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## June is Men's Health Month



SPECIAL SECTION

### REFLECTIONS *on* MEN'S HEALTH

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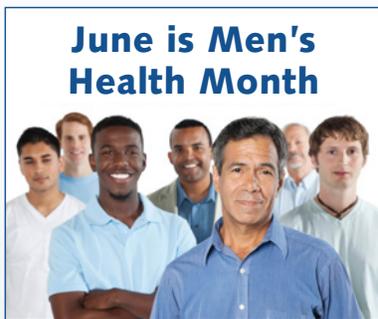
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### Reflections on Men's Health

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# Sexual Health is Essential to Healthy Living

*Your sexual health is at the center of your life.  
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The Men's Health Center at The Miriam Hospital is the first of its kind multidisciplinary center dedicated to restoring normal sexual function and improving overall health. Our staff includes experts in andrology and male sexual dysfunction, and we are the highest volume center for surgical treatment of erectile dysfunction in Rhode Island.

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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. OGRODNICZUK, 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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# 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>

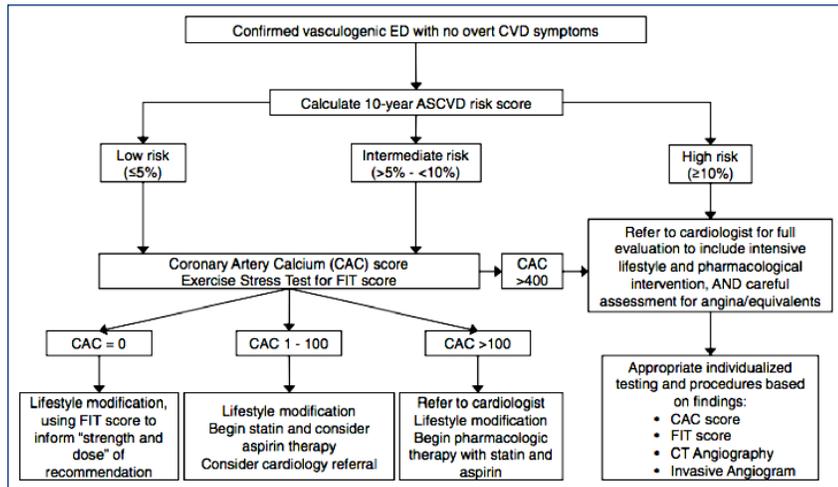
## RECOMMENDATIONS FOR EVALUATION AND MANAGEMENT OF CARDIOVASCULAR RISK IN MEN WITH ED

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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### Disclosures

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

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## 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

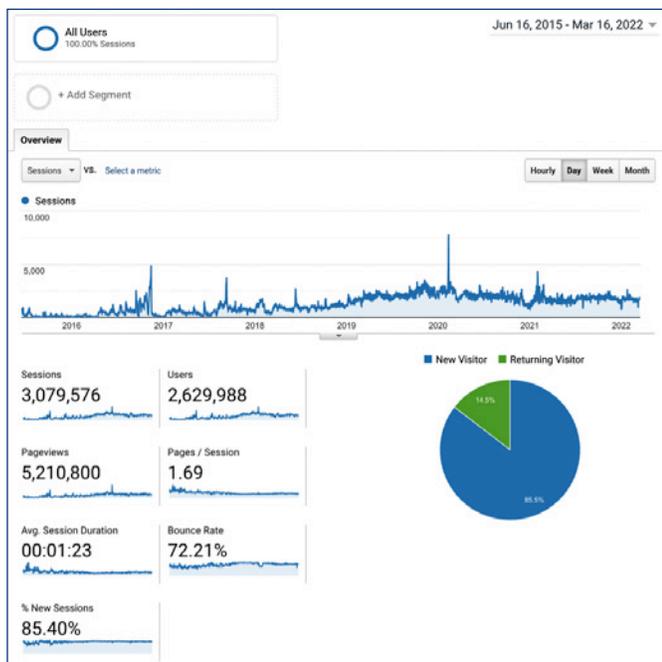
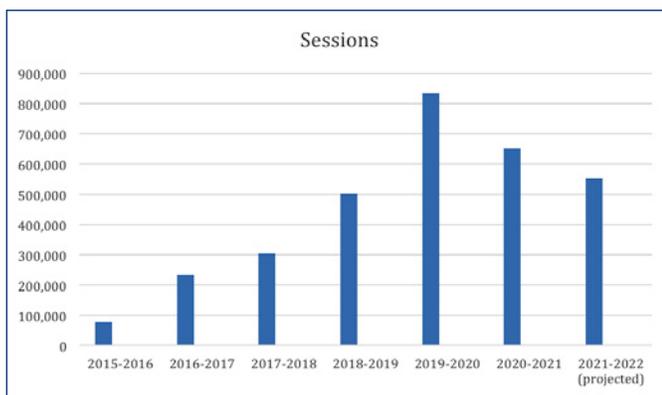


Figure 2. Sessions by year



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
bryan 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.

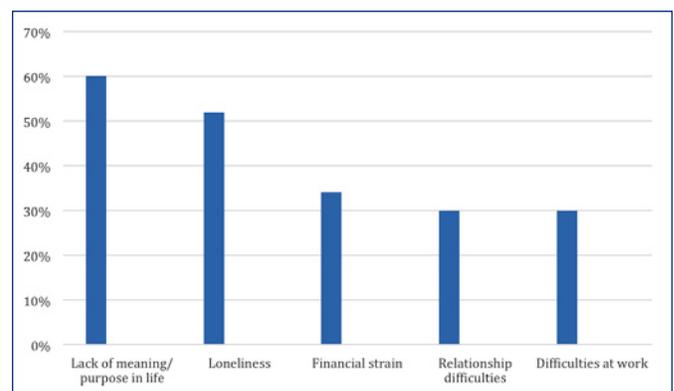
d Position: The average ranking of the website's URLs for the search terms (with 1 being the first website listed at the top search results).

**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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### Disclosures

None

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# Preconception Considerations for Male Fertility

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## 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**

Screen for sexually transmitted infections
Manage chronic disease
Review medications
Review family history of congenital disease or infertility
Consider paternal and maternal age

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), anti-hypertensives, 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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#### Disclosures

None

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