

Integrative Approaches to Men's Health

Overview

This overview focuses on how an Integrative Health approach can be useful for prevention and treatment of issues specific to men. As with all aspects of our health, men's health issues do not exist in isolation; focusing on prostate health, erectile function, testosterone, and other concerns must be done with the full picture in mind. Integrative Health emphasizes mindful awareness and general self-care along with conventional and integrative approaches to health and well-being. The Circle of Health highlights eight areas of self-care: Surroundings; Personal Development; Nutrition; Recharge; Family, Friends, and Co-workers; Spirit and Soul; Mind and Emotions; and Physical Activity. The patient narrative below provides an example of what might be covered in a men's health-focused encounter. Some studies have also showed success with certain complementary approaches, particularly supplements, when [prostate cancer](#), [erectile dysfunction](#), [benign prostatic hypertrophy](#), [testosterone deficiency](#), and other problems arise.

Meet the Patient

Keith is an 88-year-old retired teacher who is seeing you for an Integrative Health visit. His wife of 60 years died unexpectedly five years ago from a stroke. He has a history of prostate cancer (Gleason score of 8, 4+4) and is status post-prostatectomy in 2010. Before that, he had benign prostatic hypertrophy (BPH) with severe lower urinary tract symptoms with an average International Prostate Symptom Score (IPSS) of 24 and had a prostate-specific antigen (PSA) level of 27 before his prostatectomy. He now suffers from urinary incontinence and erectile dysfunction (ED) with an International Index of Erectile Function (IIEF) score of 6, but he is not interested in treatment for ED.

Keith's stated reason for coming in today is to improve his chances of living until 90, so that he can see his granddaughter, Jessica, get married. He is very close to her because she lived with him and his late wife after his daughter passed away from a drug overdose. Jessica is currently attending college locally.

Keith's son, Jeremy, 52 years old, is struggling with depression and substance abuse. Jeremy is recently divorced and moved back in with Keith. Keith is concerned that Jeremy's depression is worsening as his alcohol use increases.

Keith's other past medical history includes the following:

- He has coronary artery disease and had a four-vessel bypass in 2000.
- He has recently had bilateral cataract surgery.
- His PSA was undetectable until last year when it was 0.05 ng/dL. Just last week it increased to 0.75 ng/dL, and he is aware that this means his prostate cancer is coming back.
- His current waist circumference is 41.25 inches.

- He has left knee pain with activity, especially walking. An x-ray of the left knee two years ago revealed moderately severe degenerative joint disease (DJD).

Keith was asked by one of his primary care team members to fill out a Personal Health Inventory (PHI).

Personal Health Inventory

On his PHI, Keith rates himself a 2 out of 5 for his overall physical well-being and a 3 for overall mental and emotional well-being. When asked what matters most to him and why he wants to be healthy, Keith responds:

“My family is the most important thing in my life. I feel very grateful for the support I have, especially after my wife died a few years ago. My granddaughter is the apple of my eye. She often calls every day. I want to be around to see her get married. My son’s battle against addiction worries me greatly.”

For the eight areas of self-care, Keith rates himself on where he is, and where he would like to be. He decides to first focus on the areas of Nutrition and Mind and Emotions by cooking more for himself and learning more about meditation.

More information is available in [Keith’s PHI](#).

Introduction

This overview focuses on Integrative Health approaches that often are of special concern to men who seek medical care: prostate cancer, ED, BPH, prostatitis, testosterone deficiency, and longevity. Highlighted are key study findings unique to these specific issues or conditions.

Important Statistics

Before discussing each of various men’s health concerns, it is important to consider the overall picture.

Cancer

Cancer is the second leading cause of death in the United States, exceeded only by cardiovascular disease. One in 4 deaths in the United States is from cancer. In 2016, there were 833,308 new cases of cancer in men in the United States; that same year, 314,568 U.S. men died from cancer. For every 100,000 men, 471 new cancer cases were reported with 186 cancer deaths.¹ The number of deaths from specific cancers are summarized in Table 1, below.



Table 1. Cancer Rates in Men, United States¹

Type of Cancer	Incidence	Deaths
Prostate Cancer	192,443	30,370
Lung Cancer	113,044	80,775
Colon Cancer	73,829	27,642

Heart Disease

The prevalence of cardiovascular disease (CVD) in the United States from 2013-2016 was 61.5 million men.² More than half of those men were over age 60. The United States' total population was 331 million in 2020.³ The estimated cost of CVD for both men and women in the United States in 2010 was \$315.4 billion.⁴

Table 2. Prevalence and Mortality of Heart and Vascular Disease in U.S. Men

Heart and Vascular Disease in U.S. Men	2013-2016 Prevalence	2017 Mortality
CVD (cardiovascular disease)	61.5 million	440,460
CHD (coronary heart disease)	9.4 million	213,295

According to the U.S. Burden of Disease Collaborators, ischemic heart disease was the number one cause of years of life lost (YLL) in the United States with 562,900 deaths in 2010.⁵ This was a drop from 648,200 deaths in 1990—a 14% median decrease because of our growing population. There are other remarkable trends from this same report. The number two cause of YLL was lung cancer, with a combined 163,300 deaths for men and women. The diseases with the most marked increase in rank of YLL between 1990 and 2010 were diabetes (which moved up in rank from #15 to #7), drug use disorders (#44 to #15), and—the most striking—Alzheimer disease (#32 to #9), which led to a whopping 524% median increase in deaths.

The proportional mortality (percent of total deaths for all ages) in the United States is 35% from CVD and 23% from cancers.⁶ A large percentage of those cancer deaths are still coming from lung cancer, which is considered primarily preventable through discouraging tobacco use.

Interestingly, the high proportion of mortality from CVD in the United States in 2008 continues despite drops in the mean systolic BP from 1980 to 2008 and a steady decline in the mean total cholesterol during the same time period. In contrast to those trends, between 1980 and 2008 the United States saw steadily increasing mean fasting blood glucose levels and mean body mass index (BMI). U.S. men had significantly higher mean fasting blood sugar in 2008 than U.S. women, whereas women had modestly higher mean total cholesterol than men did in 2008.⁶ In general, U.S. men and women, gained weight at virtually the same rates between 1980 and 2008.

Mental Health

In most health systems, limited efforts, are made to integrate aspects of primary care, urology, mental health, and social support.⁷ Living with a chronic disease threatens men's sense of masculinity and self-image, as well as their perceived ability to fulfill expected social roles.⁸

In North America, 75% of the people who die by suicide are men. Men account for 75% of people with substance use disorder.⁹ Men of color seem to be at especially high risk. African American men have suicide rates of 4.5:1 over their female counterparts. In the U.S. population in general, the male to female suicide rate is 3.6:1.⁹

Some studies have found health care professionals are both less likely to diagnose mental illness in men vs. women and are less likely to act upon mental illness in men once detected.⁹ This has led many to call men's mental health care a "silent crisis" in the United States.

American boys are much more commonly diagnosed with ADHD than are girls, with a prevalence of 14.2% vs. 6.4%.⁹ There is evidence that men display more acting *out*, as opposed to acting *in*, as a symptom of mental illness. Some experts have suggested coining a new diagnosis of "male depression syndrome" or "masked depression." Acting out due to depression manifests as high levels of alcohol and drug misuse, dangerous risk taking, poor impulse control, and increased anger and irritability.⁹ Men are more likely to have comorbid depression/anxiety and substance use disorder than are women.

Uncertainty about employment and dangerous workplace environments appear related to poor mental health in men. For many men, work identity ties closely to self-identity, self-esteem, and self-worth.

A 2015 systematic review and meta-analysis examined social support and self-management interventions that promote men's health and psychosocial well-being.¹⁰ The review and analysis found that physical activity, education, and peer support (buddy systems) have a positive impact on men's quality-of-life measures. However, the authors found insufficient evidence to recommend one specific self-management support intervention over others. The study noted, "Less than 1/3 of the participants engaging with some support service are men."¹⁰ It also noted that, in contrast to physician-run standard medical care, which is usually passive, men seem to respond better to self-management support interventions. By design, these interventions develop patients' abilities to undertake management of health conditions through education, training, and support and develop their knowledge, skills, or psychological and social resources.

In 2013, Moylan explored the concept of Community Men Sheds (CMS) in Australia, in relationship to biopsychosocial and spiritual support for men.¹¹ A CMS is a physical place with a woodworking area, trade tools, equipment, and social area or "tearoom," all built into in a work shed-type setting. Men went to the CMS specifically to be with other men. These gathering places are described by its members as a place where men can simply meet and enjoy being in each other's company. A systematic literature review found that participation resulted in a greater sense of belonging to a community, increased self-esteem, and empowerment, and provided respite for families, and a venue for ideas exchange, including ideas on public health.¹¹

Summary

A variety of specific health problems are more likely to affect men, and men have different preferences for how they interact with the health care system. Some trends are shifting, and while cancer remains a significant risk for U.S. men's morbidity and mortality, CVD and metabolic risk factors, especially mean fasting blood sugar and increased rates of overweight/obesity, are even more prevalent and lethal.

This overview will focus on many of the health problems that are unique to men. However, it is important to emphasize that cardiovascular health remains the number one health risk U.S. men face. Addressing a man's mental health is also critically important to lower his risk of suicide, substance abuse disorder, and other problems. While there are many beneficial options for preventing and treating a number of uniquely male diseases or dysfunctions such as prostate cancer, ED, BPH with or without lower urinary tract symptoms (LUTS), testosterone deficiency (TD), and male longevity, it is important to keep the big picture in mind. By knowing the statistics listed above, we can focus our efforts on the most important health-related issues our nation faces.

Prostate Cancer

Gleason Score

The histologic grade of prostate adenocarcinomas is usually reported according to one of the variations of the Gleason scoring system, which provides a useful, albeit crude, adjunct to tumor staging in determining prognosis.

The Gleason score is calculated based on the dominant histologic grades, from grade 1 (well differentiated) to grade 5 (very poorly differentiated). To derive the classical score, add the two most prevalent pattern grades, yielding a score ranging from 2 to 10.

Because there is some evidence that the least-differentiated component of the specimen may provide independent prognostic information, the score is often provided by its separate components (e.g., Gleason score 3 + 4 = 7; or 4 + 3 = 7) with the most common histologic grade being denoted first. Generally, scores less than 7 are considered lower risk for progression. A score of 7 is intermediate and 8-10 is high risk. Keith's Gleason score of 4+4 puts him into the high-risk category. Gleason scores are widely used in prostate cancer research, so it is important to have a working knowledge of this scale.

Prevention

The Prostate Cancer Prevention Trial (PCPT) looked at the effects of finasteride over a period of seven years. It found finasteride led to a 30% reduction in prostate cancer prevalence, but unfortunately, there was also a trend toward more aggressive prostate cancers in the men treated with finasteride.¹² This was a large study with over 18,000 men enrolled. It should be noted that five men died of prostate cancer in the finasteride study arm with an equal number in the control arm. This was equivalent to less than 1% of the total deaths. In addition, 1,123 men died of CVD and other causes.

An 18-year-follow-up on the Finasteride Prostate Cancer Prevention Trial found that despite the reduction in low-grade prostate cancer rates in the treatment arm, the mortality rate from

prostate cancer was not reduced. This is reflected in the relative risk of prostate cancer of 0.70 in the treatment arm compared to the increase of relative risk (1.17) of high-grade prostate cancer in the finasteride arm.¹³

In 2017, Sak and colleagues did a mini review of long-term consumption of high-dose soy isoflavones in Asian men versus Western men and effect on rates of prostate cancer. The review found that Japanese men who adopt a Western lifestyle and diet have increased rates of prostate cancer comparable to their non-Asian counterparts. An interesting finding in this review was that the ability to metabolize daidzein (a soy isoflavone) to equol, the most biologically active isoflavone estrogen, by certain intestinal bacteria seems to contribute to reducing prostate cancer risk.¹⁴ A 2018 meta-analysis of 30 articles found a statistically significant association between soy consumption (especially fermented soy food) and decreased prostate cancer risk.¹⁵

Findings related to soy are much more favorable than recent reviews of the literature focused on routine consumption of vitamins or antioxidants for the prevention of prostate cancer. Little evidence supports the use of common supplements such as: vitamin D, vitamin A, vitamin C, vitamin E, lycopene, pomegranate, and selenium to prevent prostate cancer.¹⁶ A systematic review of 44 studies published in 2017 reported a lack of evidence to suggest a relationship between fish-derived omega-3 fatty acid consumption and risk of developing or preventing prostate cancer.¹⁷

In all of the prostate cancer prevention studies to date CVD is always the number one cause of death, which is in keeping with the statistics provided at the start of this overview.

Heart disease kills many more men than prostate cancer. This should be constantly and consistently reiterated and emphasized to people who are concerned about prostate cancer.⁸

Risk Factors

Recently, there has been some attention placed on calcium and dairy intake and risk of developing prostate cancer. A meta-analysis of 12 studies of over 900,000 men aged 50-70 found that high calcium intake was a risk factor for advanced prostate cancer, with a relative risk of 1.15.¹⁸ The calcium intake that was considered high ranged from 659 mg to over 2,000 mg daily, compared to 221-750 mg daily, depending on the study. A literature review also uncovered the link between increased dairy intake and prostate cancer initiation and progression.¹⁹

Considering modifiable risk factors for prostate cancer, Campi and colleagues performed a systematic review of 22 observational studies spanning 8-10 years. The evidence was mostly inconclusive in terms of prostate cancer risk factors. However, there were some notable findings regarding antihyperglycemics. The use of metformin in diabetics produced a reduction in the hazard ratio to 0.85 (CI 0.79-0.92), whereas the use of sulfonylureas increased the risk for metastatic prostate cancer.²⁰ Regular aspirin (ASA) use in men over 65 years old reduced risk, with a HR of 0.85 (CI 0.73-0.98, p=0.001). Metformin, ASA, and statins led to modest reductions in prostate cancer risk, while 5-alpha-reductase inhibitor (finasteride) reduced PCA risk but possibly increased high-grade cancer risk. Avoiding obesity (maintaining a BMI of 20-21) also reduced PCA risk. Data on diabetes and meat consumption was conflicting. The effects of

omega-3 fatty acid deficiency, elevated saturated fat intake, and high calcium intake on prostate cancer risk were inconclusive, in contrast with other meta-analyses described previously.²⁰

Most of the studies on prostate cancer indicate that the majority of people in the studies were overweight. This is not surprising, given the rates of overweight/obesity of adult U.S. males. The Alpha-Tocopherol Beta-Carotene (ATBC) study revealed that men with increased BMI had a 40% increased risk of prostate cancer compared to men with normal BMI. From this same study, a significant ($p < 0.001$) increased risk of prostate cancer mortality was associated with increasing BMI from 25-29.9 (RR=1.08), 30-34.9 (RR=1.20), and 35-39.9 (RR=1.34) for the 4,004 documented deaths from prostate carcinoma.²¹

“Two of the largest dietary and supplement studies to analyze risk of prostate cancer essentially arrived at the same conclusion—that obesity can negatively impact prostate risk or progression.”^{22(p422)} A recent meta-analysis of 11 large studies reveals that prostate cancer recurrence and mortality, especially early mortality, have been highly correlated with increasing BMI.²³ For every 5 kg/m² increase a person experiences, there is a 15% higher risk of prostate cancer.

Esposito and colleagues performed a meta-analysis of 10 studies, with 4,343 total cases of prostate cancer. It noted that men living in Westernized countries had 10-15 times the rate of prostate cancer that Asian men had. In this meta-analysis, metabolic syndrome was weakly and not significantly associated with prostate cancer. Hypertension increases the risk of prostate cancer by 15%. Two studies looked at waist circumference over 40 inches and found a 56% increased risk of prostate cancer.²⁴

Lifestyle

In terms of physical activity and prostate cancer risk, evidence is lacking, according to a 2015 systematic review.²⁵ Another 2016 systematic review revealed that physical activity does not reduce the risk of PCA; however, vigorous exercise reduced the risk of aggressive prostate tumors. Vigorous exercise was defined as anything from 75 minutes of exercise per week to more the 40 minutes of daily exercise/sports.²⁶ More research is needed to support a clinically reliable recommendation for vigorous exercise in people trying to prevent aggressive prostate cancer.

Regarding diet and PCA, there are studies on the Mediterranean diet and PCA risk. Cheng and colleagues authored a meta-analysis of 10 studies in 2019 that revealed a relative risk reduction of 0.92 for fatal prostate cancer. However there was a non-statistically significant confidence interval of 0.76-1.11.²⁷

Ornish and colleagues published a study in 2005 that focused on men with low risk prostate cancer (Gleason score less than 7). He recruited 93 men into his study with PSAs in the 4-10 range who declined conventional care, such as surgery, radiation, androgen deprivation, or watchful waiting. The experimental group undertook a comprehensive lifestyle program that included the following components: vegan diet with soy supplements (very low fat, less than 10% calories from fat); 3 gm of fish oils; 400 IU of vitamin E; 200 mcg of selenium; 2 gm of vitamin C; moderate exercise for 30 minutes six days a week; stress management for 60 minutes daily; and one hour per week of support group time. The experimental group had a

significant decrease in PSA levels and decreased growth of prostate cancer cell lines in the lab.²⁸

A two-year follow-up on this Prostate Cancer Lifestyle Trial found that 27% of the controls (n=49) and only 5% of the experimental group (n=43) went on to require conventional care for their prostate cancer ($p < 0.05$).²⁹

Follow-up studies on this original study group looked at genetic markers such as telomere length and gene expression in the prostate. In a 2008 follow-up study, lifestyle was found to modulate gene expression in the prostate. Telomeres are protective DNA and protein complexes at the end of linear chromosomes that promote chromosomal stability. Telomere shortening is counteracted by the cellular enzyme telomerase. The more telomerase, the longer the telomeres, which is healthy for the cells. Ten men from the original Ornish study were followed five years later and compared to 25 controls. Their comprehensive lifestyle changes increased their telomere length; lifestyle changes had effects at a genetic level.³⁰

A six-month randomized, intention-to-treat trial with 47 patients, done in South Carolina, looked at intensive diet, physical activity, and meditation (Mindfulness-Based Stress Reduction) in men with biochemical recurrence of prostate cancer. The patient population was remarkable for a high-level of unemployment at 60%-70%. Another remarkable feature of the patients enrolled in the study was that 77% in the intervention group (n=26) were married/partnered and 90.5% were married/partnered in the control group. Forty-eight percent of all participants had no change in PSA and 52% had an increase in PSA. After six months, PSA in the control group went up from 0.71 to 0.78 and down from 0.87 to 0.84 in the treatment group ($p = 0.45$). A sub-analysis revealed that the men with the highest increase in fruit intake and reduction of saturated fat intake had the best chance at not having PSA levels increase.³¹

The lifestyle program that is beneficial for prostate cancer and telomere length focuses on many of the same areas of self-care as the [Circle of Health](#).

Screening for Prostate Cancer

Studies have found that using PSA for screening in men aged 55-69 can reduce prostate cancer deaths by 25%-32%. Because of this, the USPSTF gives PSA screening for men 55-69 years old a grade C (small benefit). However, for the average risk man, screening for PCA with PSA caused more harm than benefit, according to the USPSTF. Two recent studies (PIVOT and ProtecT) suggest that death from prostate cancer is uncommon and that observation may be appropriate if men have low risk, localized disease, or low-risk PSA levels (PSA < 10 and Gleason < 7). Studies also looked at the use of prostate MRI and found evidence that it can reduce the cost of screening men with elevated PSA when compared with performing prostate biopsies. The take-home points from these more recent data are that PSA screening may reduce death from PCA in properly selected patients and that MRI may be a better option than ultrasound-guided prostate biopsy for those with low-risk elevated PSA. In addition, surgery for prostate cancer may not prolong life, but it can prevent disease progression. In summary, active surveillance in men with prostate cancer is a viable treatment option.³²

Supplements/Herbs

There have been some studies looking at natural treatments for prostate cancer. For example, there is interest in a particular herbal blend called Zyflamend by New Chapter. This preparation contains rosemary, turmeric, ginger, holy basil, green tea, Hu Zhang, Chinese goldthread, barberry, oregano, and Baikal skullcap. A study at Columbia University Medical Center revealed decreased concentration of androgen receptors in prostate cancer cells after 24 hours of exposure to 0.1 mcg/mL of Zyflamend.³³ A phase 1 clinical safety study of men with biopsy-proven high-grade prostatic intraepithelial neoplasia (HGPIN) found no toxicity related to Zyflamend use of 2 capsules, 3 times daily. Of the study participants, 45% had 25%-50% PSA level reduction after 18 months, with no side effects reported. In addition, at 18 months, 60% of the men had benign tissue, 26.7% had HGPIN, and 13.3% had prostate cancer.³⁴

A 2014 follow-up study on Zyflamend and the potential molecular mechanism by which it reduces prostate cancer cell progression found the primary effects of Zyflamend on prostate cancer cells were likely due to goldthread and Baikal skullcap. In cell culture (using cell line CWR22Rv1, castrate-resistant prostate cancer cells) there was 45%-80% inhibition of cell growth at 94 hours of treatment with Zyflamend. The mechanisms of action were increased histone 3 acetylation (which inhibited the expression of class I and class II histone deacetylases,) increased activation of CBP/p300 and inhibition of cell proliferation by up regulating the tumor suppressing gene p21 expression.³⁵

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

For more information on supplements to reduce prostate cancer risk visit National Cancer Institute: [Prostate Cancer, Nutrition, and Dietary Supplements—Health Professional Version](#).

Summary

In the United States, prostate cancer is the most commonly diagnosed non-skin cancer men will face. Thankfully, it has the lowest mortality rate of the top three cancers men face, as discussed in the statistics section above. Thirty-five percent of men diagnosed and treated for prostate cancer will have a biochemically defined recurrence. Unfortunately, one-third of those men will develop metastatic disease within the subsequent five years.³⁶

Encouraging men to maintain a healthy weight can lower their risk of prostate cancer, and especially early mortality related to prostate cancer. Use of Zyflamend, 2 capsules, 3 times daily for 18 months or more, in men with HGPIN, may reduce its progression to prostate cancer and may promote it turning back into benign prostatic tissue. Intensive lifestyle changes may help men with low-risk prostate cancer avoid the need for conventional prostate cancer treatments. Active surveillance of men with localized prostate cancer is a viable treatment option. Even after conventional treatment, biochemical recurrence of prostate cancer is not uncommon. Additional high-quality research is needed to help counsel those patients on their options.

Erectile Dysfunction

ED is a common issue for many men. The Massachusetts Male Aging Study found rates of ED as high as 52% in U.S. men 40-70 years-old. Of those, 70% had mild to moderate ED, and 30% had severe ED. Depending on what population you look at, the rates can run as high as 68.7%.³⁷ Many men will not ask for help with this issue unless their health care provider brings it up. The [International Index of Erectile Function \(IIEF\) questionnaire](#) can help screen for the presence and severity of ED. The IIEF meets psychometric criteria for test reliability and validity, has a high degree of sensitivity and specificity, and correlates well with other measures of treatment outcome. There is a 15-question variation called the IIEF-15 that explores five domains of sexual function and a 5-question form called the IIEF-5 that focuses entirely on erectile function. The IIEF-5 questionnaire works well as a starting point for primary care. It has demonstrated consistent and robust treatment responsiveness in studies in the United States, Europe, and Asia, as well as in a wide range of etiological subgroups.

Erectile dysfunction is not an uncommon complaint. It has been estimated that 20% of men over age 20 will suffer ED. That number climbs to 75% in men over 75 years old. The relative risk of ED drops with tobacco cessation and exercise.³² A systematic review and meta-analysis of seven studies including 478 men used the IIEF to validate outcomes. Follow-up was from 8 weeks to 2 years and included information on physical activity and exercise. With increased physical activity and exercise, there was a statistically significant improvement in patient-reported erectile function. The largest effects were from aerobic exercise with moderate to vigorous intensity. The amount of weekly exercise found to have beneficial effects ranged from 90-180 minutes.³⁸

Erectile Dysfunction and Heart Disease

Studies have revealed an increased risk of CV events in the years following diagnosis of ED. The hazard ratio for a CV event in the 9 years after ED onset ranges from 1.25-1.45.³⁹ Consider further imaging or work up for coronary heart disease in men between 40 and 60 years old with ED and a calculated ASCVD risk score of greater than or equal to 10%. In addition, consider screening all ED patients for CVD if they also present with symptoms of chest pain, presyncope, or shortness of breath.³⁹

Metabolic Syndrome

A study of 393 men between 40-70-years-old from a urology clinic looked at the correlation between rate and severity of ED and waist circumference of greater than or less than 102 centimeters (approx. 40 inches), as well as other measures of metabolic syndrome (MS). Of the study's 393 patients, 270 had some level of ED. Seventy-nine percent of the men who met the criteria for MS had ED, as compared to 62% without MS ($p < 0.001$).

Elevated fasting glucose, increased blood pressure, and increased waist circumference greater than 40 inches were most closely related to increased risk of ED. Waist circumference of over 40 inches had the greatest effect, with 2.3 times the increased relative risk. If waist circumference over 40 in is combined with and low HDL and high triglycerides, the relative risk of ED shoots up to 3.38. Most of the effects of MS and increased waist circumference were seen in 40- to 49-year-old men, and less correlation was noted in older men. This may indicate an independent risk of ED with aging.³⁷

Obesity

Researchers in Southern Brazil examined ED in 256 men 40 years and older. They found 7-19 times higher risk of ED in men over 60 depending on anthropometric indices used, including BMI and waist circumference over 102 cm (approximately 40 in). Waist circumference over 102 cm carried the highest risk of developing ED with a risk of 19.37 compared to a risk of 1.3 for BMI over 25 alone. They did not find as much correlation in men aged 40-60.⁴⁰

A randomized single-blinded trial looked at weight loss and its effect on ED in 110 Italian men 35-55 years old. They used an IIEF score of less than or equal to 21 to identify ED. Twelve percent of men less than 59 years old had moderately severe ED compared to 22% of men 60-69 years old, and 30% of the men older than 69 years of age. The men received detailed advice on weight loss and increasing physical activity. The intervention group's average BMI went down from 36.9 to 31.2, and their IIEF score improved from 13.9 to 17 ($p < 0.001$). Out of the 55 men randomized to the intervention group, 17 achieved IIEF scores at or above 22. The study also focused on waist to hip ratio and found an even higher degree of correlation between high ratios (≥ 1.0) and ED compared to BMI.⁴¹ The authors brought up the possibility that exercise improves mental health, thereby influencing erectile function. Most likely, ED is multifactorial.

Patients and clinicians often fail to appreciate that mind, body, and other influences all make significant contributions to healthy erectile function. Keep all of these areas in mind as you individualize care.

Complementary Approaches

Dietary Supplements

There is increasing interest in natural supplements that may improve erectile function. One such compound is arginine aspartate, with and without adenosine monophosphate. A small French trial involving 26 men with an average age of 56 who had mild to moderate ED tested its effects.⁴² L-arginine aspartate in a dose of 8 gm with adenosine monophosphate 200 mg was taken orally 1-2 hours before intercourse. There was significant improvement in IIEF scores ($p = 0.01-0.04$). Tolerability and safety were equal to placebo.

A 2019 study found improved efficacy of tadalafil (Cialis) when combined with Chinese herbal medicine. This same study did not report any increased side effects from adding the Chinese herbal medicine. A review and meta-analysis including 24 trials with 2,080 participants looked at supplements for ED. Of all the supplements reviewed, ginseng improved the IIEF-5 scores the most significantly, with a $p < 0.01$.⁴³ The dose of *Panax ginseng* root used ranged from 100 mg up to 1.8 g daily. The studies specifically listed Korean red ginseng as the product of choice.⁴³

Acupuncture

Acupuncture has been proposed as an option for ED. A 2019 review of 22 trials found the studies to be low-quality but did note that acupuncture may show promise as an adjunctive treatment for people suffering from mainly psychogenic ED.⁴⁴ A 2018 and a 2015 review both found that data was not of good enough quality to draw firm conclusions. The 2015 study concluded that there is not sufficient evidence to support recommending acupuncture for ED.^{45,46}

Saffron has been reported to help with ED, and there have been some preliminary reports of improved spermatogenesis with supplementation. A review of 6 trials only reported one study on spermatogenesis noting increased normal sperm morphology and motility with saffron use. Saffron was found to have a positive effect on ED but contradictory effects on sperm quality, according to the authors.⁴⁷ The saffron dosages studied were 15 mg to 200 mg daily. Better results were reported with higher doses and topical administration (gel) in diabetic patients.

Phosphodiesterase Type 5 Inhibitors

The American Urological Association (AUA) recommends men with ED be informed regarding the treatment option of an FDA-approved oral phosphodiesterase type 5 inhibitor (PDE5i), including discussion of the benefits and risks/burdens, unless contra-indicated. When prescribing men an oral PDE5i, provide instructions to maximize benefit/efficacy, including guidance on how to titrate the medication.⁴⁸ In the United States, the PDE5is available are sildenafil, tadalafil, vardenafil, and avanafil. Data suggests that men with diabetes and men who are post-prostatectomy have more severe ED at baseline and less robust responses to PDE5i. The most frequent reported adverse effects are dyspepsia, headache, flushing, back pain, nasal congestion, myalgia, visual disturbance, and dizziness. The reported adverse effects increase with increasing dosages of the PDE5i. Avoid co-administration with nitrate-containing medications due to precipitous drops in blood pressure. Do not use these medications in men with severe renal or hepatic disease. Use the medications in conjunction with sexual stimulation and not right before or after a large meal. It may also take several trials of use to determine effectiveness and proper dosing. The goal is to find a balance between efficacy and minimal adverse effects.

Summary

ED is a common problem seen in U.S. men. It may be multifactorial in etiology, but waist circumference over 102 cm (approximately 40 in) is a strong predictor of risk and severity. There are recognized associations with coronary heart disease (CHD), diabetes, and post-prostatectomy. Weight loss, increased exercise, and dietary changes can help improve erectile function. Arginine and adenosine monophosphate are options for men who do not want to use phosphodiesterase-5 inhibitors or in whom those medications are contraindicated. Acupuncture does not convincingly provide benefit in the treatment of ED. The use of PDE5is is effective in a wide range of men with a wide range of diseases. Men should receive counseling on optimization of PDE5i use.

Benign Prostatic Hypertrophy/Prostatitis

Benign prostatic hypertrophy (BPH) is one of the most common conditions affecting aging men. An estimated 40% of men over 50 years old and approximately 80% of men by 80 years old have BPH. This is possibly caused by an accumulation of dihydrotestosterone (DHT), which inhibits prostatic cell death and promotes cell proliferation, increasing the size of the prostate gland.⁴⁹ One out of two men will experience prostatitis symptoms (inflammation of the prostate gland) in their lifetime. Ninety-five percent of these are considered nonbacterial.⁵⁰ There is an antibacterial factor secreted by cells that line the prostatic ducts. It kills bacteria on contact. Zinc is an active component of this antibacterial factor.

A screening device to help determine severity of BPH-related symptoms is the [International Prostate Symptom Score \(I-PSS\)](#). It is a well-validated tool for assessing response to treatment for lower urinary tract symptoms (LUTS). One study found the IPSS to have a sensitivity and specificity of 78% and 59.4% for prostate cancer. Clinicians are strongly encouraged to use this in their practices.

Risk Factors

Risk factors for developing BPH and lower urinary tract symptoms were assessed in 778 Korean police officers. Known risk factors for progression of BPH include prostate size greater than 31 cm³, PSA greater than 1.6 ng/mL, maximum urine flow rate less than 10.6 mL a second, and post-void residual urine volume of greater than or equal to 39 mL. Researchers found that metabolic syndrome increased the risk that these men would have one or more predictors for the progression of BPH.⁵¹

Beginning in 1986 a prospective cohort study of 18,055 U.S. men, 6,461 had their IPSS reach 8-14. Men with higher BMI had increased abdominal circumference. There was a statistically significant risk of progression to severe LUTS (IPSS greater than or equal to 20) with high BMI. This suggests targeting obesity may prevent the development of worsening LUTS.⁵²

A review of BPH and obesity revealed that there is a link between obesity, BPH, and LUTS. Obesity markedly increases the risk of BPH. Higher levels of physical activity decrease the risk of BPH. Those with BMI greater than 35 compared to less than 25 have 3.53 times the likelihood of developing BPH with a prostate ≥ 40 cc in volume.⁵³

A 2015 review of 35 studies focused on designing programs to promote men's physical activity. Of all the facets of health promotion, physical activity prevails as most likely to engage men with their health.⁵⁴ The authors recommended garnering "masculine capital" by affirming competitiveness and encouraging men to strive for physical prowess. They found greater commitment to change when programs focused on strength-based approaches, provided a diverse set of delivery platforms, used technology, and offered options for group vs individual vs mixed options for both education and exercise sessions.

Medications

Long-term combination use of alpha-blockers (tamsulosin) and 5-alpha-reductase inhibitors (finasteride) leads to a reduction in the risk of the progression of BPH and LUTS.³² The combination of these two medications also reduced the risk for acute urinary retention and future need for invasive therapy. There is support in the literature for switching to finasteride alone after a year of combination with dutasteride (Avodart).³² Patients with higher BMI do worse with monotherapy for BPH with LUTS.

Supplements/Herbs

Note: As previously noted, supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

The most common herb recommended for BPH is saw palmetto (*Serenoa repens*). A recent study with 298 Italian men looked at saw palmetto at a dose of 320 mg daily of the dried ripe fruit extract for 6 months. They compared saw palmetto alone to saw palmetto with an alpha-blocker. There was similar improvement in BPH symptoms using saw palmetto with or without an alpha-blocker.⁵⁵

An excellent review of commonly used herbs and supplements used for BPH was done by Animi and colleagues.⁵⁶ The article includes tables describing the proposed mechanisms of action and other study findings for each supplement. Common possibly helpful herbs to *Urtica dioica* (common/stinging nettle), *Cucurbita pepo* (pumpkin seed oil), *Serenoa repens* (saw palmetto), *Secale cereale* (rye grass pollen), and *Pygeum africanum*, with its associated beta-sitosterols.

A randomized double-blind, placebo-controlled clinical phase 2 trial in Australia looked at a product called Prostate Eze Max. The trial was comprised of 57 men, ages 40-80. The 3-month long trial did not find any significant adverse effects. The product contains *C. pepo*, *Pygeum*, saw palmetto (660 mg daily), lycopene, and *Epilobium parviflorum* (fireweed). The dose was one capsule daily. Median IPSS decreased by 36% versus 8% in the placebo group ($p < 0.05$).⁵⁷

A systematic review reported that beta-sitosterol is likely beneficial.⁵⁸ Beta-sitosterol is in many of the plants used to treat BPH, including *Pygeum*, saw palmetto and soy. *Pygeum* was found to be of uncertain benefit. Saw palmetto was noted as likely not beneficial.⁵⁹ Studies included in a systematic review found that saw palmetto was similar in terms of IPSS effects when compared head to head with tamsulosin (Flomax) and finasteride (Proscar).⁶⁰

Another systematic review of 32 trials with 5,666 participants found no improvement of BPH symptoms with *Serenoa repens* versus placebo, even at double and triple average dosages.⁶¹ This same conclusion was made by Moran and colleagues in 2012, but expanded that to all herbal therapies for BPH and prostate cancer in that systematic review.⁶²

Zinc has been used, and older studies showed benefit. It inhibits 5-alpha reductase and binding of androgens on receptors in the prostate. Certain prescription drugs can decrease zinc levels, including diuretics, steroids, methotrexate, tetracycline and fluoroquinolones. The dose most commonly used is 25-50 milligrams daily. For long-term use, consider supplementing with 1-2.5 mg of copper to avoid deficiency. Zinc serum levels can be checked as well.⁴⁹

Supplements and herbs used for prostatitis (inflammation of the prostate, *not* BPH) include: zinc; quercetin (a flavonoid) 200-400 mg, 3 times daily; clivers (aka cleavers) as a tea 3 times daily; marshmallow root up to 6 gm daily in divided doses; cranberry; uva ursi for up to a week at a time; and kava 150-240 mg, twice daily.⁴⁹

Summary

BPH with LUTS and prostatitis are common conditions. There is a strong link between BPH and obesity. Helping men understand this risk may motivate them to adopt healthy lifestyle changes. For moderate to severe symptoms of LUTS related to BPH identified using the IPSS, the use of monotherapy or dual-therapy with peripherally acting alpha-blockers and 5-alpha-reductase inhibitors can provide substantial symptom reduction and possibly prevent progression. The use

of herbs for BPH is common in the general public. There are many positive studies on the use of various plants including *Serenoa repens* (saw palmetto); however, large systematic reviews fail to fully support their use. Beta-sitosterol has support that is more consistent in the literature. This phytosterol is widely found in nature and in the plants traditionally used to treat BPH. It can also be obtained by simply eating vegetables. Recommending a reduction in caffeine can help lessen urinary symptoms. Zinc supplementation in appropriate dosage can safely be recommended for both BPH/LUTS and prostatitis.

Testosterone Deficiency

There are no universally accepted lower limits of normal testosterone levels. Depending on the source, normal lower limits are listed from 200 ng/dL up to 337 ng/dL. Some experts suspect symptoms related to low testosterone levels can be seen at levels higher than those listed as below normal and are dependent on the individual. The prevalence estimates of testosterone deficiency (TD) range from 5%-24%. It generally is accepted that testosterone levels will decline with age. One tool to screen for TD in men is [Androgen Deficiency in Aging Males \(ADAM\)](#).⁶³ The ADAM questionnaire is highly sensitive at greater than 90%, but specificity is limited, at 40%.

Questions used as part of the Saint Louis University ADAM Questionnaire include the following:

- 1) Do you have a decrease in libido (sex drive)?
- 2) Do you have a lack of energy?
- 3) Do you have a decrease in strength and/or endurance?
- 4) Have you lost height?
- 5) Have you noticed a decreased “enjoyment of life”?
- 6) Are you sad and/or grumpy?
- 7) Are your erections less strong?
- 8) Have you noted a recent deterioration in your ability to play
- 9) sports?
- 10) Are you falling asleep after dinner?
- 11) Has there been a recent deterioration in your work performance?

Note that a positive questionnaire result is defined as a “yes” answer to questions 1 or 7 or any 3 other questions.

Risk Factors

A study conducted in Pomerania, Germany, sought to determine risk factors for testosterone decline. Of the 2,117 men enrolled, 1,490 had their total testosterone analyzed. The prevalence of TD in this group was 10.4% with an incidence of 11.7 per 1,000 person-years. The threshold used in this study was 10.4 nmol/L (300 ng/dL). An age-related decline of 0.05 nmol/L per year was found. Obesity, metabolic syndrome, diabetes, and dyslipidemia were found to increase the risk of TD. The most striking result of this study was that management of those risk factors may prevent declining total testosterone in the aging male.⁶⁴

Maintaining physical activity, ideal weight and optimal nutrition may reduce the decline of testosterone seen with normal aging.

Another study looked at U.S. men in Boston.⁶⁵ The majority of them were white. They were divided by decade of life and assessed for testosterone levels and associated risk factors. The average testosterone level was 570 ng/dL at 40 years of age and 400 ng/dL at 85 years of age. Researchers were able to quantify the effects of various life events or health parameters on total testosterone levels. For instance, loss of a spouse or a BMI increase of four to five points were equivalent to 10 years of age-related decline in testosterone levels. Developing diabetes increased the risk of having a total testosterone level of less than 300 ng/dL by 2.5-fold. Twenty-six percent of diabetics who previously were not diabetic had testosterone levels less than 300 ng/dL as compared to 9.9% who did not have diabetes. Some observers found a noticeable decline in testosterone levels in 2002 compared to 1987, but data verifying these conclusions was not elicited through a National Library of Medicine search.

Previously it has been noted that MS increases the risk of hypogonadism, type 2 diabetes, CVD, and ED. In a 2009 review, insulin resistance was found to be a very important component of MS. MS leads to endothelial dysfunction. There is new evidence linking TD to the development of MS and diabetes, but it is uncertain if this is the cause versus the effect of these conditions. Research on testosterone deprivation therapy and androgen replacement therapy is leading to a new understanding of the development of metabolic syndrome, type 2 diabetes, vascular disease, and ED.⁶⁶

Osteoporosis

Osteoporosis becomes more of a risk in men with untreated severe testosterone deficiency as they age. There is a lifetime risk of hip fracture in U.S. men of 1 in 5. This risk increases with osteoporosis. The risk of death from complications of a hip fracture is 34%. Even after 2 years of rehabilitation, a man has a 15% risk of not being able to walk again after a hip fracture.³⁹

Heart Disease

Since 2014, 22 new studies were published addressing the CVD risks of testosterone replacement therapy (TRT). None to date has proved that TRT is associated with increased risk of CV events. The 2016 Testosterone Trials for men over 65 years old identified increased arterial plaques but not increased coronary artery calcium (CAC) scores on coronary CT scans. The Testosterone Effects on Atherosclerosis Progression in Aging Men trial followed men for 3 years. Total testosterone levels of 500-900 ng/dL were achieved with TRT but there was no significant difference in the rate of change in the common carotid artery intimal-media thickness or CAC. No major adverse complications were reported either, in this study of 152 men. More recent studies suggest either a neutral or a protective CV effect for TRT.³⁹ Until we have a large, multiple-year spanning randomized or an observational case-control trial of TRT and ASCVD end point assessment, most experts recommend TRT be offered only cautiously and conservatively in men over 65 years old, unless they have osteoporosis or a high risk..

To summarize, the prescription of TRT for low testosterone for CVD reduction, sexual function, mood, or cognitive function is without support from randomized clinical trials. A 2016 systematic review analyzed 156 eligible RCTs (randomized controlled trials). TRT did not consistently demonstrate benefit for ASCVD risk, sexual function, mood and behavior, or cognition. TRT is ineffective in treating ED and not consistently effective in treating low libido. TRT did consistently improve muscle strength but this did not translate into improved physical function.⁶⁷

Improving endogenous total testosterone production is better than delivering TRT due to the negative feedback loop that occurs biochemically, and a further reduction in testicular function.

Lifestyle

A study focusing on Asian men in Singapore examined the relationship of exercise levels to testosterone levels. It also measured erectile function and prostate symptoms using the IIEF-5 and IPSS. A total of 75 men were enrolled and randomized into two groups. One group did low-volume exercise (less than 150 minutes/week). The other did high-volume exercise (greater than 200 minutes/week) with approximately 400 kcal decrease per day diet. The study lasted six months. Inclusion criteria included BMI greater than 27.5 and waist circumference greater than 90 cm. A 3%-6% weight loss from the decreased daily calories and increased exercise improved erectile function, testosterone levels, lower urinary tract symptoms, endothelial function, and quality of life in these obese men. Moderate aerobic exercise of 200-300 minutes weekly resulted in significant improvement in erectile function and testosterone levels. There was a high dropout rate of 20% in the high-volume exercise cohort. It was concluded that 200 minutes of weekly exercise is an effective treatment for moderate to severe ED. Plasma testosterone only increased in the high-volume exercise group, and it did so regardless of weight loss.⁶⁸

A study that did not support physical activity's effect on testosterone levels was done on Polish men 24-72 years old. There were 387 men enrolled. The authors found that all the hormones measured declined with age. Activity level was based on self-reporting, and high activity level was equal to more than 12,500 steps daily. Men younger than 48 showed increased estrogen levels with increased activity levels. Men older than 48 showed decreased estrogen levels with increased physical activity. It was assumed that aging caused increased estrogen levels in men. There was not a significant difference in BMI in the high-activity group compared to the baseline group. Overall, there was a lack of evidence to show increased testosterone levels were associated with high levels of physical activity.⁶⁹

Effects of Opioids

Opioid-induced androgen deficiency (OPIAD) is often under-recognized in clinical practice. OPIAD results in inappropriately low levels of gonadotropins (FSH, LH) in the face of low plasma testosterone levels. Symptoms include decreased libido, ED, fatigue, hot flashes, and depression. Signs can include decreased facial hair, anemia, decreased muscle mass, weight gain, and decreased bone mineral density. This can affect men or women and lead to infertility as well. When recognized, questions will arise regarding hormone replacement such as testosterone replacement in men. OPIAD can be seen for months to years in people being treated with morphine.

Testosterone levels can drop as quickly as a few hours after starting opioids. Once morphine therapy is interrupted, levels can recover within a few hours to days. Less is known about long-term opioid use and hypothalamus/pituitary suppression. A recent retrospective cohort study looked at risk factors for androgen deficiency in 1,585 men using daily opioids.⁷⁰ Researchers determined that the use of long-acting opioids is a key risk factor in the development of androgen deficiency. Men on long-acting opioids were more likely to be androgen deficient than men on short-acting opioids (57% vs. 35%, $P < 0.001$). As the dose increased, the likelihood of

androgen deficiency increased. Researchers found, though, that the dose was more strongly associated with androgen deficiency in men if they were taking short-acting opioids (OR 1.16 for each 10 mg increase in dose) than in men on long-acting opioids (OR 1.01).

It appears that the higher the dose of opioids, the higher the risk of hypogonadism. One can anticipate OPIAD when the range of oral morphine equivalence exceeds 100-200 mg daily. This is based on limited retrospective human data. An additional risk is taking opioids for more than one month. Even with that level of exposure, OPIAD should be reversible after opioid cessation.

Given this information, health care providers are responsible for providing full informed consent regarding the risk of developing an endocrinopathy. This should be done consistently prior to starting opioids. When deciding to replace androgen for males, a target total testosterone level of 400-700 ng/dL serves as a guideline. There are a number of different preparations of testosterone for men, including injection and topical.⁷¹

When treating patients with opioids, keep opioid-induced androgen deficiency in mind as a possible cause of low testosterone and its related symptoms.

Exercise Associated Low Testosterone

A 2018 review highlighted the need to recognize exercise-hypogonadal male condition (EHMC).⁷² This condition is rooted in overreaching or overtraining. The low testosterone levels in these men are most likely associated with high volumes of endurance exercise. They can also be associated with anaerobic sports such as American football and weight class wrestling. Symptoms of this form of hypogonadism include fatigue, sexual dysfunction, and/or low bone mineral density (BMD). Clinicians should be aware of this negative energy balance condition and screen for it in this at-risk group of men.

Summary

The risk factors for TD include aging, increasing weight, and metabolic syndrome/type 2 diabetes, which indicate insulin resistance. Not included in this overview is a discussion of environmental toxins causing endocrine disruption, which could lead to testosterone decline or dysfunction. Other significant risks are opioid exposure, especially on a chronic basis, and EHMC. Early recognition of OPIAD is important, in order to provide patients with prevention and treatment options. Greater awareness of EHMC clinically can prevent misdiagnosis of primary hypogonadism in athletes, patients with eating disorders, and weight loss enthusiasts. Although conclusive evidence is lacking, early evidence indicates that increased physical activity, especially exercise, can improve testosterone levels in the majority of men. Hormone replacement therapy, which is becoming more accepted, is an option for men suffering from symptomatic TD. However, it is not without risk, especially when it comes to cardiac events in older men.⁷³⁻⁷⁵

The "[Improving Low Testosterone Naturally](#)" tool contains more information on this important topic.

Longevity

The latest CDC annual statistics reveal the life expectancy in 2015 for U.S. men decreased by 0.2 years to 76.3 years. US women are living on average 80 years. It is a curiosity that female mammals tend to live longer than males. It is not clear what the exact physiologic mechanism is that causes this discrepancy. Most animals show disparity between sexes in longevity, except for many birds and some invertebrates. In the United Kingdom, the longevity sex difference is closing from 6 years down to 4.1 years. Reports of striking longevity of eunuchs (men castrated at a young age) at the Korean Imperial court suggest testosterone may limit the life span in male humans.⁷⁶ It may be that testosterone adds to risky and aggressive behavior in men.

Testosterone can also act as an immunosuppressant. On the other hand, low testosterone in aging males links to negative health status. Obesity leads to lower testosterone, which leads to fragility, low muscle mass, anemia, and depression. Males also have shorter telomeres, which is increasingly linking to mortality. Research is under way in nutrient sensing signaling pathways to help explain longevity related to reduced calorie intake. Insulin or insulin-like growth factor 1 (IGF-1) may turn out to be one of the causes. However, no comprehensive explanation yet exists for the gender gap in aging and longevity.⁷⁷

Physical Activity

A cohort study published in 2013 looked at longevity in men and women and its relationship to non-exercise physical activity (NEPA).⁷⁸ There were 4,232 people from Sweden enrolled for 12.5 years in the study. The NEPAs included home repairs, cutting lawn, car maintenance, bike riding, skiing, ice skating, hunting/fishing, and gathering mushrooms or berries. One could argue that bike riding, skiing, and skating are exercise, but they may be considered transportation in Sweden as opposed to formal exercise. Researchers also looked at formal exercise levels separately. They studied three outcomes, including rates of metabolic syndrome, CVD, and longevity. They found similar results for men and women. Moderate and high levels of NEPA lowered the odds ratio of metabolic syndrome (MS) despite no significant exercise. Low, moderate, and high levels of exercise reduced the risk for MS. The most significant reduction of risk for MS was 0.39, for the group with high levels of NEPA and exercise risk. High NEPA reduced relative risk of CVD by 30%. High NEPA improved longevity as well, but not level of NEPA reduced blood pressure.

Lifestyle

A prospective study with 821 Norwegian men aged 51-59 also looked at longevity.⁷⁹ The goal was to analyze the factors that contributed to living to 85 years of age. Of the men in the study, 30.7% lived to 85. They found that lifestyle factors in midlife are strongly related to mortality. The three most important factors were avoiding tobacco smoking, avoiding being overweight (BMI less than 25), and having higher levels of fitness. If people were able to achieve these three factors, the odds ratio of reaching 85 years old was 2.47 ($p < 0.001$). a maximal exercise tolerance bicycle test measured fitness levels. It was interesting to note that cholesterol level had the least effect on longevity, of all the factors measured.

Longevity is closely linked to physical activity, optimal weight, and avoiding tobacco in midlife. Cholesterol levels had no significant association with longevity in one large Norwegian study. We know that strong relationships, spirituality and religiosity, stress, educational level, financial status, and many other factors also play key roles.

Weight Loss

Tailoring the style of delivery could be as important as the content of the weight loss intervention, with men preferring simple, fact-based language with individual feedback⁸⁰ One can envision individualized interventions and personal goals. A 2018 systematic review of African American and Latino men included 7 studies and 9 articles. Rates of physical activity remain low in these groups. Several programs resulted in decreased waist circumference and a 36% reduction in CRP.⁸¹

Another systematic review of 14 trials found that caloric-reducing diets led to greater weight loss than physical activity alone. After one year, average weight loss was 3.2 kg. When diets, exercise, and behavioral change techniques were combined the average one-year weight loss was 4.9 kg compared to the no-intervention group.⁸⁰ An encouraging finding from this review was that once men engaged with the program, they tended to stick with it.

A review of nine studies that focused on intermittent vs continuous energy restriction demonstrated weight loss for both with a caloric reduction range of 15%-60% of baseline. Intermittent fasting diets resulted in 8.5 +/-4 kg weight loss compared to continuous calorie restriction of 7.1 +/-4.7 kg weight loss.⁸² Some interesting trends are that the weight loss plateaued at 6 months, and the weight returned if the diet was stopped entirely. Another clinical recommendation for optimal weight loss is to target 10% weight loss from baseline at 6 months and set a goal of -0.5-1.0 kg per week. A 2018 review of 11 RCTs concluded that intermittent and continuous energy restriction achieve comparable effects with both amount of weight lost and metabolic improvements.⁸³ Sebastiani and colleagues suggest caution with interpreting meta-analyses and their negative conclusions, because of the risk of false negatives.

Response to Stress

The U.S.-based VA Normative Aging Study looks at mortality and emotional reactivity.⁸⁴ The study included 181 men 58-88 years old; it was conducted over a 10-year period from 2002-2012. The results were based on an eight-day daily diary of stressors, physical symptoms, positive and negative affect, memory failures, pain, and social support. The goal of the study was to show that negative affect was worse for health than positive affect. Researchers also looked at decreases of positive affect in response to stressors, which is a measure of emotional reactivity. What they found was surprising, in that larger decreases in daily positive affect in response to daily stressors were associated with more than a doubling in mortality risk over the decade of follow-up. The hazard ratio was 2.32 ($p < 0.01$) for people with greater emotional reactivity with the greatest decreases in positive affect. The authors hypothesize that this may reflect greater hypothalamus/pituitary/adrenal axis (HPA) activation. One of the fascinating aspects of these results is that they draw in the importance of the dynamic nature of our human experience, as opposed to focusing on a static measure, such as baseline positive affect or negative affect, which in themselves did not influence the mortality rate over this 10-year study.

A reduction in positive affect in response to daily stressors was associated with more than double the mortality risk over a decade of follow-up.

Nutrition

The Adventist Health Study 2 (AHS-2) revealed a 12% lower risk of all-cause mortality for men and women following a vegetarian diet.⁸⁵ Men showed a greater benefit than women mainly because of the CVD risk reduction. There was not a risk reduction in cancer mortality among the vegetarians. The AHS-2 began in 2002 and had 96,000 Seventh Day Adventists enrolled. Thirty-six percent were vegan/vegetarian (4.2% and 31.6% respectively). It is interesting to note that vegans experienced the highest rate of hip fractures in a sub-analysis of the data provided from AHS-2. The greatest risk reduction of hip fractures came from eating legumes (not including soybeans or soy-based products) greater than or equal to 1 time/day compared to less than 1 time/week. Increased intake of other protein sources provided risk reduction as well, but not equal to the 64% reduction ($p=0.0003$) with legumes. This is important because in this sub-analysis of 33,208 white men and women, 305 suffered hip fractures and 127 of those were men. A hip fracture carries a high mortality risk within 1-2 years of occurrence. One explanation for the reduction in hip fractures enjoyed by daily legume eaters may be from increased lysine and hydroxylysine, as they are important in the cross-linking process of bone collagen. Lysine also promotes increased calcium absorption in the gut and reduced excretion from the kidneys.

Consuming legumes (beans) was associated with a reduced risk of hip fracture, which is a significant cause of disability and mortality in older men and women.

Marriage and Social Support

What about “marriage protection?” The theory that marriage has protective effects for male survival has persisted for over 100 years. One recent study looked at data collected from six pooled panels of the U.S. Survey of Income and Program Participation (SIPP).⁸⁶ Researchers were able to gather data from 60,000 households from 1980 to 1999. They confirmed that unmarried American men and women have higher mortality compared to married men and women. Half of studies undertaken previously, including a 2007 meta-analysis by Menzoli, did not show this protective effect. This larger pooled data also challenges previous estimates of the importance of comparing never married, widowed, divorced and/or separated populations. Men seemed to benefit more than women regarding longevity and marriage, but the gender advantage became less noteworthy in older age groups. Sullivan and colleagues, found that among 16,000 Americans, widowhood increased mortality risk by 48% with a more negative effect seen in men versus women once again. There was also greater risk for men if the death of the spouse was unexpected.⁸⁷

Growth Hormone

A review of growth hormone (GH) and longevity looked at eight controlled studies of GH versus no GH supplementation.⁸⁸ A number of small studies show GH supplementation increased lean body mass but does not seem to improve functional strength. The beneficial effect was noted in men, but not women. Side effects included edema, arthralgias, carpal tunnel syndrome, early insulin resistance, hormone sensitive tumors, and increased blood pressure. Evidence was lacking to show conclusive improvements in longevity with GH supplementation.

Summary

Male longevity is multifactorial. It is clear that fitness and non-exercise activity level influence longevity. There is growing data that diet may influence longevity, including both limiting excess calories and eating a more plant-based diet. Finally, social support, which is reflected by marriage in our culture, is very important. One might wonder if the negative effect on longevity from a sudden death of a spouse for a man reflects his need for time to tap into other social support structures in his life when his life partner passes away.

Personal Health Plan

Name: Keith

Meaning, Aspiration, Purpose (MAP):

“My intention is to live long enough to see my granddaughter Jessica get married and make sure she is well on her way in life. I also want to reduce the negative influences of recurrent prostate cancer on my life. I would also like to feel comfortable talking with my son Jeremy about his alcohol use and see him feel more socially connected to our community.”

My Goals:

- Control the left knee pain to start being more physically active again.
- Eat better food.
- Understand what the factors are that could reduce longevity and what to do about them.

Mindful Awareness:

Experience a mindful awareness practice at home using the mindful awareness CD given at the clinic visit. Consider joining a Mindfulness-Based Stress Reduction group. Find a local instructor by going to this [website](#).

Areas of Self-Care:

- Physical Activity
 - Set a goal for exercise and physical activity. Start with an obtainable goal and slowly increase both the time spent and the intensity. Start with 10 minutes of walking 3 times a week, then increase to 30 minutes of brisk walking 4 times a week. Non-exercise physical activity is also important and can include things like yard work, gardening, household chores, etc. Tai chi or qi gong classes could improve balance and functional strength.
- Surroundings
 - Get a fall risk assessment with the Physical Therapy department, which may recommend a home-safety evaluation as well. Avoiding falls and a hip fracture will help goal achievement.

- Personal Development
 - Ask about volunteering at a local school to put my love of teaching and giving back to good use. There are always children that can use extra attention. Consider attending an AA meeting with Jeremy, if he is open to this, or an Al-Anon meeting, to help you learn how to speak to him about his alcohol use disorder.
- Nutrition
 - Meet with nutritionist/dietician to slowly break away from frozen foods and soda. Consider a more plant-based diet with a daily serving of beans (legumes) and a reduction in animal fat. In addition, eat organic fruits and vegetables every day with the goal of 5-6 servings/day. Replace coffee with green tea 2-3x times/day.
- Recharge
 - Keep up the good sleep habits and seek help from the health team if sleep quality starts to deteriorate.
- Spirit and Soul
 - Hopefully with less knee pain, I will be able to enjoy outdoor activities more and nurture my connection to the earth. In addition, there is nothing stopping me from listening to the music that resonates with me every day. It is a gift I can give to myself. Continue my involvement at the local church to further enrich my spirit and soul.
- Mind and Emotions
 - Participate in an 8-week long class on Mindfulness-Based Stress Reduction. Practice what I learn for up to 60 minutes every day. Consider joining a prostate cancer support group.

Professional Care: Conventional and Complementary

- Prevention/Screening
 - Continue with routine physicals
 - Arrange fall assessment by Physical Therapy
- Treatment (e.g., conventional and complementary approaches, medications, and supplements)
 - Acupuncture
 - Shows promise for back and neck pain, headaches, and arthritis. May be helpful in maintaining a robust, active immune system, which can help keep the prostate cancer from coming back. Consider a session with a clinician from a VA hospital.
 - Zyflamend 2 capsules, 3 times daily
 - May slow or reverse rising PSA levels. May help with pain in knees from arthritis
 - Omega-3

- Improves joint tenderness and morning stiffness in patients with rheumatoid arthritis. Standardize dose based on the amount of EPA and DHA in the product. Do not take more than 2 gm per day of EPA and DHA.
- Vitamin D3 1,000 IU daily
 - Vitamin D deficiency is associated with muscle weakness and increased falls. A small study showed improved pain, sleep, and quality of life with supplements.
- Glucosamine/chondroitin 1,500 mg divided 2-3 times a day
 - Proteins found in joints that (controversially) prevent the destruction of cartilage. It has not shown benefit in back pain, but is recommended for patients with osteoarthritis of the knee. May take a few months to work.
- Topical capsaicin applied up to 3 times a day, everyday
 - This widely available cream made from cayenne peppers is useful for short-term pain relief and may help knee pain. Start with the lower concentration available over the counter and increase strength as needed. Wash hands well after application.
- Skill building and education
 - Mindfulness meditation course

Referrals/Consults

- Nutritionist/Dietician
- Acupuncturist
- Man to Man Support Groups for men who have experienced prostate cancer
 - Meetings are twice monthly and include both sharing and education for no charge.
 - 1-(800)-ACS-2345 and ask for the regional navigator.

My Support Team

- Primary Care Clinician
- Urologist
- Dietician
- Granddaughter
- Son

Next Steps

- Schedule an appointment with PT for a fall-risk assessment.
- Schedule an appointment with nutrition/dietician.
- Schedule an appointment with an acupuncturist.
- Follow up with team in 2-3 months to check progress.

Follow-Up with Keith

Keith has been working on following most of the suggestions described in his Personal Health Plan. Six months have now passed, and he is feeling well. He had a short setback with an

upper and lower respiratory infection that required antibiotics and nebulizer treatments 2 months ago. Beyond that, he has met with a nutritionist and an acupuncturist. His granddaughter, Jessica, and he have discovered they love cooking together. She comes over every Sunday, and they spend the afternoon cooking. He makes meals for the week and then freezes a few and keeps the others ready to eat in the refrigerator. He now has been able to avoid all store-bought frozen foods. He feels like his mood has improved and his energy is better. He has noticed Jeremy is more interested in socializing and has cut back on his drinking as his diet has improved. They have been going for walks together more now the weather has improved.

He was surprised how much he likes acupuncture. He has had 12 treatments now and his knee pain has lessened to the point that he is walking every day for 20-30 minutes without pain. He has noted weight loss and indeed today, his waist circumference measures 39 inches. He is also using glucosamine sulfate and thinks that may be helping as well; he denies any side effects. A friend told him about prolotherapy for knee arthritis and he is interested in trying a course of three injection treatments every 4-6 weeks.

He has discovered a love of meditation. He finds himself looking forward to his 30 minutes of meditation twice a day. He notes that his sleep is even more refreshing and his nurse practitioner at his clinic has noted his blood pressure is consistently 10 points lower than before he started meditating, even though he was not diagnosed with hypertension previously.

Finally, he is taking Zyflamend as recommended and his PSA level has not gone up in the past six months. This brings a big smile to his face as he looks you in the eye and says Jessica's wedding date is set and will be 4 months from now. "It's thanks to you that I'll be there to see my Jessica marry the love of her life. It makes me the happiest man in the world!"

Integrative Health Tools

- [Prostate Health](#)
- [Improving Low Testosterone Naturally](#)
- [Erectile Dysfunction](#)

Author(s)

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