The Intersection of Medicine and Urology

An Emerging Paradigm of Sexual Function, Cardiometabolic Risk, Bone Health, and Men's Health Centers

Martin M. Miner, MD[a],*, Joel Heidelbaugh, MD[b],
Mark Paulos, MD[c], Allen D. Seftel, MD[d], Jason Jameson, MD[e],
Steven A. Kaplan, MD[f]

KEYWORDS

- Medicine and urology • Sexual function • Cardiometabolic risk • Bone health
- Men's health centers

KEY POINTS

- Men's mental health and how they think about their health are critical to the future of men's health. Poor health choice patterns are established during those years under the age of 50 when men are twice as likely to die compared with women.
- As the future of medicine focuses on quality and value, a better understanding of the social determinants of men's health will identify potential areas of improvement.
- The presentation of a man to a clinician's office with a sexual health complaint should present an opportunity for a more complete evaluation, notably the complaint of erectile dysfunction.
- The future of men's health will be well served by integrated men's health centers that focus on the entire man, with proper education and testing and careful shared decision making between patient and provider.

[a] Department of Family Medicine and Urology, The Men's Health Center, The Miriam Hospital, The Warren Alpert Medical School of Brown University, 164 Summitt Avenue, Providence, RI 02906, USA; [b] Departments of Family Medicine and Urology, University of Michigan Medical School, Ann Arbor, MI, USA; [c] Departments of Internal Medicine and Urology, Men's Health Center, The Miriam Hospital, The Warren Alpert School of Medicine, Brown University, Providence, RI, USA; [d] Division of Urology, Cooper University Hospital, Cooper Medical School of Rowan University, Camden, NJ, USA; [e] Division of Urology, Mayo Clinic, Scottsdale, AZ, USA; [f] Benign Urologic Diseases and The Men's Health Program, Icahn School of Medicine at Mount Sinai, Mount Sinai Health System, New York, NY, USA
* Corresponding author.
E-mail address: Martin_Miner@Brown.edu

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 to addressing disparities. The National Institutes of Health Office of Research on Women's Health was established in 1990, and in 1994 the US 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]

Although decades of research have yielded many 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 care 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 life expectancy of men continues to trail that of women by nearly 5 years in 2014 (76.4 years for men and 81.2 years for women).[4]

Men's health as a concept and discipline is in a nascent state compared with women's health. Most clinicians and the public consider men's health a field concerned only with diseases of the prostate and erectile dysfunction (ED). Men's health has recently become a hot topic in these specific areas, with millions of dollars spent on remedies for prostate health, improved urinary flow, and enhanced erections and by comparison a much smaller amount directed at improved preventive health.[5]

Adult men ages 18 years to 65 years do not use or react to health care services in the same ways as women[6] and are less likely to attend preventive health care 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] The Commonwealth Fund did a mass survey in 2000 and found that "an alarming proportion of American men have only limited contact with physicians and the healthcare system in general. Many men fail to get routine check-ups, preventive care, or health counseling and they often ignore symptoms or delay seeking medical attention when sick or in pain."[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, notably the complaint of ED. In a landmark article published in 2005, Thompson and colleagues[11] confirmed that ED is a sentinel marker and risk factor for future cardiovascular events. Incident ED occurring in the 4300 men without ED at study entry enrolled in the Prostate Cancer Prevention Trial was associated with a hazard ratio of 1.25 for subsequent cardiovascular events during the 9-year study follow-up. For men with either incident or prevalent ED, the hazard ratio was 1.45.

WHO IS THE MEN'S HEALTH DOCTOR: PRIMARY CARE PHYSICIAN, UROLOGIST, OR SUBSPECIALIST?

With the advent of the Patient Protection and Affordable Care Act in March 2010, millions of men ages 18 years through 45 years who previously did not have access to health care entered the marketplace to obtain health insurance. Although urologists are typically thought of as "men's doctors" and obstetrician-gynecologists are considered "women's doctors," the issue remains: Who is to shoulder the responsibility for men's health in the decades to come? Integrated men's health centers (MHCs) to deliver health care for years to come need to be created.

The appeal of an integrated MHC is of a single, highly personal medical or urologic issue home to address all of men's health needs, including sexual health.

The MHC paradigm at the Miriam Hospital Men's Health Center is admittedly challenging to replicate at the moment. The focus encompasses becoming a lifestyle coach as it deals with the parameters of cardiometabolic medicine: lifestyle, stress management, sleep, diet, and exercise.

The following sections provide a rationale for an integrated MHC in the primary care/urology intersection, focusing on ED, Testosterone (T) deficiency, osteoporosis, cardiovascular (CV) disease, and obesity. Although this includes a preventative focus, it does not include other relevant topics of men's health, such as affective and mood disorders, domestic and partner violence, and gender-specific issues. 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 article.

ERECTILE DYSFUNCTION AND SUBCLINICAL CARDIOVASCULAR DISEASE: AN INTERSECTION OF MEDICINE AND UROLOGY

The relationship between ED and clinical CV disease (CVD) was originally based on a shared clinical risk factor model (eg, hypertension, smoking, and diabetes mellitus) and the presumed overlap in pathophysiologic mechanisms, including endothelial dysfunction, inflammation, and atherosclerosis.[12] In the early 2000s, longitudinal studies on CVD and ED revealed a 2-way relationship, positing that patients with CVD are more likely to have ED and that patients with ED are more likely to develop future CVD, even when adjusted for risk factors.[13–16] The Princeton Consensus Conference identified ED as a substantial independent risk factor for CVD,[16] and the QRISK group published one of the first risk scores to incorporate ED as an independent risk factor into their updated 10-year CV risk model, calculating a 25% increased risk for average middle-aged men.[17]

The temporal relationship between ED and subclinical CVD progression is less clear. Is ED a precursor to CVD, or does underlying CVD first manifest as ED? Available data come from cross-sectional studies correlating symptoms of ED and overt CVD or highly limited prospective cohort studies correlating ED incidence or severity with incident CV events.[13–16,18–20] A few studies have revealed a 2-year to 3-year time interval between onset of ED symptoms and CVD symptoms,[14] whereas more recent studies have examined the interrelationships between subclinical CVD (ie, early atherosclerosis), ED, and overt CVD (myocardial infarction [MI] or major adverse cardiac events [MACE]).[18–20] The Multi-ethnic Study of Atherosclerosis (MESA)[21] showed subclinical CVD is a predictor of ED, which could predict MACE. This pivotal finding provided evidence that coronary artery calcium (CAC) score can serve as a "disease score" and surrogate for accelerated atherosclerosis process in arteries, including penile arteries and vascular ED.[22]

One-half of men with sudden CVD events have no previous symptoms of CAD and between 70% and 89% of sudden cardiac events occur in men.[23–28] ED may be the single warning of this risk of sudden CVD events.[28,29] ED severity has been correlated with atherosclerotic coronary disease burden, and the presence of ED has been independently associated with CVD events.[28,29]

THE TEMPORAL RELATIONSHIP OF ERECTILE DYSFUNCTION, SUBCLINICAL CARDIOVASCULAR DISEASE, AND CLINICAL CARDIOVASCULAR DISEASE

A systematic review demonstrating that men with ED at intermediate CVD risk had a higher relative risk of CVD events compared with those at low or high CVD risk: 0.93 for

low risk, 1.51 for intermediate risk, and 1.30 for high risk.[1] Consistent with previous studies, they also showed an inverse relationship between prevalence and CV impact of age of onset on ED.[1,19,20] Relative risk of CVD events was higher among younger ED patients, with risk decreasing linearly as age in years increased.[1,19,20] This could indicate the potential usefulness of ED as a predictor in these young patients and the intermediate CVD risk score group, which commonly consists of middle-aged men, of the population who will benefit from a discussion about further testing, according to American College of Cardiology (ACC)/American Heart Association (AHA) 2013 preventive guideline.[30]

There is increasing interest in describing the burden of subclinical disease in patients with ED. The CAC score has been endorsed by recent ACC/AHA guidelines for further risk stratification of intermediate-risk patients and shown to be the single best predictor of CV risk.[21,31,32] To date, limited studies have examined CAC scores in patients with ED, showing that patients with ED have higher CAC scores compared with healthy subjects.[33] Consistent with this finding, Jackson[34] showed that among 65 ED patients aged 38 years to 73 years with no cardiac symptoms, 81% of patients had calcified plaque. Finally, Yaman and colleagues[35] categorized 60 patients with ED and 23 patients without ED according to the severity of ED measured by the International Index of Erectile Function (IIEF) and then compared CAC scores. An increasing IIEF score indicates decreasing ED severity. A significant negative correlation between IIEF scores with CAC scores was observed, implying a positive correlation between ED severity and CAC.[35]

The MESA study was the first study to explore temporal relationship between ED and subclinical CVD. Development of ED was found to occur sometime during the progression from baseline subclinical vascular disease to clinically overt CVD. A strong association was observed between baseline subclinical disease as assessed by CAC and carotid plaque and subsequent ED, highlighting the potential role of atherosclerosis testing—in particular, CAC scoring and carotid plaque—in predicting ED and overt CVD.[21] At the same time, given the strengths of ED as a predictor of future coronary and cerebrovascular events, there seem to be clear clinical implications and indications for the increased evaluation of subclinical CVD for at-risk patients before and once they develop ED.[36,37]

Few studies have examined the effect of CV risk factor modification on both ED and CVD, but much of the recent development of knowledge takes place in the men's health domain. Among the shared risk factors, modification of tobacco use, hyperlipidemia, and dietary change/weight loss/exercise in targeted patients has revealed symptomatic improvement in ED.[38–42] A randomized single-blind study of 110 obese men aged 35 years to 55 years, without diabetes, hypertension, or hyperlipidemia, who had an IIEF of 21 or less to determine the effect of weight loss and increased physical activity on erectile and endothelial function in obese men found that after 2 years, body mass index decreased more in the intervention group as did serum concentrations of interleukin 6 and C-reactive protein.[43] The mean IIEF score (Sexual Dysfuntion) in the intervention group improved from 13.9 to 17, with 17 men in the intervention group normalizing their sexual function.[43] These studies suggest that patients who are at high risk need aggressive risk factor modification, which then could delay or prevent the future onset of ED and perhaps overt CAD.

RECOMMENDATIONS FOR EVALUATION OF CARDIOVASCULAR RISK IN MEN WITH ERECTILE DYSFUNCTION

Given the relationship among ED, subclinical CVD, and clinical CVD, the authors recommend that all men with vascular ED should undergo CV risk assessment.[44,45]

In parallel, a sexual history assessment should be integrated into all CV risk assessments and may be of increased importance in populations with a lower burden of risk or predilection for more silent coronary disease as determined by the presence or absence of comorbidities or age.[44] All men should be questioned about their sexual history and functioning as part of the initial assessment of CV risk. Symptomatic men (eg, those with exertional chest pain, presyncope, or shortness of breath) with ED are presumed to have CAD and are, therefore, at high risk for CVD events and as such should undergo CV stress testing.[44,45]

The authors recommend evaluation of fasting plasma glucose, serum creatinine (estimated glomerular filtration rate), albumin/creatinine ratio, fasting lipids, and assessment of the cardiometabolic syndrome component, which may be used to further characterize CV risk.[44] The authors recommend measurement of total T levels, particularly for patients who have failed a trial of phosphodiesterase type 5 inhibitors.[44] Based on established guidelines, the authors recommend considering T supplementation for men with total T less than 300 ng/dL who are symptomatic (eg, decreased libido, decreased spontaneous erections, low energy, increased fatigue, or loss of muscle mass and strength).[46] The authors do not recommend T supplementation for total T greater than 350 ng/dL.[46]

The 2013 ACC/AHA risk assessment guidelines are an appropriate starting point for CAD risk stratification in younger, middle-aged men with ED or in diabetic men with ED.[45] Due to a reliance on a small number of traditional risk factors and the strong reliance of age in the risk estimates, the authors propose more advanced testing for all men aged 40 years to 60 years with vasculogenic ED because these patients normally do not score as high risk with the new ACC/AHA risk estimator and likely have significant unaccounted-for risk.[45]

Men who seem at high risk for CV events based on ASCVD score greater than 10% should be referred to a cardiologist.[47] The authors suggest that all other men with vasculogenic ED and no overt CVD symptoms undergo further noninvasive evaluation using CAC scoring as the primary diagnostic test to detect subclinical atherosclerosis for the purpose of advanced risk stratification.[47,48] Exercise stress testing with calculation of the FIT Treadmill Score may also have appropriate roles in the evaluation of men with vasculogenic ED.[49] In addition, imaging of CAC with the latest multidetector scans takes only a few seconds, and the cost of the test is currently less than $200 in many metropolitan areas in the United States.[50,51]

Given the limitations of other markers for CVD risk assessment and in light of the growing body of evidence supporting the use of CAC as a diagnostic and prognostic tool, the authors support the use of CAC scoring as the first diagnostic test for further risk assessment in all low-risk and intermediate-risk men 40 years to 60 year old with confirmed vasculogenic ED without overt CVD symptoms.[51,52]

This approach treats atherosclerosis as a continuum that can be impacted by many traditional and nontraditional risk factors that result in inflammation, subclinical atherosclerosis, and finally clinically apparent CVD.[53] In keeping with this theory, the presence of subclinical atherosclerosis has been shown to predict future CVD complications and death.[54] The growth of technology over the past 2 decades has allowed for direct measurement of subclinical atherosclerosis and, therefore, further stratifying individual risk for a CVD event.[51] The authors propose the use of CAC score to guide initiation of pharmacotherapy in low-risk and intermediate-risk patients and to guide intensity of therapy in high-risk patients.[47,51,54]

AN UPDATE ON TESTOSTERONE REPLACEMENT THERAPY AS ANOTHER EXAMPLE OF THE POTENTIAL OF THE MEN'S HEALTH CENTER

In March 2015, all US commercial T products underwent an FDA-mandated label change that restricted the indicated population and warned against the possible risk of MI and stroke.[55] Investigators from the responsible FDA team subsequently published their rationale and perspective in a leading medical journal in 2015.[56]

The actions by the FDA were extensively covered by the lay and medical media, and contributed to concerns that T therapy (TTh) is associated with previously under-recognized risks and is overprescribed. The label change regarding indicated populations created an unusual situation in which TTh prescriptions for a large majority of men with well-recognized condition of T deficiency, also known as adult-onset hypogonadism, suddenly became off-label literally overnight, adding to the concern that physicians are prescribing T for no reason other than "normal aging."[57] These changes may have reduced the willingness of many professionals to consider treatment of affected men with T deficiency. In addition, health insurers have created policies based on these changes to justify reduced coverage for T products.

CHANGES TO THE FOOD AND DRUG ADMINISTRATION LABEL

Although the addition of a CVD warning to the label for TTh products received considerable attention, warnings of this type are not uncommon. It states, "Long term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, epidemiologic studies and randomized controlled trials have been inconclusive for determining the risk of major adverse cardiovascular events (MACE), such as nonfatal myocardial infarction (MI), nonfatal stroke, and cardiovascular (CV) death, with the use of testosterone compared to nonuse. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in men."

In addition, the language for indications was changed by the FDA to provide an inclusive list of conditions causing hypogonadism, termed *classical hypogonadism*, and removing the term *idiopathic*, which accounted for a large majority of treated cases prior to the issuing of the warning. Finally, a statement was added as follows: "Safety and efficacy of AndroGel 1.62% in men with 'age-related hypogonadism' (also referred to as 'late-onset hypogonadism') have not been established."[55]

STATUS OF PUBLISHED STUDIES LEADING TO ADDITION OF CARDIOVASCULAR RISK WARNING

The FDA pharmacovigilance team identified only 4 studies suggesting increased CV risks with T therapy. The first, in 2010, was a 6-month placebo-controlled T gel study in frail men, with limited mobility, in which more CV events were noted in the T arm compared with the placebo arm.[58] A majority of these events, however, were not clinically significant and included nonspecific changes on electrocardiogram, palpitations, and pedal edema not associated with heart failure. The FDA's own written assessment indicated they dismissed these results as concerning because the numbers of MACEs were too few for evaluation.[59]

The second study, by Vigen and colleagues,[60] reported that men who subsequently received TTh had an absolute rate of MI, stroke, or death of 25.7% at 3 years after angiography compared with 19.9% in untreated men. Soon after publication it was discovered the investigators had reversed their results, because the absolute rate of events was only 10.1% among men who received TTh and 21.2% in untreated men.

Later, the investigators revealed they had miscategorized more than 1000 individuals in the original publication, and nearly 10% of the all-male population was discovered to be women.[61]

A third study by Finkle and colleagues[62] reported increased rates of nonfatal MI in the 90 days after a T prescription compared with the prior 12 months. Apart from serious methodological concerns (the period prior to the prescription represents physician prescribing behavior rather than a natural rate of MI), there was no control group of hypogonadal men who did not receive a T prescription, so it is unknown whether rates of MI were higher, lower, or unchanged in this population. Finally, a meta-analysis of placebo-controlled Testosterone Trials reported increased CV events for men who received T.[63] As the FDA noted, however, this study's results were confounded by incorrect data culled from the component studies and an overly broad definition of what constituted a CV event.[59] The FDA's own analysis indicated that the number of important CV events were similar in the T-treated and placebo-treated groups.[59] At least 6 other meta-analyses found contradictory results, with no increased T-associated CV risks.[64–70] The largest of these suggested decreased risks for men at high CV risk due to cardiometabolic disorders.[64]

Substantial literature indicates that low T levels are associated with increased mortality, coronary artery disease (severity and incidence), increased fat mass, and decreased lean mass. Two observational studies reported reduced mortality, by half, in men with low T who received TTh compared with untreated men.[71,72] Several small to moderate-sized placebo-controlled trials showed CV benefits with T administration in men with known CV disease, specifically angina and heart failure.[73–77]

Although the new FDA warning is accurate in that some studies did report increased CV risks with T administration whereas others did not, the strength of the few studies suggesting any increased risk was remarkably weak. The European Medicines Agency performed its own review and declined to add a new CV warning.[78]

REVIEW OF NEW CARDIOVASCULAR STUDIES

Since the FDA advisory committee meeting in 2014, 22 new studies were published addressing CV risks of TTh, including 11 clinical trials and 11 observational data analyses. Five of these studies comprise the Testosterone Trials. None has proved that T is associated with an increased risk of CV events.

In 2016, the primary results of the Testosterone Trials were published.[79] This was arguably the most important Testosterone Trial to date, representing the first large, government-funded, multicenter, placebo-controlled trial involving 790 men 65 years or greater assigned to either T gel or placebo for 1 year. The trial included a second year to monitor for safety outcomes. The Testosterone Trials confirmed that T therapy improved sexual function, sexual desire (increase in T levels was associated with significantly increased sexual activity, as assessed by the Psychosexual Daily Questionnaire as well as significantly increased sexual desire and erectile function), physical activity, and mood. Rates of MACE were identical in the first year for the T arm and placebo arms, with N = 7. In the second year, however, there were only 2 MACEs in the T arm compared with 9 in the placebo arm, albeit not statistically significant.

Subsequently, Budoff and colleagues[80] presented results of CT angiography in subset of 138 men from the Testosterone Trials. Compared with placebo, T treatment was associated with a significantly greater increase in noncalcified and total plaque volume but not in calcified plaque. No major CV events occurred in either treatment group. First, the volume of noncalcified plaque has not been associated with CV outcomes, so the significance of this finding is unknown. Second, CAC scores do have a

well-established association with CV outcomes, and this measure did not change with T administration. Finally, there were no adverse CV events in this subgroup, and as discussed previously, for the entire study population of 790 men in the Testosterone Trials there were a greater number of MACEs in the placebo arm than the T arm (16 vs 9, respectively).[80]

Testosterone's Effects on Atherosclerosis Progression in Aging Men was a 3-year placebo-controlled, double-blind, parallel-group randomized trial involving 308 men 60 years or older with low or low-normal T levels[81]; 156 participants were randomized to receive 7.5 g of 1% T and 152 were randomized to receive placebo gel packets daily for 3 years, with dose adjustment targeted to achieve T levels between 500 ng/dL and 900 ng/dL. Results were that T administration for 3 years versus placebo did not result in a significant difference in the rates of change in either common carotid artery intima-media thickness or CAC. No MACEs were reported because this trial was only powered to evaluate atherosclerosis progression and, therefore, these findings should not be interpreted as establishing CV safety of T use in older men.

SUMMARY OF CARDIOVASCULAR STUDIES BECAUSE FOOD AND DRUG ADMINISTRATION LABEL CHANGE

Although the newly added CV warning to T products mandated by the FDA is technically accurate, in that some studies have reported increased CV risks and others have not, it is incomplete to note the few observational studies reporting an increased CV risk that are weak with regard to scientific evidence and quality and omit studies that provide evidence to the contrary. Specifically, the overall safety results from the Testosterone Trials revealed fewer MACEs for men who received T compared with placebo by 9 to 16, respectively. Two observational studies showed reduced hazard ratio of MACEs for men whose T levels normalized with treatment compared with those whose T levels failed to normalize, indicating suboptimal treatment may increase CV risk. The attention raised by the FDA investigation into CV risk seems to have prompted additional studies, together with published results from the Testosterone Trials, yet not a single study has emerged to provide evidence to support concerns that T therapy increases CV risk. On the contrary, the totality of evidence of these studies strongly suggests either a neutral or a protective CV effect for T therapy.

Thus, the MHC provides the infrastructure to affect change as seen in this comprehensive review of T replacement therapy. The MHC provides for a comprehensive and thoughtful evaluation and treatment plan to ensure that T replacement therapy is given in accordance with both the FDA guidelines and the latest CV contributions.

FINAL EXAMPLE OF THE POTENTIAL OF THE MEN'S HEALTH CENTER: OSTEOPOROSIS IS A MEN'S HEALTH CONCERN: INCIDENCE AND GENDER DISPARITIES

Osteoporosis is the most common metabolic bone disease in the United States and worldwide. The National Osteoporosis Foundation estimates that there are 10 million Americans with osteoporosis and an additional 43 million with low bone mineral density (BMD).[82] In 2005, more than 2 million incident fractures were reported in the United States alone.[83] Worldwide, osteoporosis causes more than 8.9 million fractures annually, resulting in an osteoporotic fracture every 3 seconds.[84] The economic burden of incident osteoporosis related fractures is staggering and the direct medical cost of osteoporosis related fractures in the United States is estimated to be more than $13.8 billion.[85]

With the US population 50 years of age or older predicted to increase by 60% from 2000 to 2025, the economic burden of osteoporosis related fractures is estimated to

increase to 23.5 billion dollars, and at least 25% of this cost will be attributed to treating osteoporosis related fractures in men.[86] In 2010 the National Osteoporosis Foundation estimated that there were 2.8 million men with osteoporosis and another 14.4 million men with low bone mass.[86] Worldwide, men account for 25% of hip fractures,[87] and in the United States men account for nearly 30% of all hip fractures.[88] By 2050, the worldwide incidence of hip fracture in men is projected to increase by 310% compared with 240% in women.[86] In 2025, the estimated number of hip fractures occurring worldwide in men will be similar to that observed in women in 1990.[86]

The estimated lifetime risk of an osteoporosis-related fracture in US men is at least 1 in 5.[86] This is in contrast to the 1 in 7 lifetime risk of prostate cancer. Studies of older men's knowledge about osteoporosis demonstrated that 83% of men did not believe that they were susceptible to osteoporosis, and 43% could not correctly define osteoporosis. Osteoporosis-related fractures in men lead to significant disability, diminished quality of life, and increased mortality.[87] One in 6 men will sustain a hip fracture by age 90, and a man's risk of death from complications of a hip fracture is 34%.[88] After a hip fracture 15% of men are unable to walk at 2 years, and only 34% are able to walk without an assisting device.[88]

Despite these remarkable statistics, significant gaps still remain in the management of osteoporosis in men. A study of 51,000 adults admitted with a hip fracture in the state of North Carolina showed that only 2.2% of men admitted with a fracture received treatment of osteoporosis, and men were 75% less likely than women to be treated.[89] Of those men who did receive treatment, two-thirds received calcium and vitamin D only.[90]

GAPS IN TREATMENT IN MALE OSTEOPOROSIS ARE SIGNIFICANT

Although the health and economic impact of osteoporosis on men is well described, there remains a paucity of research on osteoporosis therapies in men. A systematic review and meta-analysis of osteoporosis treatment efficacy in men could identify only 22 randomized clinical trials that evaluated the efficacy of a treatment of osteoporosis or low BMD for adult men that reported fracture outcomes.[91] A prior systematic review and meta-analysis completed in 2011 included only 5 studies reporting fracture outcomes and concluded that "the evidence of the efficacy of osteoporosis treatment to reduce fracture risk in men was inconclusive."[92]

Vertebral fractures are a marker of bone fragility and indicate a higher risk of fractures. The presence of 1 or more prevalent vertebral fractures on lateral spine radiographs is a strong predictor of future incident vertebral fractures and a moderate predictor of nonvertebral fractures independent of BMD.[93] The National Osteoporosis Foundation recommends routine DXA screening for all men over 70 and for men over 50 based on risk factor profile.[94]

Treatment includes making healthy lifestyle changes, including getting 1000 mg to 1200 mg of calcium daily through dietary sources and using supplements if dietary sources are insufficient.[95] Vitamin D supplementation to achieve blood 24-hydroxyvitamin D levels of at least 30 ng/mL is also recommended as is 30 minutes to 40 minutes of weightbearing exercises 3 times to 4 times per week, limiting alcohol to fewer than 3 drinks per day, and smoking cessation, recommended for all men.[95]

Treatment with a specific bone-forming medication is indicated in any man with a low impact fracture, a T score—2.5 SD below mean for normal young white men, or T score from −1 to −2.5 with high 10-year risk of fracture greater than or equal to 20% overall or 3% at the hip using FRAX or long-term glucocorticoid therapy greater

than 7.5 mg daily. Currently there are 5 FDA-approved drugs for treatment of osteoporosis in men, including alendronate, risedronate, zoledronic acid, teriparatide, and denosumab. Response to treatment should be monitored by serial BMD at the hip and spine every 1 year to 2 years, and markers of bone turnover or bone formation may be considered.[95]

Recently updated guidelines from the American College of Physicians for treatment of low BMD and osteoporosis to prevent fractures in men and women reiterate that low BMD as measured by dual-energy x-ray absorptiometry is an imperfect predictor of fracture risk, identifying less than one-half of the people who go on to have an osteoporotic fracture.[96] There is low-quality evidence showing the appropriate duration of treatment is uncertain, although high-risk patients may benefit from more than 5 years of treatment.[96] Newer imaging modalities to improve on fracture risk estimation include quantitative CT and trabecular bone score. Quantitative CT improves quantification of tissue density within a region of interest and trabecular bone score can provide information regarding bone architecture and quality rather than bone quantity.[97]

THE COMPONENTS OF A MEN'S HEALTH CURRICULUM: AN OUTGROWTH OF THE MEN'S HEALTH CENTER

A dedicated men's health curriculum is long overdue and would be a natural outgrowth of an MHC. Such a curriculum would begin with a deep understanding of the social determinants of men's health, why men do or do not seek health care, and, most importantly, how they view and address their acute and chronic health conditions. Teaching men's health should not be limited to conditions solely focused on urologic or CV conditions but should focus on the interaction between the 2 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 health care issues. Health care providers need to be adequately trained to care for men who have sex with men, transgendered patients, and complex geriatric men. The future will see fellowships based on such curricular platforms to train men's health specialists.

Men's health should be categorized into 4 general categories:

1. Conditions that are unique to men (eg, prostate cancer, prostate disease, and ED)
2. Diseases or illnesses that are more prevalent in men compared with women (eg, CV disease, stroke, and renal disease)
3. Health issues for which risk factors and adverse outcomes are different in men (eg, obesity)
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 (eg, access to care)

A men's health curriculum must be rooted in the deep understanding of the impact of masculinity factors on health care 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 explain men's self-representation and internalization of notions of masculine social norms that drive or avoid the receipt of appropriate health care services. Understanding poor health status and literacy in men includes considering how masculinity and gendered social

determinants of health (eg, 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.

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 with expertise in the aforementioned arenas.

BUILDING A MEN'S HEALTH CENTER

Before developing a business plan for a MHC, it has to be decided what and whom it will encompass, organization, revenue versus expenses, sustainability, and opportunities for growth. To build a successful enterprise, there must be a buy-in from leadership (in either an academic or private practice setting) as well as a cadre of specialties, including partnerships with various subspecialists in cardiology, endocrinology, psychiatry, orthopedics, and dermatology, who are truly vested in the need for integration of thought, goals, and vision. In the past, most MHCs have focused on sexual health and administration of T.

This is a time of great stress on the medical system and health care providers. The adaptation of the patient-centered medical home model, electronic medical records, and increasing scrutiny of testing and outcomes all add to the burden of clinical management of male patients. Men tend to present to health care providers later with symptoms and far more advanced along the disease spectrum than their female counterparts. A men's health program and concentration can allow those symptoms men see as vital to a healthy life (eg, sexual function) and propel them to 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 program or MHC established to address these needs.

THE FUTURE OF MEN'S HEALTH

Men's health has received both praise and skepticism over the past decade, with some bona fide controversy. The importance of men focusing on their health with regular preventive care is highlighted by numerous awareness events throughout the year, including Men's Health Month in June, and November, which highlights prostate cancer, testicular cancer, and mental health in men during that month. Because women make up to 80% of the health care decisions for their families, including men, the future of men's health can be positively affected by a better understanding of men's health issues by women. Many MHCs have notoriously treated thousands of men with T or injections for ED without progressing through the proper guidelines of national organizations, often charging patients hundreds of dollars for proprietary treatments that could be offered for much less with standard prescriptions. The future of men's health will be well served by integrated MHCs that focus on the entire man, with proper education and testing and careful shared decision making between patient and provider.

The latest annual statistics from the Centers for Disease Control and Prevention (www.CDC.gov) show for the first time in decades the life expectancy in 2015 for US men decreased by 0.2 years to 76.3 years.[98] Age-adjusted cancer deaths was the only area of improvement because 9 of the 10 top causes of death increased, including heart disease, chronic lower respiratory disease, unintentional injuries, stroke, Alzheimer disease, diabetes, kidney disease, and suicide. Despite improvement in most other age groups and races over the past decade, middle-aged (ages 45–54 years) white Americans have slowly been experiencing an increase in all-cause mortality due to significant increases in poisonings (including opioids), suicide, and chronic liver disease. The largest gap in life expectancy between men and women occurred in 1979 (7.8 years favoring women) and decreased to 4.8 years in 2010 and has remained fairly stable since. As men's health specialists hope to continue to decrease the life expectancy gap between men and women, addressing these concerning trends will be critical, especially dealing with the opioid crisis in America.

Men's mental health and how they think about their health are critical to the future of men's health. Poor health choice patterns are established during those years under the age of 50 where men are twice as likely to die compared with women. Being male is the single largest demographic factor for early death.[99]

Addressing these important men's health issues will not be easy. As the future of medicine focuses on quality and value, a better understanding of the social determinants of men's health will identify potential areas of improvement. Advocating for men's health will become more important in the years to come because access to care and costs of care are limiting factors in a population that has not typically focused on their own health. Reaching boys and men at all stages of life with important health behavior education will allow them to live their lives to the fullest. The American Urological Association Men's Health Checklist is a comprehensive outline of health topics for providers to address for various ages of men. Women and other social support systems can have a positive impact on male health, which ultimately improves the lives of men, women, and children. Men's health is family health!

REFERENCES

1. Fontanarosa PB, Cole HM. Theme issue on men's health: call for papers. JAMA 2006;295:440–4.
2. Agency for healthcare research and quality. Evidence Based Report. December, 2005.
3. National Center for Health Statistics Fact Sheets. December, 2005.
4. National Center for Health Statistics. Health, United States, 2015: with special feature on racial and ethnic health disparities. Hyattsville (MD). 2016.
5. Penson D, Kreiger JN. Men's health. Are we missing the big picture? JGIM 2001; 16:717–71.
6. Schlichthorst M, Sanci LA, Pirkis J, et al. Why do men go to the doctor? Socio-demographic and lifestyle factors associated with healthcare utilisation among a cohort of Australian men. BMC Public Health 2016;16(Suppl 3):1028.
7. Courtenay WH. Constructions of masculinity and their influence on men's well being: a theory of gender and health. Soc Sci Med 2000;50:1385–401.
8. Rose I, Kim MT, Dennison CR, et al. The contexts of adherence for African Americans with high blood pressure. J Adv Nurs 2000;32:587–94.
9. Plascencia A, Ostfield AM, Gruber SB. Effects of sex on differences in awareness, treatment, and control of blood pressure. Am J Prev Med 1988;4:315–26.

10. Sandman D, Simantov E, An C. Out of Touch: American Men and the Health Care System. The Commonwealth Fund. March 2000.
11. Thompson IM, Tangen CM, Goodman PJ, et al. Erectile dysfunction and subsequent cardiovascular disease. JAMA 2005;294(23):2996–3002.
12. Vlachopoulos CV, Terentes-Printzios DG, Ioakeimidis NK, et al. Prediction of cardiovascular events and all-cause mortality with erectile dysfunction: a systematic review and meta-analysis of cohort studies. Circ Cardiovasc Qual Outcomes 2013;6:99–109.
13. Fung MM, Bettencourt R, Barrett-Connor E. Heart disease risk factors predict erectile dysfunction 25 years later: the Rancho Bernardo Study. J Am Coll Cardiol 2004;43:1405–11.
14. Montorsi P, Ravagnani PM, Galli S, et al. Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: the COBRA trial. Eur Heart J 2006;27:2632–9.
15. Hotaling JM, Walsh TJ, Macleod LC, et al. Erectile dysfunction is not independently associated with cardiovascular death: data from the Vitamins and Lifestyle (VITAL) study. J Sex Med 2012;9:2104–10.
16. Nehra A, Jackson G, Miner M, et al. The Princeton III consensus recommendations for the management of erectile dysfunction and cardiovascular disease. Mayo Clin Proc 2012;87:766–78.
17. Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ 2017;357:j2099.
18. Banks E, Joshy G, Abhayaratna WP, et al. Erectile dysfunction severity as a risk marker for cardiovascular disease hospitalisation and all-cause mortality: a prospective cohort study. PLoS Med 2013;10:e1001372.
19. Inman BA, Sauver JL, Jacobson DJ, et al. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. Mayo Clin Proc 2009; 84:108–13.
20. Chew KK, Finn J, Stuckey B, et al. Erectile dysfunction as a predictor for subsequent atherosclerotic cardiovascular events: findings from a linked-data study. J Sex Med 2010;7:192–202.
21. Feldman DI, Cainzos-Achirica M, Billups KL, et al. Subclinical vascular disease and subsequent erectile dysfunction: the Multiethnic Study of Atherosclerosis (MESA). Clin Cardiol 2016;39:291–8.
22. Jackson G, Boon N, Eardley I, et al. Erectile dysfunction and coronary artery disease prediction: evidence-based guidance and consensus. Int J Clin Pract 2010; 64:848–57.
23. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation 2013;127(1):6–245.
24. Fox CS, Evans JC, Larson MG, et al. Temporal trends in coronary heart disease mortality and sudden cardiac death from 1950 to 1999: the Framingham Heart Study. Circulation 2004;110:522–7.
25. Kuller L, Cooper M, Perper J. Epidemiology of sudden death. Arch Intern Med 1972;129:714–9.
26. Podrid PJ, Myerburg RJ. Epidemiology and stratification of risk for sudden cardiac death. Clin Cardiol 2005;28:I3–11.
27. Ni H, Coady S, Rosamond W, et al. Trends from 1987 to 2004 in sudden death due to coronary heart disease: the Atherosclerosis Risk in Communities (ARIC) study. Am Heart J 2009;157:46.

28. Shin D, Pregenzer G, Gardin JM. Erectile dysfunction: a disease marker for cardiovascular disease. Cardiol Rev 2011;19:5–11.
29. Gandaglia G, Briganti A, Jackson G, et al. A systematic review of the association between erectile dysfunction and cardiovascular disease. Eur Urol 2014;65:968–78.
30. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2935–59.
31. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: executive summary. J Am Coll Cardiol 2010;56:2182–99.
32. Blaha MJ, Yeboah J, Al Rifai M, et al. Providing evidence for subclinical CVD in risk assessment. Glob Heart 2016;11(3):275–85.
33. Chiurlia E, D'Amico R, Ratti C, et al. Subclinical coronary artery atherosclerosis in patients with erectile dysfunction. J Am Coll Cardiol 2005;46:1503–6.
34. Jackson G. Erectile dysfunction and asymptomatic coronary artery disease: frequently detected by computed tomography coronary angiography but not by exercise electrocardiography. Int J Clin Pract 2013;67:1159–62.
35. Yaman O, Gulpinar O, Hasan T, et al. Erectile dysfunction may predict coronary artery disease: relationship between coronary artery calcium scoring and erectile dysfunction severity. Int Urol Nephrol 2008;40:117–23.
36. Gibson AO, Blaha MJ, Arnan MK, et al. Coronary artery calcium and incident cerebrovascular events in an asymptomatic cohort. JACC Cardiovasc Imaging 2014;7:1108–15.
37. Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med 2008;358:1336–45.
38. Kostis JB, Dobrzynski JM. The effect of statins on erectile dysfunction: a meta-analysis of randomized trials. J Sex Med 2014;11:1626–35.
39. Cui Y, Zong H, Yan H, et al. The effect of statins on erectile dysfunction: a systematic review and meta-analysis. J Sex Med 2014;11:1367–75.
40. Kałka D, Domagała Z, Dworak J, et al. Association between physical exercise and quality of erection in men with ischaemic heart disease and erectile dysfunction subjected to physical training. Kardiol Pol 2013;71:573–80.
41. Gupta BP, Murad MH, Clifton MM, et al. The effect of lifestyle modification and cardiovascular risk factor reduction on erectile dysfunction. Arch Intern Med 2011;171:1797.
42. DeLay KJ, Haney N, Hellstrom WJ. Modifying risk factors in the management of erectile dysfunction: a review. World J Mens Health 2016;34:89–100.
43. Esposito K, Giugliano F, Di Palo CD, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. JAMA 2004;291:2978–84.
44. Miner M, Nehra A, Jackson G, et al. All men with vasculogenic erectile dysfunction require a cardiovascular workup. Am J Med 2014;127:174–82.
45. Shah NP, Cainzos-Achirica M, Feldman DI, et al. Cardiovascular disease prevention in men with vascular erectile dysfunction: the view of the preventive cardiologist. Am J Med 2016;129:251–9.
46. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with Androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2010;95:2536–59.
47. Same R, Miner M, Blaha M, et al. Erectile dysfunction: an early sign of cardiovascular disease. Curr Cardiovasc Risk Rep 2015;9:49–57.

48. Blaha MJ, Silverman MG, Budoff MJ. Is there a role for coronary artery calcium scoring for management of asymptomatic patients at risk for coronary artery disease? Clinical risk scores are not sufficient to define primary prevention treatment strategies among asymptomatic patients. Circ Cardiovasc Imaging 2014;7(2): 398–408.
49. Ahmed HM, Al-Mallah MH, McEvoy JW, et al. Maximal exercise testing variables and 10- year survival: fitness risk score derivation from the FIT Project. Mayo Clin Proc 2015;90(3):346–55.
50. Yeboah J, McClelland RL, Polonsky TS, et al. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. JAMA 2012;308(8):788–95.
51. Hecht H, Blaha M, Berman D, et al. Clinical indications for coronary artery calcium scoring in asymtomatic patients: expert consensus statement from the society of cardiovascular computed tomography. J Cardiovasc Comput Tomogr 2017;11:157–68.
52. Blaha MJ, Dardari ZA, Blumenthal RS, et al. The new intermediate risk group: a comparative analysis of the new 2013 ACC/AHA risk assessment guidelines versus prior guidelines in men. Atherosclerosis 2014;237(1):1–4.
53. Gofman JW. The quantitative nature of the relationship of coronary artery atherosclerosis and coronary heart disease risk. Cardiol Dig 1969;4:28–38.
54. Pastuszak AW, Hyman DA, Yadav N, et al. Erectile dysfunction as a marker for cardiovascular disease diagnosis and intervention: a cost analysis. J Sex Med 2015;12:975–84.
55. FDA Drug Safety Communication: FDA cautions about using testosterone products for low testosterone due to aging; requires labeling change to inform of possible increased risk of heart attack and stroke with use 2015. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm436259.htm. Accessed December 14, 2017.
56. Corona G, Isidori AM, Buvat J, et al. Testosterone supplementation and sexual function: a meta- analysis study. J Sex Med 2014;11(6):1577–92.
57. Nguyen CP, Hirsch MS, Moeny D, et al. Testosterone and "Age Related Hypogonadism"–FDA concerns. N Engl J Med 2015;373(8):689–91.
58. Basaria S, Coviello AD, Travison TG, et al. Adverse events associated with testosterone administration. N Engl J Med 2010;363:109–22.
59. US Food and Drug Administration. Citizen petition denial response From FDA CDER to Public Citizen. Published July 16, 2014. Accessed August 31, 2014. Available at: http://www.citizen.org/documents/2184_FDA%20Denial%20of% 20Petition_July%2016, %202014.pdf. Accessed April 28, 2016.
60. Vigen R, O'Donnell CI, Baron AE, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. JAMA 2013;310(17):1829–36.
61. Morgentaler A, Lunenfeld B. Testosterone and cardiovascular risk: world's experts take unprecedented action to correct misinformation. Aging Male 2014; 17(2):63–5.
62. Finkle WD, Greenland S, Ridgeway GK, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. PLoS One 2014; 9(1):e85805.
63. Xu L, Freeman G, Cowling BJ, et al. Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. BMC Med 2013;11:108.

64. Corona G, Maseroli E, Rastrelli G, et al. Cardiovascular risk associated with testosterone-boosting medications: a systematic review and meta-analysis. Expert Opin Drug Saf 2014;13(10):1327–51.

65. Borst SE, Shuster JJ, Zou B, et al. Cardiovascular risks and elevation of serum DHT vary by route of testosterone administration: a systematic review and meta-analysis. BMC Med 2014;12:211.

66. Calof OM, Singh AB, Lee ML, et al. Adverse events associated with testosterone replacement in middle-aged and older men: a meta-analysis of randomized, placebo-controlled trials. J Gerontol A Biol Sci Med Sci 2005;60(11):1451–7.

67. Fernández-Balsells MM, Murad MH, Lane M, Lampropulos JF. Clinical review 1: adverse effects of testosterone therapy in adult men: a systematic review and meta-analysis. J Clin Endocrinol Metab 2010;95(6):2560–75.

68. Haddad RM, Kennedy CC, Caples SM, et al. Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. Mayo Clin Proc 2007;82(1):29–39.

69. Isidori AM, Giannetta E, Gianfrilli D, et al. Effects of testosterone on sexual function in men: results of a meta-analysis. Clin Endocrinol (oxf) 2005;63(4):381–94.

70. Shores MM, Smith NL, Forsberg CW, et al. Testosterone treatment and mortality in men with low testosterone levels. J Clin Endocrinol Metab 2012;97(6):2050–8.

71. Muraleedharan V, Marsh H, Kapoor D, et al. Testosterone deficiency is associated with increased risk of mortality and testosterone replacement improves survival in men with type 2 diabetes. Eur J Endocrinol 2013;169(6):725–33.

72. English KM, Steeds RP, Jones TH, et al. Low-dose transdermal testosterone therapy improves angina threshold in men with chronic stable angina: a randomized, double- blind, placebo-controlled study. Circulation 2000;102(16):1906–11.

73. Caminiti G, Volterrani M, Iellamo F, et al. Effect of long-acting testosterone treatment on functional exercise capacity, skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure a double-blind, placebo-controlled, randomized study. J Am Coll Cardiol 2009; 54(10):919–27.

74. Malkin CJ, Pugh PJ, West JN, et al. Testosterone therapy in men with moderate severity heart failure: a double-blind randomized placebo controlled trial. Eur Heart J 2006;27(1):57–64.

75. Pugh PJ, Jones RD, West JN, et al. Testosterone treatment for men with chronic heart failure. Heart 2004;90(4):446–7.

76. Iellamo F, Volterrani M, Caminiti G, et al. Testosterone therapy in women with chronic heart failure: a pilot double-blind, randomized, placebo-controlled study. J Am Coll Cardiol 2010;56(16):1310–6.

77. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Testosteronecontaining_medicines/human_referral_prac_000037.jsp&mid=WC0b01ac05805c516f. Accessed December 14, 2017.

78. Snyder PJ, Bhasin S, Cunningham GR, et al. Testosterone trials investigators. Effects of testosterone treatment in older men. N Engl J Med 2016;374(7): 611–24.

79. Budoff MJ, Ellenberg SS, Lewis CE, et al. Testosterone treatment and coronary artery plaque volume in older men with low testosterone. JAMA 2017;317(7): 708–16.

80. Basaria S, Harman SM, Travison TG, et al. Effects of testosterone administration for 3 years on subclinical atherosclerosis progression in older men with low or low-normal testosterone levels: a randomized clinical trial. JAMA 2015;314: 570–81.

81. Campion JM, Maricic MJ. Osteoporosis in men. Am Fam Physician 2003;67(7): 1521–6.
82. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. Osteoporos Int 1997;7(5):407–13.
83. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a world-wide projection. Osteoporos Int 1992;2(6):285–9.
84. Stevens JA, Rudd RA. The impact of decreasing U.S. hip fracture rates on future hip fracture estimates. Osteoporos Int 2013;24:2725–8.
85. Day, Cheeseman J. Population projections of the United States by age, sex, race, and hispanic origin: 1995 to 2050, U.S. bureau of the census, current population reports. Washington, DC: U.S. Government Printing Office; 1996. p. 25–1130.
86. Schnell S, Friedman SM, Mendelson DA, et al. The 1-year mortality of patients treated in a hip fracture program for elders. Geriatr Orthop Surg Rehabil 2010; 1(1):6–14.
87. Pande I, Scott DL, O'Neill TW, et al. Quality of life, morbidity, and mortality after low trauma hip fracture in men. Ann Rheu Dis 2006;65(1):87–92.
88. Ip TP, Leung J, Kung AWC. Management of osteoporosis in patients hospitalized for hip fractures. Osteoporos Int 2010;21(Suppl 4):605–14.
89. Kiebzak GM, Beinart GA, Perser K, et al. Undertreatment of osteoporosis in men with hip fracture. Arch Intern Med 2002;162(19):2217–22.
90. Nayak S, Greenspan S. Osteoporosis treatment efficacy for men: a systematic review and meta-analysis. J Am Geriatr Soc 2017;65(3):490–5.
91. Schwarz P, Jorgensen NR, Mosekilde L, et al. The evidence for efficacy of osteoporosis treatment in men with primary osteoporosis: a systematic review and meta-analysis of antiresorptive and anabolic treatment in men. J Osteoporos 2011;2011:2598–618.
92. Kim SH, Choi HS, Rhee Y, et al. Prevalent vertebral fractures predict subsequent radiographic vertebral fractures in postmenopausal Korean women receiving antiresorptive agent. Osteoporos Int 2011;22:781.
93. Schousboe JT, Vokes T, Broy SB, et al. Vertebral fracture assessment: the 2007 ISCD official positions. J Clin Densitom 2008;11(1):92–108.
94. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2012;97(6):1802–22.
95. Qaseem A, Forciea MA, McLean RM, et al, For the Clinical Guidelines Committee of the American College of Physicians. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. Ann Intern Med 2017;166:818–39.
96. Expert Panel on Musculoskeletal Imaging, Ward RJ, Roberts CC, et al. ACR appropriateness criteria osteoporosis and bone mineral density. J Am Coll Radiol 2017;14(5S):S189–202.
97. Kochanek KD, Murphy SL, Xu J, et al. Deaths: final data for 2014. Natl Vital Stat Rep 2016;65(4):1–122.
98. Neese R, Kruger DJ, Nesse RM. Economic transition, male competition, and sex differences in mortality rates. Evol Psychol 2007;5:358–74. Available at: www. CDC.gov.
99. AUA Men's Health Checklist: Am Urological Assn Publication 2014.