

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

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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.¹ 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.² Recent data indicate that 68.6% of men aged 20 years and older are overweight,³ 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.⁴

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.⁵ 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,⁶ and are less likely to attend preventive healthcare visits.⁷ 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.^{8,9} 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.¹⁰

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, Thompson¹¹ 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.¹² 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.^{13,14} 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.¹⁵⁻¹⁸ 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.^{19,20} Because of the common risk factors and pathophysiological processes, men with CVD are more likely to have ED and vice versa.²¹⁻²⁵ ED severity has been correlated with atherosclerotic coronary disease, and the presence of ED has been independently associated with CVD events.^{26,27} 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.²⁷

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.^{27,28}

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.²⁷ 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.²⁸ Of course, this is seen especially in comorbid disease states with increased inflammatory markers and reduced testosterone levels.²⁹⁻³¹ 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.^{32,33} 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.³² 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.³³ 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.¹⁴ 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.³⁴ Riedner et al performed a case-controlled study of 242 men referred for elective coronary angiography.³⁵ 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.³⁵ In contrast, Riedner did not find an association between ED and probability of CAD in men ≥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.³⁶ 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.³⁶

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.³⁷ 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.³⁸

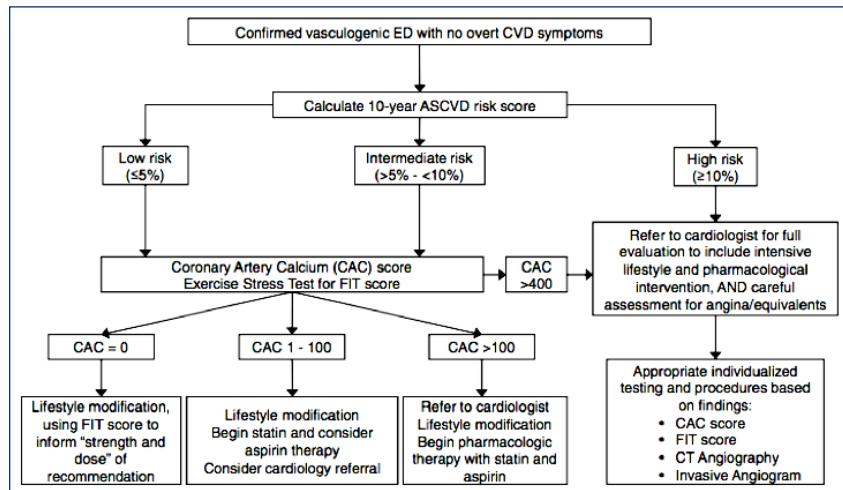
RECOMMENDATIONS FOR EVALUATION AND MANAGEMENT OF CARDIOVASCULAR RISK IN MEN WITH ED

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.³⁹ We also recommend measurement of total testosterone levels, particularly for patients who have failed a trial of phosphodiesterase type 5 inhibitors.⁴⁰ 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).⁴⁰⁻⁴³ We do not recommend testosterone repletion for total testosterone >12 nmol/L (>350 ng/dL).⁴³ 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.⁴⁴

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.⁵⁶ 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.³⁹ 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."³⁷

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.⁴⁴ (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.⁴⁵⁻⁴⁸

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).⁴⁹⁻⁵⁰ 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.³⁹ Exercise stress testing with calculation of the FIT Treadmill Score may also have appropriate roles in the evaluation of men with vasculogenic ED.⁵¹ 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.⁵² 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.⁵³ 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.⁵⁴ 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.⁵⁵ The Dallas Heart study demonstrated the value of CAC in risk reclassification in a younger population (Mean age 44.4 ±9 years).⁵⁶ 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).⁵³ 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.⁵³

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.⁵⁷ 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

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

Drs. Paulos and Harisaran have no disclosures

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