Commerce, Senate Finance, Senate Judiciary, House Corporations, and House Finance RIMS-related bills heard in committee

### May 9, Monday

Webinar on National Academy for State Health Policy (NASHP) Analysis of Rhode Island Hospitals' Operating Costs and Financial Performance  
RIMS Finance Committee meeting:  
**Kwame Dapaah-Afriyie, MD**, Chair

### May 10, Tuesday

RIMS Foundation Board Meeting:  
**Catherine Cummings, MD**, Chair  
Health Services Council Meeting  
Senate Finance RIMS-related bill heard in committee

### May 11, Wednesday

Rhode Island Department of Health (RIDOH) Board of Medical Licensure and Discipline (BMLD)  
Governor's Overdose Intervention and Prevention Task Force: **Sarah Fessler, MD**, RIMS Past President  
House Education, House Finance, and House HHS RIMS-related bills heard in committee

### May 12, Thursday

Senate Education and House Finance RIMS-related bills heard in committee  
Rhode Island Foundation Annual Meeting

### May 13, Friday

Baby Formula Shortage Update: RIDOH; Neighborhood Health Plan of RI (NHPRI); Rhode Island Health Care Association (RIHCA); RIMS staff

### May 16, Monday

State House Update: **Michael Migliori, MD**, Public Laws Committee, Chair; **Peter Karczmar, MD**, RI Medical Political Action Committee (RIMPAC), Chair  
CNESMS/NED Spring Meeting, **Alyn Adrain, MD**, and **Peter Hollman, MD**, Delegates; **Sarah Fessler, MD**, Alternate Delegate and **Elizabeth Lange, MD**, RIMS President and Alternate Delegate  
New England Delegation to the AMA Political Candidates meeting, **Peter Hollman, MD**

### May 17, Tuesday

Office of the Health Insurance Commissioner (OHIC) Health Insurance Advisory Committee (HIAC): **Catherine A. Cummings, MD**, Past President  
National Government Services Key Stakeholder Monthly Meeting  
Senate HHS, Senate Housing & Municipal Government, and Senate Judiciary RIMS-related bills heard in committee

### May 18, Wednesday

RIDOH Primary Care Physicians Advisory Committee (PCPAC): **Elizabeth Lange, MD**, President  
Senate Judiciary, Senate Education, Senate Environment & Agriculture, House Education, House Finance, and House HHS RIMS-related bills heard in committee

### May 19, Thursday

Health Information Technology (HIT) Steering Committee  
Meeting with American Civil Liberties Union of RI (ACLU-RI) regarding legislation  
RIMS Climate Change and Health Committee, 2nd meeting  
Senate Finance, Senate Judiciary, and House Finance RIMS-related bills heard in committee

### May 20, Friday

Baby Formula Shortage Update: RIDOH, NHPRI, RIHCA and RIMS  
**Elizabeth Lange, MD**, President



### Rita Towers joins RIMS' Physician Health Program Team

The Rhode Island Medical Society recently welcomed

**RITA TOWERS, MSW, LCSW**, to its staff as a full-time Clinical Associate for the Physician Health Program. Ms. Towers has a Master's Degree in Social Work from Boston College. She has worked in mental health and health care settings in various capacities for the past thirty years. Her previous clinical work has included serving as a medical social worker for the South-coast Hospital Group and more recently as a Member Advocate for Neighborhood Health Plan of Rhode Island. Her strong case management skills will be a welcome addition to the Physician Health Program and she will work in collaboration with **KATHLEEN BOYD, MSW, LICSW**, Program Director.

### May 23, Monday

RI Physician Compact (SB 2606) bill meeting with Senators, Senate staff, and other stakeholders

### May 24, Tuesday

Senate Floor passes RI Physician Compact bill, heads to House  
AMA Advocacy Resource Center webinar regarding modernization of Medical Injury Compensation Reform Act in California  
Senate Commerce, Senate HHS, Senate Judiciary and House Environment & Natural Resource Committees considers multiple RIMS-related bills

### May 25, Wednesday

Senate Education and House HHS hears and considers multiple RIMS-related bills

### May 26, Thursday

Governor's Overdose Task Force (GOTF): Racial Equity Work Group  
New England Delegation Candidate Interviews: **Peter Hollman, MD**, and **Alyn Adrain, MD**, Delegates; **Sarah Fessler, MD**, Alternate Delegate and **Elizabeth Lange, MD**, RIMS President and Alternate Delegate  
House Judiciary considers multiple RIMS-related bills

### May 27, Friday

Baby Formula Shortage Update: RIDOH, NHPRI, RIHCA and RIMS,  
**Elizabeth Lange, MD**, President



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## Rhode Island Hospital awarded \$12M to establish first Injury Control Center of Biomedical Research Excellence

PROVIDENCE – Rhode Island Hospital recently announced it has received a \$12.1 million federal grant from the National Institute of General Medical Sciences, part of the National Institutes of Health (NIH), to establish the first Injury Control Center of Biomedical Research Excellence (COBRE).

The Injury Control COBRE will investigate all phases of injury control from prevention of injury occurrence to defining optimal treatment of and rehabilitation from injuries.

“I am extremely proud that Rhode Island Hospital will host the first-of-its-kind Injury Control COBRE,” said **SAUL N. WEINGART, MD**, president, Rhode Island Hospital and Hasbro Children’s Hospital. “Accidents and injuries correlate directly with other negative health effects like chronic pain, substance use disorder, and adverse mental health outcomes. So, it’s important this grant will support innovation in injury prevention and treatment that provides better outcomes for patients.”

“Nationally, injuries account for 27% of all emergency department visits and in 2020 resulted in 278,345 fatalities,” said Principal Investigator **MICHAEL J. MELLO, MD, MPH**, Director of the Injury Prevention Center at Rhode Island Hospital. “This award will allow us to build research infrastructure that is critically needed to understand and prevent injuries.”

The Injury Control COBRE will support studies by early career investigators and will house the Injury Control Digital Innovation Core led by **MEGAN RANNEY, MD, MPH**, and the Injury Control Research to Practice and Policy Core led by **FRANCESCA BEAUDOIN, MD, PhD**.

“Together, these cores provide infrastructure to enhance the rigor and dissemination of injury science,” Dr. Beaudoin said. “We will educate the community of injury prevention experts in topics like cutting-edge methods for analyzing injury data and disseminating research findings for different target audiences, from policy makers to the public.”

“Technology has great potential to reduce injuries, but is underutilized in communities,” said Dr. Ranney. “Under this grant, we will establish a COBRE that will position researchers in Rhode Island to lead the way in innovative injury control research on topics such as childhood abuse, firearm violence, and motor vehicle crashes. Our innovative cores will also ensure that our research is used for good.”

The first research projects the COBRE will fund include: “Derivation of a clinical prediction rule for pediatric abusive fractures” and “A prospective study of posttraumatic stress symptom development and cannabis use among trauma exposed injured emerging adults following Emergency Department discharge”. One additional research project will also be named in the first year of the grant.

Members of Rhode Island’s Congressional delegation supported Rhode Island Hospital’s application for the NIH grant to establish the COBRE.

The five-year Phase 1 grant includes \$800,000 for a pilot to support 16 additional injury control investigators at the COBRE. ❖

## Lifespan’s Norman Prince Spine Institute opens new Providence location

PROVIDENCE – The Norman Prince Spine Institute (NPSI) at Lifespan, an arm of the Norman Prince Neurosciences Institute (NPNI), recently announced the opening of its new Providence location at 690 Eddy Street, adjacent to the Rhode Island Hospital campus. The newly renovated building, with three stories and nearly 17,000 square feet of space, replaces the Spine Institute’s existing smaller evaluation and treatment space within Rhode Island Hospital. Ample on-site parking promises to ease access for patients often experiencing mobility issues.

“Lifespan’s investment in this new facility for the Norman Prince Spine Institute is illustrative of our commitment to our patients and meets our need for patient care space as the demand for multidisciplinary spine care grows. Whether chronic back and neck pain, degenerative disc disease, spinal trauma, spinal deformity, spinal tumors, or congenital spinal disorders, these all inhibit patients’ wellbeing, and we are dedicated to their treatment,” said **ZIYA L. GOKASLAN, MD**, neurosurgeon-in-chief at Rhode Island and The Miriam Hospitals, and clinical director of Lifespan’s Norman Prince Neurosciences Institute.

NPSI provides the highest level of comprehensive, multidisciplinary care for spine patients, including non-surgical interventions (physical therapy, chiropractic care, acupuncture, and pain intervention procedures); minimally invasive and endoscopic spine procedures; and complex reconstructive surgeries. NPSI not only offers cutting-edge care for Rhode Island and the larger New England community but also serves as a national and international destination center for spine care, education, and research.

“Spine care means something unique to every patient, but every patient looks to us to improve their function, minimize their pain, and regain enjoyment of the things they have missed out on. With this new location, we can offer patients a broader spectrum of well-coordinated care than ever,” said **ADETOKUNBO A. OYELESE, MD, PhD**, director of the spinal surgery division and director of the Norman Prince Spine Institute at Rhode Island Hospital.

NPSI’s services will also continue to be offered at its Newport Hospital and The Miriam Hospital, and at offices in Bristol, Smithfield, and East Greenwich. ❖

## Transitions



### James E. Fanale, MD, CNE's President/CEO, to retire in early 2023

PROVIDENCE – Care New England Health System has announced the intention of its President and CEO, **DR. JAMES E. FANALE**, to retire effective early 2023, staying on to guide a new CEO as well as provide strategic advice to the Board.

“Many years ago, it was my passion for caring for others which led me to practice as a geriatrician, which I still do to this very day, aside from serving as CNE’s president and CEO. It was one of the best decisions I ever made, because it gave me the opportunity to pursue my true passion of caring for others. I am proud to look back on my career, feeling that I’ve made a difference,” said Dr. Fanale. “Now, after having spent my career doing what I enjoy and feeling that I’ve effectively improved access to state-of-the-art healthcare for all individuals who come to CNE, it’s time to leave the office behind and be with my wonderful wife and children.”

He added, “When you’re a physician, and a healthcare system leader, you can see the result of your actions. There is a personal reward that can never be matched. I wish that for everyone, no matter what industry they are in.”

Charles Reppucci, Care New England’s Board Chair, added, “I thank Dr. Fanale for his many years of leadership and look forward, upon his retirement, to his continued support and guidance of a new CEO and the Board. He is a stalwart supporter of CNE and a respected community leader on healthcare quality and accessibility. His successes and accomplishments are extraordinary.

“As a practicing physician and CEO, his healthcare perspectives have been a benefit to Rhode Island, and we all owe him a debt of gratitude. Upon his retirement, Jim will continue in a consultative role. Representatives from the Board, executive and clinical leadership, and Dr. Fanale, will comprise members of a Search Committee to identify a successor. Then, continuing to work alongside a new CEO will be an experienced executive transition team.” ❖



### Arthur J. Sampson named Lifespan interim CEO, president

PROVIDENCE – Lifespan Corp. announced on May 20 that **ARTHUR J. SAMPSON** has been named interim CEO and president of Lifespan, effective June 1. The appointment follows the mid-April resignation of **DR. TIMOTHY J. BABINEAU**.

Sampson most recently served as the president and CEO of The Miriam Hospital, after previously serving as president and chief executive officer of Newport Hospital.

Sampson holds a master’s degree in health care administration from the George Washington University and served administrative residencies at The Johns Hopkins Hospital in Baltimore and Union-Truesdale Hospital (now Charlton Memorial Hospital) in Fall River, Massachusetts. Sampson is a fellow of the American College of Healthcare Executives.

**LAWRENCE A. AUBIN, SR.**, chairperson of Lifespan’s board of directors, sent a message to Lifespan’s more than 15,000 employees on May 20th, notifying them of the appointment. He said Sampson will lead the nonprofit hospital company while the Lifespan board of directors conducts a national search for a permanent successor to replace Babineau, who will serve the board in an advisory role through the end of September.

“Arthur is an agile and strong leader and works well with individuals at all levels of the organization,” Aubin said. “We are fortunate to have him rejoining Lifespan during this transition period, bringing his institutional knowledge, expertise and experience to continue the important work laid out in our Lifespan 2025 strategic plan.”

Aubin said the Lifespan board of directors will initiate a national search for a new president and chief executive officer “in the coming weeks,” with the most immediate steps in the process involving the selection of an executive search firm and a search committee to support the search. ❖

## Recognition

### HCV healthcare leaders will kick off July 30th WaterFire in honor of World Hepatitis Day

PROVIDENCE – After a two-year hiatus due to the COVID-19 pandemic, RI's HCV medical, public health and advocacy leaders will reunite and re-commit to HCV elimination. On July 30th, in honor of July 28th's World Hepatitis Day, healthcare workers across disciplines, from across Rhode Island, will join in collaboration, celebration and support of what can be achieved together.

This year's theme is, "Test to Treat," to get all Rhode Islanders with HCV diagnosed and promptly treated and cured. RI Defeats Hep C is partnering with WaterFire for the event and will honor five lead torch bearers who continue to light the way in preventing illness, death and suffering due to HCV through the challenges of COVID-19.

They are: Jennifer Clarke MD, MPH; Alan Epstein, MD; Osvaldo Lugo; Megan M. Pinkston-Camp, MA, PhD; and Sophie Sprecht-Walsh, LPN.

Kickoff is at Waterplace Park at 8:05 pm.

#### 2022 Lead torch bearers



#### JENNIFER CLARKE MD, MPH

An internal medicine physician, women's health expert and researcher, Dr. Clarke began working in the RI's women's prison in 1998 to provide primary medical care and conduct public health research. She received an NIH Career Development Award to improve reproductive health care for women released from jail; directed a project

to evaluate Title X services at the RI Department of Corrections (RIDOC) and the reproductive health needs of incarcerated women, and conducted a study to decrease unplanned pregnancies and HIV/STD risk among incarcerated women at community re-entry. As RIDOC medical director from 2015-2020, Dr. Clarke spearheaded provision of medications to treat opioid use disorder – a cornerstone of HCV prevention – and initiated an HCV-elimination program.



Torch bearers at the 2018 RI Defeats Hep C WaterFire Lighting. [YVONNE COYLE, WATERFIRE.]



#### ALAN EPSTEIN, MD

Dr. Epstein is director of gastroenterology at Roger Williams Medical Center and an assistant professor at Boston University School of Medicine. Dr. Epstein has been treating HCV since 1990, starting with three times weekly interferon injections, through myriad clinical trials, to today's direct acting antiviral agents. Dr. Epstein founded the

RI branch of the American Liver Foundation in 1994 and was named its New England Clinician of the year in 2015. He has tirelessly supported HCV access for all patients with the Rhode Island Hepatitis Action Coalition and other advocacy groups. This grandfather hopes to see HCV eliminated by 2030.



#### OSVALDO LUGO

Osvaldo Lugo is a prevention specialist for AIDS Care Ocean State (ACOS), home of RI's syringe services program. He has been working on HCV prevention via harm reduction since before harm reduction was a term used widely in RI. Lugo is the key person for community-based HCV screening and runs ACOS' Street Outreach program.

He has contributed tremendously to HCV-related research and expansion of harm reduction services in RI. He worked at all previous HCV WaterFires conducting HCV screening.



#### MEGAN M. PINKSTON-CAMP, MA, PhD

Dr. Pinkston-Camp is an associate professor of psychiatry and human behavior and medicine, Alpert Medical School of Brown University, clinical health psychologist, Department of Psychiatry, Rhode Island and Miriam Hospitals, and behavioral medicine track coordinator for Brown's Clinical Psychology Training Program. She has been engaged in work dedicated to persons living with HIV and HCV for nearly 30

years in different regions of the country. She provided evidence-based assessment and care for patients living with HCV/HIV coinfection during the interferon era. She facilitated the longest running support group for persons living with HCV in RI. Dr. Pinkston-Camp feels fortunate to have walked alongside many individuals on their HCV journey; they have inspired her academic writings and grants that attend to the intersection of HCV, HIV, substance use, alcohol use and mental health.



#### SOPHIE SPRECHT-WALSH, LPN

Sophie Sprecht-Walsh has been providing nursing care in Rhode Island since 2008. She has dedicated her career to working with persons living with and at risk for viral hepatitis and HIV and caring for persons with substance use disorders. She provides comprehensive HCV education, counseling, screening, diagnostic testing, patient navigation,

and HCV care to drug-involved populations and patients on opioid agonist therapy. She facilitates streamlined HCV treatment to expand access and optimize cure. For years she has contributed to research to eliminate HCV and ameliorate the opioid crisis. Ms. Sprecht-Walsh served on the medical boards of Clinica Esperanza and Project Weber Renew and is currently co-chair of the GAIA Vaccine Foundation. ❖

## Did you know? Nearly 70% of smokers want to Quit.<sup>1</sup>

# QUITWORKS<sup>SM</sup>-RI

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- **FREE** phone-based counseling and virtual support tools
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<sup>1</sup> [www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/cessation/quitting/index.htm](http://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/quitting/index.htm)



## Recognition



### American Liver Foundation honors Thomas Sepe, MD, at May gala

BOSTON – **THOMAS SEPE, MD**, was among the honorees recognized by The American Liver Foundation (ALF) at the ALF New England Legacy Gala held at the Exchange Conference Center on May 5th. The award recognizes individuals who have made an outstanding contribution to the liver community, fields of biotechnology, medical innovation, and philanthropy.

Dr. Sepe is director of The Liver Center at University Gastroenterology (UGI) in Providence and a clinical professor of medicine at Brown University. He is also a long-serving ALF New England Medical Advisor.

He oversees UGI's clinical trials unit in liver disease, which has conducted more than 70 research trials in hepatitis C infection. The unit is now focused on disease-specific drug therapy for NASH (non-alcoholic steatohepatitis) and cirrhosis.

"We are thrilled to have the opportunity to honor those making significant contributions to the liver community," said Lorraine Stiehl, ALF's chief executive officer. "With nearly 100 million Americans affected by liver disease, their collective work is more important now than ever."

"The American Liver Foundation, University GI, and I all share the same vision – to find new treatments and cures for all forms of liver disease," Dr. Sepe said. "While we have a lot of work to do, I am deeply honored to have received this grand award for our accomplishments thus far." ❖

### Rhode Island Hospital Trauma and Burn Centers achieve reverification

PROVIDENCE – Rhode Island Hospital has achieved reverification from the American College of Surgeons (ACS) Committee on Trauma and the American Burn Association (ABA). This achievement comes on the heels of the hospital's pediatric division receiving reverification of its trauma and burn centers, making Rhode Island Hospital home to the only comprehensive adult and pediatric Level 1 trauma and burn center in New England.

ABA verified burn centers meet evidence-based standards that establish a threshold for high quality burn care and have demonstrated proficiency in a wide range of burn treatments. ACS verified trauma centers have confirmed that they have the necessary resources for delivering optimal trauma care to injured patients and have demonstrated both readiness and performance in trauma care.

"The Burn Center at Rhode Island Hospital is the only verified and accredited burn center in the state with the most advanced technology to provide superior treatment for each patient," said **DAVID HARRINGTON, MD**, the center director. "Our care is comprehensive through all phases from injury through reconstruction and rehabilitation, to final recovery. We are honored to be able to serve those in our community who have suffered a burn injury."

Rhode Island Hospital's adult trauma center reverification extends through January 2024 and adult burn center verification extends through January 2025. ❖

## Appointment

### Ana Tuya Fulton, MD, MBA, named CNE Chief Population Health Officer

WARWICK – **ANA TUYA FULTON, MD, MBA**, has been named Care New England's Chief Population Health Officer. She will maintain her current titles of Chief Medical Officer of Integra, and Executive Chief of Geriatrics & Palliative Care at Care New England.



She will serve as the primary Care New England system leader for setting the overall strategy for value-based care within the CNE Health System. In her capacity as Chief Population Health Officer, Dr. Fulton will also work with key regulatory bodies to reduce the cost trends in health care across Rhode Island and work to improve quality, access, service, and equity. She will also oversee the creation of new programs to continue to advance innovation and population-based strategy and the expansion of Integra's nationally recognized nascent hospital-at-home program for its most frail members which was created before the CMS program came into effect.

Since 2008, Dr. Fulton has worked for Care New England in various roles, including as Chief of Medicine at Butler Hospital, Director of Geriatrics and Chief of Geriatrics for Care New England, and most recently as Medical Director for Integra Community Care Network. ❖

## In Memoriam



**MARLENE CUTITAR, MD**, 60, passed away in mid May, succumbing to cancer. She is survived by Donald Acevedo, of Warwick.

A native of North Smithfield, RI, Dr. Cutitar was a 1979 graduate of The Wheeler School in Providence. She was a Brown alumna, who earned her bachelor of science degree in 1983, and her medical degree in 1986. She did her residency and fellowship at Rhode Island Hospital and The Miriam Hospital. Her areas of expertise were in surgical oncology, breast surgery and general surgery, as well as gastrointestinal surgery.

Dr. Cutitar was a Clinical Assistant Professor of Surgery at the Alpert Medical School of Brown University, and a member of the Clinical Faculty Advisory Committee (CFAC). She was also a member of the American Medical Women's Association and the RI Chapter of the American College of Surgeons.

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On April 29th, 2022, she was named a "Top Doc" in breast surgery by Rhode Island Monthly, an honor she had also received in 2019.

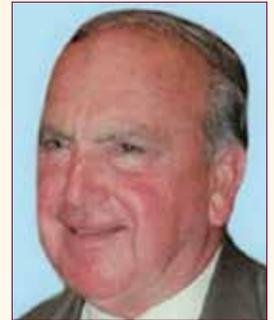
The Rhode Island Medical Women's Association (RIMWA) is planning a celebration of her life during the summer. She served as treasurer of the organization, and past president. In an announcement of her passing to RIMWA members, the Board of Directors remembered her as "an esteemed colleague, dear friend, gifted teacher, enthusiastic mentor, and surgeon extraordinaire to so many. It is simply not possible to imagine Rhode Island (and national) medicine without her shining presence over the past 35 years." ❖

## Obituary



**JOSEPH A. IZZI, Sr., MD**, age 87, passed away May 8, 2022 after a long illness at

home, surrounded by his loving family. He was the beloved husband of Barbara (Sabella) for 54 years and was a loving father to Dr. Joseph A. Izzi, Jr. (Lori) and Dr. Jason R. Izzi (Kimberly), and adoring Grandpy to his wonderful grandchildren Santino and Jayci. He was the loving brother of the late Carolyn Marano, and brother of Dr. Roger A. Izzi, Jr.



He graduated from La Salle Academy, Providence College and The University of Bologna Medical School. He did his internship and orthopedic residency at Rhode Island Hospital. Upon finishing his residency, he served as a Lt. Commander in the U.S. Navy and was stationed in De Nang, Vietnam during the Tet Offensive.

Dr. Izzi was a board-certified orthopaedic surgeon who practiced for 45 years in Providence and North Providence. He was a member of the Providence Medical Society, RI Orthopaedic Society, American College of Surgeons, International College of Surgeons, The American Academy of Orthopaedic Surgeons, University of Bologna Alumni Association, Eastern Orthopaedic Society and The Irish American Orthopaedic Society.

Contributions in his memory may be made to St. Jude Children's Hospital, [www.stjude.org](http://www.stjude.org). ❖