Men's Health Issues

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician, behavioral health professional or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

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Faculty Disclosure

Contributing faculty, Lori L. Alexander, MTPW, ELS, MWC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for physicians, physician assistants, nurses, and behavioral health professionals seeking to enhance their knowledge of issues related to men's health.

Accreditations & Approvals

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NetCE designates this continuing education activity for 15 ANCC contact hours.

This activity was planned by and for the healthcare team, and learners will receive 15 Interprofessional Continuing Education (IPCE) credits for learning and change.

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AACN Synergy CERP Category A.

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This activity is designed to comply with the requirements of California Assembly Bill 1195, Cultural and Linguistic Competency.

About the Sponsor

The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

Disclosure Statement

It is the policy of NetCE not to accept commercial support. Furthermore, commercial interests are prohibited from distributing or providing access to this activity to learners.

Course Objective

The purpose of this course is to provide health and mental healthcare professionals with necessary information regarding conditions and health issues that affect men in order to facilitate more effective diagnosis, treatment, and care. As

male-specific factors influence the provision and compliance to therapy, tools to ensure effective patient education for men are provided to increase the likelihood of positive outcomes.

Learning Objectives

Upon completion of this course, you should be able to:

1. Identify diseases that are more prevalent among men than among women.
2. Describe the health implications of male gender identity and identify strategies to improve communication with male patients.
3. Explain the diagnosis and treatment of benign prostate conditions and prostate cancer.
4. Apply guideline recommendations for prostate cancer screening.
5. Describe various treatment options for prostate cancer.
6. Distinguish among benign testicular conditions.
7. Discuss the diagnosis and treatment options for testicular cancer.
8. Discuss the differences between male and female breast cancer.
9. Discuss the diagnosis and treatment options for sexual dysfunction (premature ejaculation and erectile dysfunction).
10. Recognize the signs and symptoms of late-onset hypogonadism.
11. List factors affecting male infertility.
12. Describe the prevention, control, and screening of sexually transmitted infections.
13. Identify issues of particular concern for men who have sex with men.
14. Discuss the effects of substance misuse, depression, and stress/anger on the physical and psychosocial well-being of men.
15. Discuss the importance of educating men about the need for screening, routine health maintenance, and healthy lifestyle.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

There are many reasons to be concerned about health issues that are unique to or more common in men. In 1900, women outlived men by an average of two years; that gap widened to seven years in 1970 through 1990 [1]. Advances in diagnosis and treatment, as well as heightened awareness of disparities in men's and women's health, led to a narrowing of the gap to slightly less than five years in 2014 [1]. Still of concern, however, is the high number of men's deaths that are potentially avoidable. Many factors contribute to the disparity in mortality and morbidity between men and women, but the factor thought to have the most significant impact on the health of men relates to male gender identity, including a tendency for risky behavior [2; 3; 4; 5].

The concept of men's health was established to focus on the high rates of morbidity and mortality. Thus, men's health encompasses both male-specific conditions, such as those related to the prostate, as well as diseases that affect men at a higher rate compared with women. A discussion of all diseases that affect men is beyond the scope of this course. However, the leading causes of death among men are presented and discussed in the context of how they compare with the causes of death in women.

Among the male-specific conditions addressed are prostate disease (e.g., prostatitis, benign prostatic hypertrophy [BPH], cancer), testicular conditions (e.g., testicular torsion, epididymitis, varicocele, cancer), premature ejaculation, erectile dysfunction, late-onset hypogonadism, infertility, and sexually transmitted infections (STIs). Prostate cancer is discussed in considerable detail. Prostate screening and treatment have been controversial issues in health care, and the most recent recommendations for how to discuss screening and treatment options are included. Also provided are brief overviews of male breast cancer, a rare disease but one that is rising in prevalence, and health issues of specific concern for men who have sex with men (MSM), a growing population seen in the primary care setting.

The psychosocial well-being of men is integral to overall health. The link between anger and stress and disease is mentioned, as is the major role of substance misuse in mortality and morbidity. Alcohol misuse and depression have both been underdiagnosed in men, especially older men, and strategies for screening are explored.

The course closes with suggestions for fostering enhanced healthy behaviors among men, with recommendations for reaching out to men, ensuring appropriate health screening, and encouraging healthy behaviors.

OVERVIEW OF MEN'S HEALTH ISSUES

The concept of men's health emerged in response to the documented trends in greater mortality rates for men compared with women. Over the past decade, attention to the causes of death and disease in men has increased, and a growing body of scientific literature has begun to elucidate gender differences in physiologic, psychologic, and sociologic aspects of disease. These differences have a strong influence on the health of men as well as on the response to treatment and health behaviors.

Men's health lacks the same type of clinical focus as women's health; that is, men's health does not have the equivalent of a specialist (gynecologist) to provide care for the reproductive tract. Care of the male reproductive tract is assumed by primary care physicians, urologists, endocrinologists, reproductive specialists, and possibly, oncologists. The discipline of andrology is in its early stages, and some have proposed that this discipline should be expanded beyond the reproductive tract to include all men's health issues, with a goal of developing appropriate training programs and establishing a distinct specialty [6]. Men's health programs at large academic centers as well as free-standing centers in large cities are providing multidisciplinary diagnostic and management services targeted to men.

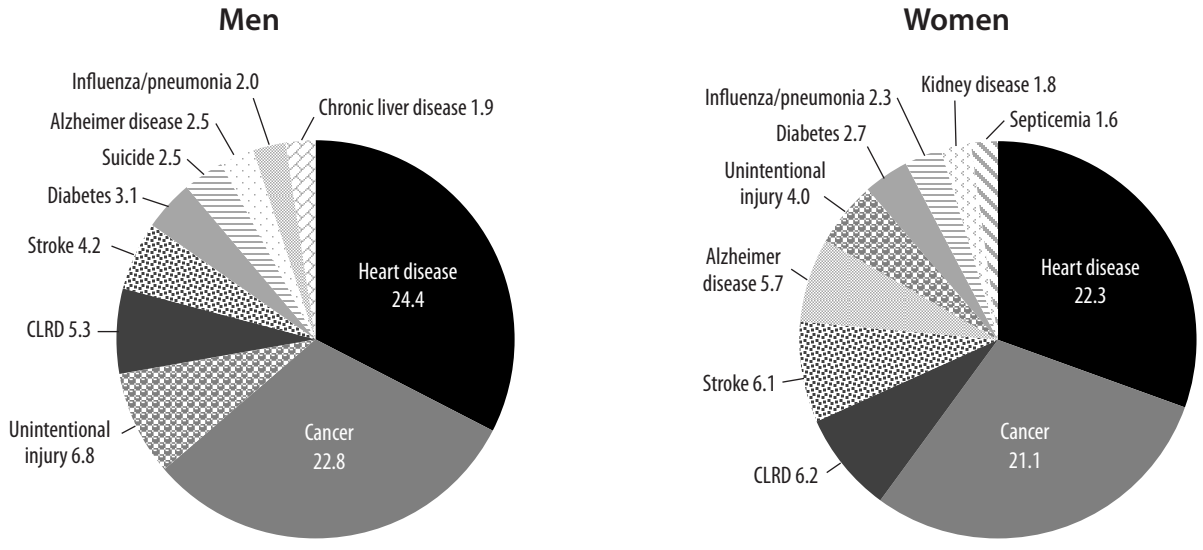
As defined by most organizations around the world, the field of men's health encompasses a broad range of health issues, including diseases that are more prevalent among men than women or that differ with regard to risk factors, diagnosis, and treatment. Men's health also addresses the psychologic and social influences on men and acknowledges the need to model healthier attitudes beginning in boyhood.

Several initiatives have helped to promote awareness of men's health among the public, policy arena, and scientific community, including establishment of the Men's Health Network, a nonprofit organization based in Washington, DC, and targeted peer-review journals such as the *Journal of Men's Health* and the *American Journal of Men's Health*.

MORBIDITY AND MORTALITY AMONG MEN

In general, the leading causes of death among men and women are the same; what differs are the age at the time of death, the number of deaths caused by each disease, and the ranking of the causes (***Figure 1***) [7; 8]. The overall death rate in 2016 was higher for male than female individuals (all ages) (880.2 vs. 819.3 per 100,000) [9; 10]. Cardiovascular disease and cancer are the two leading causes of death for both men and women, but a greater percentage of men die of each cause [9; 10]. Deaths related to cardiovascular disease and cancer account for approximately 47% of the total number of deaths among all men [7]. In 2015, the percentage of deaths for men was lower than that for women for Alzheimer disease, cerebrovascular diseases, influenza/pneumonia, and chronic lower respiratory diseases [7; 8]. The causes of death differ within the male population according to age and race/ethnicity, highlighting disparities related to socioeconomic status, cultural differences, access to care, and possibly, genetic predisposition for specific diseases (***Table 1***) [11].

THE LEADING CAUSES OF DEATH AMONG MEN AND WOMEN, 2015



CLRD = chronic lower respiratory disease.

Source: [7; 8] *Figure 1*

TEN LEADING CAUSES OF DEATH FOR MEN ACCORDING TO RACE/ETHNICITY, 2015

Leading Causes of Death	Mortality Rate and Rank					
	All Men	White	Black/ African American	Hispanic/ Latino	Asian/Pacific Islander	American Indian/ Alaskan Native
Cardiovascular diseases	24.4% (1)	24.6% (1)	23.9% (1)	20.6% (1)	22.8% (2)	19.2% (1)
Cancer	22.8% (2)	23.0% (2)	21.4% (2)	20.2% (2)	26.1% (1)	17.0% (2)
Unintentional injuries	6.8% (3)	6.8% (3)	6.5% (3)	10.3% (3)	5.5% (4)	13.1% (3)
Chronic lower respiratory diseases	5.3% (4)	5.6% (4)	3.2% (7)	2.7% (7)	3.2% (7)	3.9% (7)
Cerebrovascular diseases	4.2% (5)	4.1% (5)	4.9% (4)	4.6% (4)	6.4% (3)	2.9% (8)
Diabetes mellitus	3.1% (6)	2.9% (6)	4.2% (6)	4.5% (5)	3.9% (5)	4.1% (6)
Suicide	2.5% (7)	2.6% (8)	—	2.6% (8)	2.6% (6)	4.1% (6)
Alzheimer disease	2.5% (8)	2.6% (7)	—	2.1% (10)	2.0% (9)	—
Influenza and pneumonia	2.0% (9)	2.0% (9)	1.7% (10)	—	3.3% (6)	1.8% (10)
Chronic liver disease	1.9% (10)	1.9% (10)	—	4.2% (6)	—	5.7% (4)
Assault (homicide)	—	—	4.9% (5)	2.4% (9)	—	2.2% (9)
Kidney disease	—	—	2.7% (8)	—	2.0% (10)	—
Septicemia	—	—	1.9% (9)	—	—	—

Source: [11] *Table 1*

Review of the leading causes of death demonstrates that many men's deaths are potentially avoidable. Most notable is the third leading cause of death for all men: unintentional injuries [11]. Unintentional injuries cause substantially more deaths among men than women, for whom it is the sixth leading cause of death [12]. Suicide is the seventh leading cause of death among all men; this cause of death is not included in the top 10 causes for women. In addition, homicide is among the ten leading causes of death for black, Hispanic/Latino, and American Indian/Alaska Native men [13; 14; 15]. Several of the other leading causes of death among men are associated with chronic diseases, for which modification of risk factors and early detection can improve outcomes.

Gender differences exist in the prevalence of specific cancers and in deaths related to cancers [16]. The lifetime probability of being diagnosed with invasive cancer is higher for men than women (***Table 2***) [16]. The rate of deaths associated with cancer of the urinary bladder, esophagus, lung, and liver and intrahepatic bile duct are higher among men than among women (***Figure 2***) [16]. Although prostate cancer is the most prevalent cancer in men and receives widespread attention, lung cancer is responsible for a greater percentage of cancer-related deaths among men (24% vs. 10%) [16].

MALE GENDER IDENTITY AND IMPLICATIONS FOR HEALTH

An increasing amount of research is supporting a relationship between men's risk for disease and death and male gender identity, and the traditional male role has been shown to conflict with the fostering of healthy behaviors [4; 17]. Male gender identity is related to a tendency to take risks, and the predilection for risky behavior begins in boyhood [17; 18; 19]. In addition, boys are taught that they should be self-reliant and independent and should control their emotions, and societal norms for both boys and men dictate that they maintain a strong image by denying pain and weakness [4; 18; 19].

Issues related to male gender identity have several important implications for health. First, risky behavior is associated with increased morbidity and mortality. Second, the concept of masculinity leads to inadequate help- and information-seeking behavior and a reduced likelihood to engage in behavior to promote health [4; 18; 19]. These behaviors appear to be rooted in a decreased likelihood for men to perceive themselves as being ill or at risk for illness, injury, or death [4]. Third, male gender identity, coupled with lower rates of health literacy, creates special challenges for effectively communicating health messages to men [5; 20; 21]. Gender differences in health-related behaviors are consistent across racial/ethnic populations, although specific behaviors vary according to race/ethnicity [17].

Risky Behavior

Risky behavior affects health and well-being beginning at a young age. The overall rate of fatal injuries is approximately two times higher among boys than girls (0 to 19 years of age) [22]. Motor vehicle accidents are the leading cause of death for both genders, especially in the age category of teenage drivers (15 to 19 years of age). Although not all of these injuries and deaths are related to risky behavior, Youth Risk Behavior Surveillance (YRBS) data indicate that many of them are related; other risky behaviors identified in this survey are related to morbidity and mortality in adolescence and are also contributors to habits that affect health in adulthood. The 2017 YRBS showed that the rate of risky behaviors is predominantly higher among male respondents (***Table 3***) [23]. The rates of many of these behaviors continued to be higher among male adults (***Table 4***), which plays a role in premature deaths among men [1; 24].

Men's predilection for risky behavior is reflected in the high rate of unintentional injury, which accounts for 6.8% of deaths among men (compared with 4.0% for women) [7; 8]. There is wide variation in this rate across race/ethnicity, with much higher rates among American Indian/Alaska Native men (13.1%) and Hispanic/Latino men

COMPARISON FOR LIFETIME RISK FOR CANCERS FOR MEN AND WOMEN		
Cancer Type	Lifetime Risk	
	Men	Women
All sites	39.3%	37.7%
Lung and bronchus	6.7%	5.9%
Colon and rectum	4.4%	4.1%
Melanoma of the skin	3.7%	2.5%
Non-Hodgkin lymphoma	2.4%	1.9%
Kidney and renal pelvis	2.1%	1.2%
Leukemia	1.8%	1.3%

Source: [16] *Table 2*

TEN LEADING CANCER TYPES FOR THE ESTIMATED NEW CANCER CASES AND DEATHS BY SEX, UNITED STATES, 2019

Estimated New Cases

			Males		Females		
Prostate	174,650	20%			Breast	268,600	30%
Lung & bronchus	116,440	13%			Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%			Colon & rectum	67,100	8%
Urinary bladder	61,700	7%			Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%			Melanoma of the skin	39,260	4%
Kidney & renal pelvis	44,120	5%			Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%			Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%			Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%			Pancreas	26,830	3%
Pancreas	29,940	3%			Leukemia	25,860	3%
All Sites	**870,970**	**100%**			**All Sites**	**891,480**	**100%**

Estimated Deaths

			Males		Females		
Lung & bronchus	76,650	24%			Lung & bronchus	66,020	25%
Prostate	31,620	10%			Breast	41,760	14%
Colon & rectum	27,640	9%			Colon & rectum	23,380	8%
Pancreas	23,800	7%			Pancreas	21,950	7%
Liver & intrahepatic bile duct	21,600	7%			Ovary	13,980	5%
Leukemia	13,150	4%			Uterine corpus	12,160	4%
Esophagus	13,020	4%			Liver & intrahepatic bile duct	10,180	3%
Urinary bladder	12,870	4%			Leukemia	9,690	4%
Non-Hodgkin lymphoma	11,510	4%			Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%			Brain & other nervous system	7,850	3%
All Sites	**321,670**	**100%**			**All Sites**	**285,210**	**100%**

Source: [Reprinted with permission of Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7-34.] *Figure 2*

COMPARISON OF RISKY BEHAVIORS IN YOUTH (9th THROUGH 12th GRADES)		
Behavior	**Male Respondents**	**Female Respondents**
Rarely or never wore a seat belt (when riding with someone else)	6.6%	5.1%
Rode with a driver who had been drinking alcohol	15.7%	17.1%
Sent a text or e-mail message while driving a car (or other vehicle)	38.2%	40.2%
Drove after drinking alcohol	6.8%	4.1%
Carried a weapon (gun, knife, or club)	24.2%	7.4%
Was in a physical fight	24.2%	17.2%
Ever smoked cigarettes daily	9.8%	7.8%
Ever tried smoking cigarettes	30.7%	27.3%
Ever used electronic vapor product (e-cigarettes, e-cigars, e-pipes, vape pipes, vaping pens, e-hookahs, hookah pens)	44.9%	39.7%
Used smokeless tobacco (chewing tobacco, snuff, or dip) on at least 1 day during the previous 30 days	8.9%	1.9%
Had >5 drinks of alcohol within a couple of hours on >1 of the previous 30 days	12.8%	14.1%
Ever used marijuana	35.2%	35.9%
Drove after using marijuana	14.6%	11.3%
Ever used hallucinogenics	7.6%	5.5%
Ever used ecstasy	5.0%	2.9%
Ever used cocaine	6.1%	3.5%
Ever used heroin	2.4%	0.9%
Ever used methamphetamines	3.4%	1.4%
Source: [23]		*Table 3*

RISKY BEHAVIOR AMONG ADULTS		
Behaviors[a]	**Men**	**Women**
Non-seat belt use	16%	11%
"Heavy" drinking (five or more drinks on the same occasion on at least five days of the last month)	9.3%	3.2%
Five drinks or more in a day at least one day within the previous month	30.0%	16.4%
Current smoking	21.2%	16.8%
Use of illicit drugs[a]		
Any illicit drug (past month)	12.8%	7.7%
Cannabis (past month)	10.9%	6.0%
Psychotherapeutic drug (nonmedical use in past month)	2.6%	2.3%
[a]Data for behaviors are based on individuals 18 years of age and older; the data on use of illicit drugs are based on individuals who were 12 years of age and older.		
Source: [1; 24]		*Table 4*

(10.3%) [11]. The trend of more fatal unintentional injuries among men is evident in countries around the world; an analysis of accidental deaths among men and women in 36 countries showed higher rates for men [2]. Across all age-groups, the rates were higher in the United States than the median rate for all countries. Accidental deaths are related primarily to motor vehicle injuries, violence, and occupation, and the rates in all categories are higher for men than for women. The rate of death related to motor vehicle injuries for men is slightly higher than for women (21 vs. 14 per 100,000), and the percentage of fatal unintentional firearm-related injuries deaths occur overwhelmingly more often among men (84.7%) than women (22.0%) [25]. Similarly, fatal occupational injuries occur predominantly in men (57% vs. 6%) [26].

Substance misuse plays a significant role in both risky behavior and the development of chronic diseases. As demonstrated by the YRBS data, the use of tobacco, alcohol, and illicit drugs begins in the teenage years, with more boys than girls engaging in such behavior [23]. Among adults, substance misuse continues to be more prevalent among men than women [27]. Misuse of tobacco, alcohol, and drugs are associated with high rates of unintentional injuries, violence, STIs, and masking of depression [25; 28; 29; 30].

The rate of tobacco use among men has declined over the past decade, but the rate continues to be higher than that among women [31]. The Centers for Disease Control and Prevention (CDC) estimates that men who smoke increase their risk of death from lung cancer by 25 times, with tobacco being the cause of approximately 90% of all lung cancer deaths in men [32]. In addition, smoking is a significant risk factor for many cancers, especially those that are more prevalent among men, and is linked to a two to four times greater likelihood of cardiovascular disease or stroke [32].

Excessive alcohol use is the third leading lifestyle-related cause of death for both men and women, and long-term use of alcohol is a well-recognized contributor to several chronic diseases [33]. Even consumption that is considered to be less than "hazardous" (three to five drinks per day) has been associated with increased morbidity and mortality [34].

Help- and Information-Seeking Behavior

Help- and information-seeking behavior related to male gender identity is another factor that affects men's health. In general, men are reluctant to seek health care or talk about their health because they see such help-seeking as a sign of weakness or vulnerability and a threat to their masculinity [4; 35; 36]. These reports are substantiated by data on utilization of healthcare resources, which indicate that men have fewer healthcare visits (physician's office, emergency department, or home visit) than women; in 2017, 15.2% of men had no healthcare visits, compared with 13.3% of women [37]. In addition, men are more likely to lack a usual source of health care (28% vs. 14%) [38]. Men have reported several reasons for not having a usual source of care, and the reasons vary among racial/ethnic populations [39]. The reason given most often is that they are seldom or never sick, and this may be related to men's perceptions of invulnerability [39; 40]. Other reasons given include not finding time and not being able to take time away from work [38]. Cultural values, such as *machismo*, lead many Hispanic men to avoid health care until there is no other choice [40]. This may contribute to the low rate of healthcare use among Hispanic men, which is the lowest across racial/ethnic populations [40]. Other reasons for the low use of healthcare services among Hispanic men are lack of health insurance, low understanding of the healthcare system, fear of poor functional outcomes, and a low perception of the quality of the patient-clinician interaction [40]. In the black population, men have reported to avoid healthcare services because of fears and concerns about their negative health behaviors and history [41].

Lower rates of healthcare use among men have a negative impact on preventive care, and rates of routine health assessments and recommended vaccinations and screening procedures have been lower among men than among women [42]. Several factors contribute to the avoidance of screening tests, including men's belief that they are healthy; their focus on their present, rather than future, health; the need for more information about the screening procedure; and other issues related to masculinity [42]. For example, black men have reported avoiding screening for prostate and colorectal cancer because they see these procedures as "violating their manhood" [41; 43].

Among men who do have physician office visits, many are not forthcoming about symptoms or information they seek [44]. Because of their traditional discomfort with expressing feelings and emotions, they are less likely to seek help for psychosocial problems or emotional symptoms [17; 45]. Men tend to be more motivated to seek health care for male-oriented conditions, such as erectile dysfunction or sports-related injuries, or when their health or symptoms interfere with their routine activities [45].

Communicating Effectively with Men

Effective communication is essential in the healthcare setting but can be challenged by several factors. Specific challenges in communicating with men are related to male gender identity as well as to low health literacy and language and cultural barriers.

Male Gender Identity

Men's beliefs about masculinity and traditional male roles affect health communication, and healthcare practitioners should consider male-specific beliefs and perceptions when communicating with male patients. For example, because men tend to focus on present rather than future health, concepts of fear, wellness, and longevity often do not work well in health messages [40]. Instead, healthcare practitioners should focus more on "masculine" concepts, such as strength, safety, and performance, all of which tie into men's perceptions of their roles as providers and protectors. To address men's reluctance to admit pain, practitioners should avoid asking questions such as "Do you have pain?" and instead use phrases such as "Most men I see with this condition say they have quite a bit of pain—what about you?" Using numbers/statistics and metaphors relating the body to a machine may also help to communicate effectively by addressing male gender identity. In addition, practitioners should be nonjudgmental about their male patients' health and risk behaviors and develop open lines of communication to encourage them to express their health concerns.

Health Literacy, Language, and Culture

According to the National Assessment of Health Literacy, 14% of individuals in the United States have "below basic" health literacy, which means they lack the ability to understand health information and make informed health decisions [21; 46]. The findings of the assessment demonstrated that the rate of "below basic" literacy was higher among men than women (16% vs. 12%) [21]. Although the rate of "basic" health literacy was similar for men and women, rates of "intermediate" and "proficient" health literacy were lower for men [21]. Similar rates of health literacy have been found in subsequent studies, with rates of adequate health literacy consistently lower among men and even lower among non-white men [47; 48]. In one study, the rate of adequate health literacy was 48% among white men (compared with 63% among white women) and 23% among non-white men (compared with 30% among non-white women) [48].

Recognition of the importance of adequate health literacy to good health outcomes has led to assessment of health literacy being deemed "the newest vital sign," with development of an assessment tool by that name [48; 49]. The Newest Vital Sign (NVS) tool has been shown to demonstrate the health literacy status in fewer than three minutes, with results that are comparable to those of more extensive literacy tests [48]. Clinicians are encouraged to use this tool to assess the literacy of their patients, especially those of racial/ethnic minorities, and to adapt discussions to literacy levels and provide low-literacy educational resources.

Compounding health literacy are language and cultural barriers, which have the potential for far-reaching effects, given the growing percentages of racial/ethnic populations. According to U.S. Census Bureau data from 2017, 21.8% of the American population speak a language other than English, and of those, 8.5% speak English less than "very well" [50]. Clinicians should ask their patients what language they prefer for their medical care information, as some individuals prefer their native language even though they have said they can understand and discuss symptoms in English [51]. Translation services should be provided for patients who do not understand the clinician's language. "Ad hoc" interpreters (family members, friends, bilingual staff members) are often used instead of professional interpreters for a variety of reasons, including convenience and cost. However, clinicians should check with their state's health officials about the use of ad hoc interpreters, as several states have laws about who can interpret medical information for a patient [52]. Even when allowed by law, the use of a patient's family member or friend as an interpreter should be avoided, as the patient may not be as forthcoming with information and the family member or friend may not remain objective [52]. Children should especially be avoided as interpreters, as their understanding of medical language is limited and they may filter information to protect their parents or other adult family members [52]. Individuals with limited English language skills have actually indicated a preference for professional interpreters rather than family members [53].

Most important, perhaps, is the fact that clinical consequences are more likely with ad hoc interpreters than with professional interpreters [54]. A systematic review of the literature showed that the use of professional interpreters facilitates a broader understanding and leads to better clinical care than the use of ad hoc interpreters, and many studies have demonstrated that the lack of an interpreter for patients with limited English proficiency compromises the quality of care and that the use of professional interpreters improves communication (errors and comprehension), utilization, clinical outcomes, and patient satisfaction with care [55; 56].

Clinicians should use plain language in their discussions with their patients who have low literacy or limited English proficiency. They should ask them to repeat pertinent information in their own words to confirm understanding, and reinforcement with the use of low-literacy or translated educational materials may be helpful.

MALE-SPECIFIC DISORDERS

Among male-specific disorders, prostatic conditions are perhaps of most concern to men and have raised the most questions in the healthcare community about diagnosis, screening, and treatment. Sexual health issues, such as premature ejaculation and erectile dysfunction, are also of substantial concern to men, and treatments for these conditions gained increased attention beginning in the late 1990s. The prevalence of many STIs is on the rise, especially among younger men, posing a significant public health problem [57]. Infertility is an issue for many younger men, and interest in late-onset hypogonadism has increased, primarily because of the debate about the use of testosterone replacement therapy. Much attention has also been focused on the unique healthcare needs of a minority population—MSM. (This term has become preferred as a more accurate description because of the variation in how such men identify themselves sexually [58].) Another minority population is that of men with breast cancer, a disease that has become more prevalent since the 1980s. The diseases and conditions noted here by no means represent all of those related to the health care of men. Topics were chosen on the basis of their impact on the overall health of men and the implications for care.

Primary care and family medicine physicians and other general healthcare providers are at the forefront of managing all of these male-specific conditions. Consultation with and referral to specialists, such as urologists, endocrinologists, reproductive specialists, and oncologists, should be carried out as appropriate, and follow-up should be continued with the primary healthcare provider.

DISEASES AND CONDITIONS OF THE PROSTATE

Prostate tissue undergoes changes as men age, and as such, prostatic conditions predominantly occur in older men. The three primary problems related to the prostate are prostatitis, BPH, and prostate cancer. These conditions can be challenging to diagnose because lower urinary tract symptoms, such as frequency, urgency, and dysuria, can be associated with all three conditions. Furthermore, the most serious of the prostate conditions—prostate cancer—usually produces no symptoms in the early stage of the disease. In addition to the diagnostic challenge created by similar, or no, symptoms, the interpretation of prostate-specific antigen (PSA) levels is difficult, and decisions regarding who and when to screen for prostate cancer are not easy.

PROSTATITIS

Inflammation of the prostate is classified into four categories according to a system developed by the National Institutes of Health (NIH) International Prostatitis Collaborative Network [59]. These categories are:

- Acute bacterial prostatitis
- Chronic bacterial prostatitis
- Chronic prostatitis (nonbacterial)/chronic pelvic pain syndrome (subcategorized as A [inflammatory] and B [noninflammatory])
- Asymptomatic inflammatory prostatitis

Both acute and chronic bacterial prostatitis occur in approximately 5% to 10% of men with symptoms related to prostatitis. Chronic nonbacterial prostatitis/chronic pelvic pain syndrome is the most common type, occurring in approximately 90% of symptomatic men [60]. These three types of prostatitis are addressed here; asymptomatic inflammatory prostatitis is an incidental finding during evaluation of another genitourinary condition such as prostate cancer or infertility [61].

It has been estimated that prostatitis accounts for approximately 2 million outpatient visits per year in the United States, with a direct cost of care of nearly $4,000 per patient per year [61]. The condition can have a substantial impact on the quality of life, causing pain and sexual dysfunction, as well as decreased libido and erectile and ejaculatory dysfunction [62; 63].

Chronic prostatitis/chronic pelvic pain syndrome has the greatest impact on the quality of life of all types of prostatitis. Studies have found that the effect of chronic pelvic pain syndrome on the quality of life is similar to that of angina, congestive heart failure, diabetes mellitus, and Crohn disease [61]. Symptoms fluctuate over time; one study showed that 43% of men had symptoms within 11 months of follow-up, and another showed that 31% of men had moderate or marked improvement during two years of follow-up [64; 65]. Chronic prostatitis/chronic pelvic pain syndrome also causes patient anxiety at the initial visit. Most men with symptoms worry that they have an infection (71%) or cancer (68%), and concerns at one-year follow-up have included worsening symptoms without treatment, cancer, infection, and need for surgery [65]. These concerns have led to an increased number of physician visits [65].

Prevalence

The prevalence of prostatitis has been reported to be approximately 8%, ranging from about 2% to 10% [66]. In patients younger than 35 years of age, the most common variant of the syndrome is acute bacterial prostatitis. Among older patients, nonbacterial prostatitis (NIH types II and IV) is the most common [67]. The results of studies have suggested that the symptoms of prostatitis increase the risk for BPH, lower urinary tract symptoms, and prostate cancer [66].

Etiology

The cause of acute and chronic bacterial prostatitis is usually lower urinary tract infection with gram-negative organisms, most notably *Escherichia coli* [60; 61]. Most men with prostatitis, however, have no evidence of urinary tract infection [61]. Other causes may include a primary voiding dysfunction problem; presence of *Chlamydia trachomatis*, *Ureaplasma* species, or *Trichomonas vaginalis*; uncommon organisms (e.g., *Mycobacterium tuberculosis*); HIV; cytomegalovirus; and inflammatory conditions (e.g., sarcoidosis) [67].

The risk factors for prostatitis have not been clearly defined. In a study of 463 men with chronic prostatitis/chronic pelvic pain and 121 asymptomatic age-matched controls, the lifetime prevalence of several self-reported medical conditions were significantly greater among the men with prostatitis, specifically neurologic disease (41% vs. 14%); hematopoietic, lymphatic, or infectious disease (41% vs. 20%); psychiatric conditions (29% vs. 11%); nonspecific urethritis (12% vs. 4%); and cardiovascular disease (11% vs. 2%) [68]. The authors of that study noted that more research is needed to determine if such conditions contribute to the pathogenesis of chronic prostatitis/chronic pelvic pain. A history of STIs has been noted to be associated with an increased risk for prostatitis symptoms [66].

Diagnosis

Several other urogenital conditions should be considered in the differential diagnosis of prostatitis, including BPH, cystitis, erectile dysfunction, prostate cancer, STI, and urolithiasis [69; 70]. Of the four types of prostatitis, acute bacterial prostatitis is the easiest to diagnose and treat. Symptoms of this condition include dysuria and urinary frequency and may also include signs of systemic infection, such as chills and fever [70]. Pain most commonly occurs in the prostate/perineum and scrotum and/or testes, and may also occur in the penis or lower back [70]. Urine samples should be cultured to determine the causative micro-organism.

Chronic bacterial prostatitis is distinguished from acute disease by time, being defined by persistence of symptoms for at least three months, and systemic symptoms are usually absent [58; 70]. The condition should be suspected when the patient's history includes recurrent urinary tract infections, usually with the same bacterial strain [61]. The patient should complete an NIH Chronic Prostatitis Symptom Index to obtain a baseline score for the severity of symptoms [59]. This index includes questions related to three domains—pain, urinary symptoms, and quality-of-life impact—and has been shown to be a valid, reliable tool for measuring prostatitis symptoms [70; 71]. Computed tomography (CT) can determine if there are structural or functional abnormalities of the urinary tract [60; 61].

The diagnostic evaluation for acute or chronic bacterial prostatitis should include a urinalysis and urine culture [61; 70]. There is no criterion-standard method for diagnosing chronic prostatitis/chronic pelvic pain syndrome [61; 69]. The Meares-Stamey four-glass test was developed in the late 1960s to screen for prostatitis; the test involves collecting urine samples before and after prostatic massage, as well as collecting prostatic fluid during the massage [72]. Cultures are done on the specimens, and the presence of micro-organisms in the prostatic fluid indicates chronic prostatitis [61; 72]. The accuracy and reliability of the test has not been established, and studies have shown that the test is not used often, even by urologists [61; 69]. There is also a two-glass version of the test that has correlated well with the four-glass version, but that, too, is not often used [61]. The Meares-Stamey test is not helpful for diagnosing chronic pelvic pain syndrome. Men who have substantial lower urinary tract symptoms and pelvic pain may be candidates for urodynamic evaluation, as voiding dysfunction is common in such cases [61].

Treatment Options

No U.S.-based guidelines have been developed, to date, for the treatment of prostatitis, but the European Association of Urology included recommendations for the treatment of prostatitis in its 2008 guidelines on the management of urinary and male genital tract infections [70]. These guidelines note that high doses of a parenteral antibiotic are often needed for acute bacterial prostatitis, and a broad-spectrum penicillin, a third-generation cephalosporin, and a fluoroquinolone are options [70]. An aminoglycoside may be added to any of these antibiotics as initial therapy [70]. A 10-day course of a fluoroquinolone can be used for less severe infections [70].

For chronic bacterial prostatitis, the choice of antibiotic depends on the sensitivity of the microorganism, and the antibiotic should be one that penetrates the prostate [61]. The typical first-line treatment is a four- to six-week course of a fluoroquinolone, and treatment is usually more effective if begun soon after symptoms begin [61; 70; 73; 74]. Trimethoprim may also be considered [70].

Treatment for chronic prostatitis/chronic pelvic pain syndrome is complex; evidence on the effect of traditional treatment options has been conflicting, and treatment options are often not effective in managing symptoms. The most commonly studied pharmacologic options are antibiotics, alpha-blockers, anti-inflammatory agents, steroid inhibitors, and muscle relaxants, and often, a combination of these agents provides the most effective management [74]. Antibiotics, particularly fluoroquinolones, have improved symptoms, even in some patients in whom a bacterial cause has not been identified [74]. Studies have shown that an antibiotic and an alpha-blocker is more effective than an antibiotic alone [70]. A meta-analysis showed that alpha-blockers, antibiotics, and a combination of the two all significantly improve symptoms (according to scores on the NIH Chronic Prostatitis Symptom Index), with the combination providing the greatest benefit [75]. However, another meta-analysis showed that these same agents—alone and in combination—were not associated with a statistically or clinically significant decrease in symptom scores [76]. The combination of an alpha-blocker (doxazosin) with an anti-inflammatory agent (ibuprofen) and a muscle relaxant (thiocolchicoside) led to a statistically and clinically significant reduction in the total score on the NIH Chronic Prostatitis Symptom Index in one systematic review; according to the findings of another systematic review, the three-agent combination was not superior to monotherapy [74; 76]. Researchers have cautioned that publication bias may cause overestimation of the beneficial effects of alpha-blockers and that the placebo effect has been significant in many studies [75; 76]. Addressing a hypothesis that the pain related to chronic prostatitis may have a neuropathic origin, pregabalin has been evaluated as a management strategy, but a systematic review found that the drug did not improve symptoms and caused side effects in a large percentage of men [77].

Trigger point release/paradoxical relaxation training to release trigger points in the pelvic floor musculature was found to significantly improve symptoms in men who had chronic prostatitis/chronic pelvic pain syndrome [63]. Seventy percent of the men in the study had a significant decrease in the score on the NIH Chronic Prostatitis Symptom Index, with improvement in pelvic pain, urinary symptoms, libido, ejaculatory pain, and erectile and ejaculatory dysfunction [63].

BENIGN PROSTATIC HYPERTROPHY

BPH is one of the most common conditions among aging men, with the disease usually developing after 40 years of age and increasing in frequency with age [78]. Serious complications and mortality are rare, but the condition has an impact on the quality of life, with symptoms that interfere with normal daily activities and sleep [78]. Complete evaluation is necessary for an accurate diagnosis of BPH; the condition must be differentiated from prostate cancer, which is associated with similar early symptoms. In addition, early detection of BPH leads to early treatment, which can control

progression of the disease, preventing such complications as urinary tract infection, acute urinary retention, and obstructive nephropathy [79].

Prevalence and Etiology

The prevalence of BPH increases with age, from approximately 8% of men 31 to 40 years of age to approximately 90% of men in their 80s [80; 81]. Risk factors identified in one study included increased age, prostatic volume, and peak urinary flow rate [82]. Other factors, including some that are modifiable, include obesity, diet, dyslipidemia, hypertension, alcohol use, and smoking [83]. The relative risk for BPH (and common comorbidities) may be higher for black and Hispanic men than for white men and is thought to be related in part to genetic differences based on race/ethnicity; however, observational studies have produced variable results [81; 84].

Diagnosis

As previously noted, distinguishing BPH from other prostate-related diseases is often difficult, as lower urinary tract symptoms are similar for a variety of conditions. The American Urological Association (AUA) evidence-based guidelines for the management of BPH recommend the following tests [78]:

- Medical history
- Assessment of lower urinary tract symptoms
- Determination of severity and bother of symptoms
- Physical examination
- Urinalysis

Determination of a serum PSA level is also recommended if the patient has a life expectancy of more than 10 years (and the diagnosis of prostate cancer will alter management), and a frequency-volume chart is recommended if substantial nocturia is a predominant symptom [78]. Routine measurement of a serum creatinine level is not recommended as part of the initial evaluation of men with lower urinary tract symptoms related to BPH [78].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The National Institute for Health and Care Excellence recommends offering men with lower urinary tract symptoms information, advice, and time at initial assessment to decide if they wish to have prostate-specific antigen (PSA) testing if their symptoms are suggestive of benign prostatic enlargement.

(https://www.nice.org.uk/guidance/cg97. Last accessed June 12, 2019.)

Level of Evidence: Expert Opinion/Consensus Statement

In obtaining a history, clinicians should ask about urinary tract symptoms, sexual function, previous surgical procedures, and general health issues in an attempt to identify other causes of voiding dysfunction or comorbidities that may complicate treatment. Diabetes, cerebrovascular disease, and Parkinson disease can cause urinary symptoms secondary to neurogenic bladder, and STIs or trauma may cause urethral stricture [85]. It may be appropriate to have the patient keep a diary of voiding habits (frequency, volume, etc.) [78].

Assessment of symptoms is an integral aspect of the initial evaluation for BPH, as it helps to determine the severity of disease. The AUA Symptom Index is the recommended assessment tool; this seven-question instrument has been validated for clarity, test/retest reliability, internal consistency, and criteria strength [78; 86]. The Index addresses [86]:

- Urinary frequency
- Hesitancy
- Nocturia
- Incomplete emptying
- Urgency
- Weak urinary stream
- Intermittence

Symptoms should be discussed with the patient and questions addressed as necessary [78].

The physical examination should include a digital rectal examination (DRE) to determine the size, consistency, and shape of the prostate [78]. A symmetrically firm and enlarged prostate by DRE is indicative of BPH [79]. The true size of the prostate is often underestimated by DRE compared with transrectal ultrasound [78]. Examination should also include neurologic evaluation to assess the patient's general mental status, ambulatory status, neuromuscular function of the lower extremities, and anal sphincter tone [78].

A urinalysis (dipstick test) to screen for hematuria, proteinuria, pyuria, and other abnormalities can help to rule out such conditions as bladder cancer, carcinoma in situ of the bladder, urinary tract infection, urethral strictures, distal urethral stones, and bladder stones, which are less likely if the results of urinalysis are normal [78].

Treatment Options

According to the AUA guideline, the benefits, risks, and costs of treatment options should be discussed with patients who have moderate-to-severe symptoms (AUA Symptom Index score of 8 or more) who are bothered enough by the symptoms to consider therapy [78]. The treatment options for BPH include:

- Watchful waiting
- Medical therapy (minimally invasive procedures)
- Surgical interventions

The AUA guideline recommends watchful waiting as the preferred approach for men who have mild symptoms (a score of less than 8 on the AUA Symptom Index) [78]. This approach may also be taken for men with moderate-to-severe symptoms (score of 8 or more) who are not bothered by the symptoms and have no complications [87]. Watchful waiting should include yearly evaluations similar to the initial one [78]. Symptoms may be reduced by avoiding decongestants and antihistamines, decreasing fluid intake at bedtime, and reducing the amount of caffeine and alcohol intake [78].

Among the options for medical treatment are five alpha-blockers that have FDA-approved indications for BPH (***Table 5***). The AUA guideline notes that four of these drugs—alfuzosin, doxazosin, tamsulosin, and terazosin—have similar clinical effectiveness and slight differences in adverse events profiles [78]. The fifth drug, silodosin, was approved in 2008, and peer-reviewed studies were not available for the literature review of the AUA guideline update. A study of pooled data from two phase III studies showed that silodosin led to rapid improvement in symptoms (within three to four days) that was sustained for 12 weeks [88].

The primary adverse events associated with alpha-blockers have been orthostatic hypotension, dizziness, fatigue (asthenia), and ejaculatory problems [78]. These drugs should not be used for men who are taking medication for erectile dysfunction, as the interaction between the two drugs can cause profound hypotension [79].

Two 5-alpha reductase inhibitors, finasteride and dutasteride, are also approved for treatment of BPH-related symptoms and are recommended options in the AUA guideline [78]. This is less effective than therapy with alpha-adrenergic antagonists for relieving lower urinary tract symptoms, leading to an average improvement of 3 points on the AUA Symptom Index [78]. The advantage of 5-alpha reductase inhibitors is that they also act to prevent progression of disease and reduce the size of the prostate. As such, the AUA notes that these drugs should be used only for men who have evidence of prostatic enlargement [78]. Men should be made aware of the need for long-term therapy with either of these drugs, and clinicians should also discuss the possible adverse events, which include decreased libido, ejaculatory dysfunction, and erectile dysfunction. These effects usually resolve within one year [78; 79].

In 2011, the FDA issued a safety announcement that the Warnings and Precautions section of the labels of 5-alpha reductase inhibitors was revised to include new safety information about the increased risk of a diagnosis of high-grade prostate cancer [92]. The revision came after FDA review of two

PHARMACOLOGIC THERAPY FOR BENIGN PROSTATIC HYPERTROPHY	
Agent	**Daily Dose**
Alpha-blockers	
Alfuzosin ER (Uroxatral)	10 mg
Doxazosin (Cardura) and doxazosin ER (Cardura XL)	4–8 mg
Silodosin (Rapaflo)	8 mg
Tamsulosin (Flomax)	0.4–0.8 mg
Terazosin (Hytrin)	1–2 mg
5-alpha reductase inhibitors	
Dutasteride (Avodart)	0.5 mg
Finasteride (Proscar)	5 mg
Combination (alpha-blocker and 5-alpha reductase inhibitor)	
Dutasteride/tamsulosin (Jalyn)	1 capsule (0.5 mg dutasteride and 0.4 mg tamsulosin hydrochloride)
Phosphodiesterase 5 inhibitors	
Tadalafil (Cialis)	5 mg
Source: [89; 90; 91]	*Table 5*

prostate cancer prevention trials, in which finasteride and dutasteride reduced the incidence of lower risk forms of prostate cancer but were associated with an increased incidence of high-grade prostate cancer [92].

The AUA guideline also supports the use of combination therapy with an alpha-blocker and a 5-alpha reductase inhibitor for men with lower urinary tract symptoms and evidence of prostate enlargement, as demonstrated on volume measurement, PSA level as a proxy for volume, or on DRE [78]. A fixed-dose combination of dutasteride (0.5 mg) and tamsulosin (0.4 mg) is available, and the results at four years showed that, for men with a baseline prostate volume ≥40 mL and PSA level of ≥1.5 ng/mL, the combination led to greater reductions in the relative risk of clinical progression, acute urinary retention, or BPH-related surgery than either drug alone [93].

The AUA guideline also notes that anticholinergic agents are appropriate and effective options for managing BPH-related symptoms in men who do not have an elevated post-void residual and when symptoms are predominantly irritative [78].

Phosphodiesterase type-5 inhibitors have also been shown to be effective for reducing the symptoms associated with BPH [94]. This class of drugs also offers advantages over other drugs in its rapid onset of action, fewer adverse events, and enhanced sexual function [94]. Potential adverse events include back pain, dyspepsia, headache, and dizziness [95]. In 2011, the first phosphodiesterase type-5 inhibitor—tadalafil—was approved by the FDA for BPH-related symptoms, with indications for symptoms in men who have prostate enlargement, with or without erectile dysfunction [95]. Before prescribing tadalafil, clinicians should ensure that patients are not taking drugs that interact with tadalafil, such as nonselective alpha-blockers, nitrates, and cytochrome P450 inhibitors [95].

Saw palmetto, a commonly used alternative therapy for BPH, is not recommended for BPH-related symptoms, as the most recent data have shown no clinically meaningful effect on symptoms [78].

Minimally invasive therapies such as transurethral needle ablation and transurethral microwave thermotherapy are treatment options for men with bothersome moderate or severe symptoms [78].

However, the AUA guideline notes that, although these therapies improve symptoms, flow rate, and quality of life, the outcomes are not as good as those after transurethral resection of the prostate [78].

Surgical interventions are typically reserved for worsening disease and severe symptoms that do not respond to medical treatment. The AUA guideline recommends surgery for patients who have renal insufficiency secondary to BPH; recurrent urinary tract infections, bladder stones, or gross hematuria due to BPH; or symptoms refractory to other therapies [78]. The most common procedure is transurethral resection of the prostate, which comprises 90% of all prostate surgeries done for BPH and is the benchmark for therapy [78; 96]. Open prostatectomy; transurethral laser ablation or enucleation; laser resection; photoselective vaporization; and transurethral incision, vaporization, and resection are other surgical options, and the selection of intervention is based on the surgeon's experience, the patient's anatomy, and a discussion of the benefits and risk of complications [78].

PROSTATE CANCER

Prostate cancer is the most commonly diagnosed cancer among men, accounting for 19% of all cancer diagnoses in men and the second leading cause of cancer-related deaths, responsible for 9% of cancer-related deaths in men [16]. The lifetime risk of a prostate cancer diagnosis is approximately 15% [16].

Prostate cancer is a complex issue for both men and their healthcare providers for many reasons, including variation in tumor biology, lack of specific symptoms, accuracy of levels of PSA and its several derivatives, questions about optimum treatment, and, most notably, controversy surrounding screening.

Prevalence and Etiology

The estimated number of prostate cancer diagnoses in 2019 is 174,650, with an estimated 31,620 deaths [16]. The highest prevalence is found among black men (179.2 per 100,000), and the lowest is among Asian American and Pacific Islander men (56.0 per 100,000) [16]. The death rate related to prostate cancer is also highest for black men, with a rate that is more than twice that for men of all other races/ethnicities (39.8 per 100,000 vs. 18.1 [white], 19.1 [American Indian and Alaska Native], 15.9 [Hispanic/Latino], and 8.6 [Asian American and Pacific Islander]) [16]. The mortality rate associated with prostate cancer decreased 2.3% per year between 2007 and 2016, in part, because of improvements in early detection and treatment [16].

The known risk factors for prostate cancer are advanced age, black race, and a family history of the disease (especially when diagnosed at a younger age) [16; 97]. The risk for prostate cancer may also be increased for men with symptoms of prostatitis [66].

Prevention

Several studies have been undertaken to determine the efficacy of measures to prevent prostate cancer through either chemoprevention agents or dietary supplements. The chemoprevention agents evaluated belong to the class of 5-alpha reductase inhibitors, a class of drugs approved for the treatment of BPH. One drug in this class, finasteride, was evaluated in the first large-scale chemoprevention study, the Prostate Cancer Prevention Trial (PCPT), a seven-year study involving nearly 19,000 men 55 years of age or older. In that study, finasteride significantly reduced the prevalence of prostate cancer (18% vs. 24% for the placebo group) [98]. Dutasteride was shown to decrease the risk of prostate cancer in the REDUCE trial, and extended follow-up indicated a low rate of new prostate cancer diagnoses [99; 100]. The initial results of the PCPT and REDUCE trials led the American Society of Clinical Oncology (ASCO) and the AUA to develop a joint guideline recommending finasteride and dutasteride for the prevention of prostate cancer [90]. However, reanalysis of the results of the trials showed that the risk for high-grade prostate cancer was increased and the reduction in prostate cancer risk was seen primarily for less fatal subtypes of prostate cancer that are often not treated [100; 101]. In 2011, the FDA

decided against approving the two drugs for the prevention of prostate cancer, noting that the risk-benefit profile is not favorable for chemoprevention [91; 101; 102]. As stated earlier, the FDA revised the labels of all 5-alpha reductase inhibitors to note the increased risk of higher grade prostate cancer associated with the drugs [92]. The ASCO/AUA guideline was withdrawn, and experts have called for more research to determine whether 5-alpha reductase inhibitors have a role in the prevention of prostate cancer [101; 102; 103].

Dietary supplements have not been shown to substantially reduce the prevalence of prostate cancer. In the Selenium and Vitamin E Cancer Prevention Trial (SELECT), a randomized study of more than 35,000 men, neither of those two vitamins, alone or in combination, prevented prostate cancer in relatively healthy men [104]. A subsequent phase III trial showed that selenium supplementation had no effect on prostate cancer risk among men with high-grade prostatic intraepithelial neoplasia [105]. There is insufficient evidence for the routine recommendation of other dietary supplements, such as soy, lycopene, or green tea, to prevent prostate cancer [106; 107].

Screening

There is no question that available screening methods and enhanced awareness has led to an increased number of men in whom prostate cancer is diagnosed at an earlier stage. The primary benefit of screening is a lower stage and grade of cancer at the time of diagnosis, and the high rate of localized disease at the time of diagnosis (92% to 96%) reflects, in part, the increased number of cancers that are detected earlier through screening [102; 108; 109]. Despite this benefit, an effect of screening on mortality has not been clearly demonstrated. After 13 years of follow-up in the National Cancer Institute's Prostate, Lung, Colon, and Ovary (PLCO) trial, there was no benefit of annual screening on mortality [110]. A meta-analysis (five randomized controlled trials) similarly demonstrated no effect of screening on prostate cancer-specific or overall mortality [111]. However, data from the European Randomized Study of Screening for Prostate Cancer demonstrated that screening reduced the risk for prostate cancer death by 7% to 9% per year [112].

In addition to a lack of effect on mortality, screening is associated with high rates of false-positive results, overdiagnosis and subsequent overtreatment, and complications. Among men who had four PSA tests, the cumulative risk for at least one false-positive result was 12.9% [102]. Rates of overdiagnosis have been estimated at 17% to 50%, and 23% to 42% of all screen-detected prostate cancers are overtreated [102; 113]. Furthermore, treatment is associated with complication rates of 20% to 50% [102; 114]. These findings have led several expert panels to update their screening recommendations (***Table 6***) [97; 102; 108; 114; 115; 116; 117]. Overall, experts recommend against routine screening for most men and emphasize the need to consider life expectancy and the patient's age and risk factors for the disease. The age to start a discussion about screening varies slightly among the guidelines. The AUA guideline notes that decisions about screening should be individualized for men younger than 55 years who are at high risk for the disease (positive family history or black race) [114]. The guideline also states that the greatest benefit of screening appears to be for men 55 to 69 years of age and strongly recommends shared decision making for men in this age-group. The ACS guideline notes that screening should be discussed beginning at 50 years of age for men at average risk and before 50 years of age for men at higher risk [108]. The NCCN guideline suggests that clinicians talk to patients about the risks and benefits of a baseline DRE and PSA beginning at 40 years of age [97]. The American College of Physicians (ACP) recommends that clinicians inform their male patients, 50 to 69 years of age, about the limited potential benefits and substantial harms of screening [115].

RECOMMENDATIONS FOR PROSTATE CANCER SCREENING			
Organization	**Year of Publication**	**Screening Recommendation**	**Notes**
American Cancer Society	2010	—	Discuss the potential benefits, risks, and uncertainties associated with prostate cancer screening with men ≥50 years
American Society of Clinical Oncology	2012	Discourage general screening for men with a life expectancy of ≤10 years, as the harms outweigh the benefits	Discuss the individual appropriateness of screening with men who have a life expectancy >10 years
American Urological Association	2018	No routine screening in men 40 to 54 years of age at average risk	Decisions should be individualized for men younger than 55 years who are at high risk. Shared decision-making should take place for men 55 to 69 years of age, for whom screening is of greatest benefit.
American College of Physicians	2013	No routine screening with PSA for average-risk men younger than 50, men older than 69, or men with a life expectancy of less than 10 to 15 years	Clinicians should inform men 50 to 69 years of age about limited potential benefits and substantial harms of screening and should individualize decision based on patient's general health, life expectancy, and preferences.
National Comprehensive Cancer Network	2019	—	Offer baseline PSA testing (with DRE) to healthy, well-informed men 45 to 75 years of age. Men 45 to 75 years of age with serum PSA values less than 1 ng/mL should be screened every 2 to 4 years. Consider PSA testing only in very healthy patients older than 75 years of age.
U.S. Preventive Services Task Force	2018	No routine screening for men 70 years of age and older. For men 55 to 69 years of age, the decision should individualized.	Clinicians should discuss the potential benefits and harms of screening.
Source: [97; 102; 108; 114; 115; 116; 117]			*Table 6*

Researchers continue to investigate ways to make screening more effective. Using a higher PSA threshold for biopsy for older men and less frequent screening for men with low PSA levels are strategies that may reduce the risk of overdiagnosis as well as prostate cancer-related mortality [118].

Informed decision making is integral in selecting approaches to screening, with every guideline emphasizing the need to discuss the potential benefits, harms, and limitations associated with screening with their male patients. The American Cancer Society notes that men should receive information about screening directly from their healthcare provider or be referred to reliable and "culturally appropriate" sources [108]. Decision aids

can be especially useful in helping men and their healthcare providers weigh the benefits and risks of screening, and studies of decision aids have led to improved knowledge and have increased men's desire for an active role in decision making [108; 114; 119; 120; 121]. The NCCN guideline offers talking points for discussion, and ASCO provides a decision aid tool (https://www.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/2012-psa-pco-decision-aid.pdf).

Despite the continued emphasis on informed decision making, the percentage of men who report having had a discussion with their healthcare providers about screening has been suboptimal, with a rate of about 63% to 66% of the general male population [122; 123]. Black men were most likely to have had a discussion, and men without a usual source of care were the least likely [123].

For men who choose to have screening for prostate cancer, the combination of DRE and PSA is the preferred method, providing better predictive value than either method alone [102]. The sensitivity of PSA testing is higher than that of DRE, especially for tumors that are more aggressive [109]. However, the PSA level can vary as a result of several factors.

PSA and Its Derivatives

In an effort to enhance the specificity of PSA testing, variations of the PSA test have been developed, including free PSA, PSA density, PSA velocity, and complexed PSA [97]. Each has its benefits and limitations, and the AUA notes that none increases the benefits-harms ratio of screening [114]. Levels of free PSA have been shown to be significantly lower in men with prostate cancer than in men without the disease [97]. The FDA has approved percent-free PSA for the early detection of prostate cancer in men with PSA levels between 4 ng/mL and 10 ng/mL [97].

PSA density is the result of dividing the PSA level by the volume of the prostate, as measured by transrectal ultrasonography, and a higher result suggests a greater likelihood of prostate cancer [97]. Greater PSA density has correlated with the presence of prostate cancer, as well as with the pathologic stage of the tumor and its aggressiveness and progression after treatment [124]. The use of PSA density has been limited by the lack of precision of total PSA, of measurement of prostate volume, and of the need to carry out transrectal ultrasonography [97]. In addition, PSA density does not offer much benefit compared with other PSA derivatives [97]. PSA velocity is the rate at which a PSA level increases over a period of time, and it has been most helpful for longitudinal monitoring of men younger than 50 years of age who have normal PSA levels and no prostate enlargement [97]. A high PSA velocity alone should not prompt biopsy but instead, aid in decision making [97]. The test is not useful for men with PSA values greater than 10 ng/mL [97]. The ratio of complexed PSA to total PSA provides information comparable to the ratio of free to total PSA, and the use of complexed PSA has been approved as a detection aid (in conjunction with DRE) for men 50 years of age or older; however, the test is not widely used in practice [97].

Threshold for Biopsy

Prostate cancer is found in about 25% of biopsy specimens, illustrating a problem regarding a well-defined threshold at which to obtain a biopsy specimen [125]. Although most cancer is detected with use of a PSA threshold of 4 ng/mL, some studies have shown that prostate cancer is subsequently found in men with levels in the range of 2.5–4.0 ng/mL [97]. The NCCN concluded that while these values have been used by many, a level of 3.0 ng/mL is supported by trials and would more robustly limit the risk of overdetection. However, there was not a consensus among NCCN panel members regarding limiting the option to biopsy to prespecified PSA thresholds [126]. The NCCN panel also concluded that DRE alone is not an absolute indication for biopsy in men with low PSA, as the positive predictive value of DRE in this population is poor. However, a very suspicious DRE, independent of PSA, could indicate high-grade cancer in men with normal PSA values, and therefore, biopsy should be considered in these men [126].

CLASSIFICATIONS OF RISK OF BIOCHEMICAL RECURRENCE				
Risk Level	**Tumor**	**Gleason Score**	**PSA Level (ng/mL)**	**Other**
Very low	T1c	≤6	<10	Biopsy cores: <3 positive, ≤50% cancer in any core PSA density: <0.15 ng/mL/g
Low	T1–T2a	≤6	<10	—
Intermediate	T2b–T2c	7 (or PSA level as noted)	10–20 ng/mL	—
High	T3a (or other criteria)	8–10 (or other criteria)	>20	—
Very high	T3b–T4 (locally advanced)	Primary Gleason pattern 5 (or other criteria)	—	Biopsy cores: >4 with Gleason score 8–10
NCCN = National Comprehensive Cancer Network, PSA = prostate-specific antigen.				
Source: [126]				*Table 7*

Diagnosis and Staging

Men with early prostate cancer are usually asymptomatic. More advanced disease may be associated with changes in urinary habits, such as a slowing of the urinary stream, sense of incomplete voiding, nocturia, and frequency, as well as dysuria, hematuria, or pain in the lower back or pelvis. Because many of these symptoms are similar to those linked to benign prostate conditions, prostate cancer cannot be diagnosed on symptoms alone. The diagnostic methods are the same as those used for screening: PSA, DRE, and transrectal ultrasonography. In performing the DRE, the clinician should focus on the size, consistency, and abnormalities within or beyond the gland. Prostate cancers are characteristically hard, nodular, and irregular.

In its 2013 Best Practice Statement on PSA, the AUA emphasizes the importance of PSA in staging, noting that the PSA level predicts response of prostate cancer to local therapy [127]. Response is most likely in men with a PSA level <10 ng/mL [127].

Biopsy of the prostate with analysis of the tissue provides the most definitive diagnostic procedure. It also gives evidence of the aggressiveness of the tumor when cancer is detected. The pathologist quantifies the aggressiveness of the tumor with use of the Gleason score, assigning a number between 2 and 10 (with 10 representing the most aggressive). Pathologic review involves both staging according to the American Joint Committee on Cancer staging manual and classification of the tumor with the Gleason score [128]. Further staging with imaging (CT, MRI, bone scan) is done only for tumors that are confined to the prostate with a Gleason score of 8 or higher or a PSA level of greater than 20 ng/mL or for tumors that extend beyond the prostate or are symptomatic [97]. As part of the Choosing Wisely campaign, the AUA notes that a routine bone scan is not necessary for men with newly diagnosed prostate cancer with a PSA level <20.0 ng/mL and a Gleason score of ≤6 [127].

Treatment Options

Recognizing that many prostate cancers have an indolent natural history, guidelines recommend that treatment decisions be based on the patient's estimated life expectancy and the risk of biochemical recurrence [126]. Risk of biochemical recurrence has been classified by the NCCN into five categories (***Table 7***) [126].

A new prostate cancer grading system was developed during a 2014 consensus conference of the International Society of Urological Pathology (ISUP). The new system resulted in changes to the assignment of Gleason pattern based on pathology. This system assigns grade groups from 1 to 5, derived from the Gleason score. Many experts believe that the ISUP grade groups enable patients to better understand their true risk level and limit overtreatment. The NCCN has accepted the new grade group system. Patients remain divided into very-low-, low-, intermediate-, high-, and very-high-risk groups [126].

The primary options for localized prostate cancer are watchful waiting (also known as active surveillance), radiation therapy (either three-dimensional external-beam radiation or brachytherapy), and radical prostatectomy. Other options include androgen-deprivation therapy (ADT, also referred to as hormone therapy), chemotherapy, cryosurgery, and immunotherapy.

Each treatment option is associated with benefits and harms, and clinicians should discuss each option in detail and provide educational resources and decision aids [129; 130; 131]. To gain a true understanding of a patient's preferences, treatment options should be discussed only after the patient has described his preferences [132]. Clinicians should carefully assess their patients' understanding of treatment options; studies of underserved men have shown low comprehension of common terms used in prostate cancer treatment discussions [133; 134]. Attention should also be paid to how to best communicate risk. A study has shown that such terms as "number needed to treat," "odds ratio," and "relative risk reduction" were confusing to men [135]. In that study, men best understood information when it was presented as an absolute risk reduction and in a positive context; men preferred that treatment options be discussed in terms of the probability of an increase in survival (rather than a decrease in mortality) and that the discussion include the impact of treatment on patient-centered quality-of-life outcomes [135].

Active Surveillance

Active surveillance has also been referred to as watchful waiting, but the terms have not always been defined the same way, and researchers are calling for a distinction between the two terms. Active surveillance is being used increasingly to describe an approach in which men with localized prostate cancer are followed up closely for clinical signs to prompt curative treatment [136]. The lack of universal definitions for these two terms has hampered research to determine the appropriateness of active surveillance as a management approach [136; 137]. Some studies are now beginning to distinguish the two approaches, with watchful waiting defined as observation and provision of palliative care when prostate cancer becomes symptomatic, and active surveillance defined as close follow-up (with DRE, PSA levels, and biopsies) and provision of treatment at signs of progression [138].

Choosing active surveillance rather than definitive treatment is difficult because of the myriad advantages and disadvantages to the approach (***Table 8***) [126]. Data on active surveillance have also conflicted. In a cohort of 450 men followed up for a median of nearly seven years, the rate of prostate cancer-specific mortality was low [139]. Two later systematic reviews indicated that the evidence was insufficient to determine whether active surveillance with curative intent was an appropriate option for men with localized prostate cancer [136; 137]. Most recently, radical prostatectomy was compared with active surveillance, and the intervention did not significantly reduce all-cause or prostate cancer-specific mortality through at least 12 years of follow-up [140]. In addition, a cost-effectiveness analysis demonstrated that active surveillance was most effective and least expensive compared with several interventions (brachytherapy, intensity-modulated radiation therapy, or radical prostatectomy) [138].

ADVANTAGES AND DISADVANTAGES OF ACTIVE SURVEILLANCE FOR PROSTATE CANCER	
Advantages	**Disadvantages**
Ensure that small indolent cancers are not treated unnecessarily	Lack of definitive prompt for treatment may lead to missed opportunity for cure
Avoid side effects of treatment that may be unnecessary	Cancer may progress or metastasize before treatment
Maintain quality of life and normal activities	Treatment of larger, more aggressive cancer may be more complex, with increased side effects
Decrease initial costs	Living with an untreated cancer increases anxiety Must carry out frequent medical examinations and biopsies Timing and value of long-term natural history of untreated disease is undetermined Long-term natural history of untreated disease is uncertain
Source: [126]	*Table 8*

The NCCN Panel recommends active surveillance for all men with very-low-risk prostate cancer and a life expectancy of less than 20 years and believes that surveillance should be considered for men with very-low-risk prostate cancer and a life expectancy of 20 years or more [126]. In addition, the Panel recommends active surveillance for all men with low- and favorable intermediate-risk prostate cancer and a life expectancy of less than 20 years and believes that it should be considered for men with low- and favorable intermediate-risk and a life expectancy of 10 years or more [126]. With active surveillance, recommended monitoring is measurement of a PSA level no more than every 6 months, unless clinically indicated, and a DRE and repeat biopsy no more than every 12 months [126].

Radiation Therapy

Radiation therapy is an option for men at various levels of risk for biochemical recurrence, except for men for whom active surveillance is recommended [126]. Radiation to pelvic lymph nodes may be considered for men with intermediate risk and should be done for men at high risk [126]. Radiation therapy offers progression-free survival similar to that of prostatectomy while avoiding the complications associated with surgery [126].

The advent of three-dimensional (3D) CRT, which integrates external-beam radiation with CT images, has allowed for the delivery of higher radiation doses but with a lower risk of side effects because of enhanced precision [126]. About half of men will have temporary bladder or bowel symptoms during treatment with external-beam radiation therapy [126]. The disadvantage to external-beam radiation therapy is the time needed for treatment, as the recommended duration of treatment is eight to nine weeks [126].

Intensity-modulated radiation therapy (IMRT), a second-generation 3D technique, has been used increasingly in clinical practice [141]. IMRT reduced the risk of gastrointestinal toxicities and rates of salvage therapy compared with 3D-CRT in some retrospective, population-based studies, but treatment cost was increased [142; 143]. More recently, moderately hypofractionated image-guided IMRT regimens have been tested in randomized trials, but additional research is needed [126].

Brachytherapy has been used increasingly for men with early localized prostate cancer; however, increasing evidence suggests that technical advancements in brachytherapy may have a role in treatment of high-risk localized and locally

advanced prostate cancer [126; 144; 145]. This approach is a recommended option as monotherapy for men at low risk and a life expectancy of at least 10 years and in combination with external-beam radiation therapy for men at intermediate risk, regardless of life expectancy [126; 146]. Complications are increased when the two forms of radiation therapy are used together [126]. Brachytherapy alone yields control rates comparable to those of surgery (approximately 90%), and added advantages are short treatment duration, minimal risk of incontinence, and short-term preservation of erectile function; the seeds are implanted in one procedure, and men typically recover in one day [126]. Disadvantages include the need for general anesthesia and a risk of acute urinary retention [126].

Radical Prostatectomy

Radical prostatectomy is an option for men with a life expectancy of at least 10 years who have clinically localized disease that can be completely excised [126]. It also may be an option for men with high-risk disease and for select patients with very-high-risk disease, although several factors (e.g., PSA >10 ng/mL, stage T2b or higher, Gleason score 9 or 10, higher number of biopsy cores with high-grade cancer, more than 50% core involvement) predict unfavorable outcome in these patients [147]. Radical prostatectomy is a salvage option for patients experiencing biochemical recurrence after primary external beam radiation therapy, but morbidity remains significantly higher than when the treatment is used as initial therapy [148; 149]. This treatment option has been most often associated with the highest survival rates but also with side effects that have been reported to have a significant impact on quality of life, such as impotence, incontinence, urethral stricture, and surgery-related morbidity [126; 150; 151]. Despite the potential side effects, the sense of being cancer free has led men who chose to have radical prostatectomy to be satisfied with their decision [152]. Laparoscopic and robot-assisted procedures have been found to yield results similar to those for open procedures, but rates of incontinence and erectile dysfunction may be higher [126]. The AUA notes that no conclusive benefit to pelvic lymph node dissection has been found [127]. Such dissection for clinically localized disease may not be necessary if the PSA is less than 10 ng/nL and the Gleason score ≤6 [127].

Androgen Deprivation Therapy (ADT)

ADT involves medical or surgical castration (with luteinizing hormone-releasing hormone [LHRH] agonists or orchiectomy, respectively). It is recommended as an adjunct to radiation therapy or prostatectomy for men with local or locally advanced disease and at high or intermediate risk for recurrence [126]. Meta-analyses have shown clinical benefit for adjuvant ADT after either radiation therapy or prostatectomy or neoadjuvant therapy before radiation therapy [153; 154].

Both NCCN and ASCO recommend ADT as initial treatment for metastatic prostate cancer [126; 155]. Researchers have evaluated the timing of ADT—early (before symptoms occur) or delayed—and early therapy has provided no overall survival benefit and only a modest decrease in risk for prostate cancer-specific mortality; because of this, the ASCO guideline does not make a recommendation for early ADT [155]. Several studies have demonstrated that intermittent ADT is as effective as continuous ADT for metastatic or locally advanced disease, with better quality of life and fewer side effects [156; 157; 158].

Use of ADT as a primary therapy for men with localized prostate cancer has increased significantly among men at low and intermediate risk, but this approach should not be considered standard [126; 146]. ADT is associated with several adverse events, including osteoporosis, increased risk for fracture, obesity, insulin resistance, and increased risk for cardiovascular disease and diabetes [126].

Chemotherapy

The use of chemotherapy is typically reserved for men with metastatic castration-resistant prostate cancer, and docetaxel-based regimens have been shown to confer survival benefit [159; 160]. The duration of therapy is not well-defined, but 10 cycles were used in the phase III trials in which these regimens were evaluated.

Cryosurgery

Cryosurgery is a minimally invasive procedure that is an option for prostate cancer (of any grade) that is clinically confined to the prostate in men at low, intermediate, or high risk [161]. The five-year biochemical disease-free survival rates have ranged from 48% to 92%, depending on the risk of recurrence, but long-term data on prostate cancer-specific survival are not yet available and there are no clearly defined guidelines for patient selection for cryosurgery as a salvage procedure [161]. The authors of a meta-analysis published in 2007 and updated in 2018 concluded that it was difficult to determine the relative benefits of this treatment because of the poor quality of the available studies [162].

Options for Metastatic Castration-Resistant Prostate Cancer

Since 2010, three agents, an immunotherapy, and a radiopharmaceutical have been approved for metastatic castration-resistant prostate cancer. Cabazitaxel (Jevtana), enzalutamide (Xtandi), and abiraterone acetate (Zytiga) are indicated for treatment following docetaxel [126]. Sipuleucel-T (Provenge), an autologous cellular immunotherapy, is approved for men with metastatic castration-resistant prostate cancer who are asymptomatic or minimally symptomatic. Lastly, radium 223 dichloride (Xofigo) was approved in May 2013 for the treatment of metastatic castration-resistant prostate cancer with bone metastases (but not visceral involvement) [126].

Prognosis

Survival after treatment of prostate cancer is related to the extent of the tumor at the time of diagnosis, and the relative five-year survival rate is 100% for localized or regional prostate cancer [16]. The five-year survival rate is substantially lower (30%) when prostate cancer is metastatic at the time of diagnosis [16].

Follow-up

Primary care physicians, nurses, and other health-care professionals who see patients on a regular basis play an important role in the follow-up evaluation for men who opt for active surveillance, as well as for those who have been treated by an oncologist. After treatment for prostate cancer, men should be followed up with an annual DRE and PSA testing every 6 to 12 months for five years and annually thereafter [163]. Primary care clinicians can also aid in the management of the side effects of treatment and screening for secondary cancers.

Case Study

Patient A is an active man, 59 years of age, who missed his yearly DRE and PSA. The results of these tests had been within normal limits in all previous examinations. At his next examination, a firm prostate nodule, approximately 2 mm in diameter, is palpated, and the PSA level is 14 ng/mL. A needle biopsy of the prostate is performed within one week of the PSA measurement. The biopsy shows several sites containing cells indicative of adenocarcinoma of the prostate, with a Gleason score of between 8 and 9.

After carefully evaluating the treatment options for an aggressive tumor, Patient A chooses radical prostatectomy and seeks care at an institution where nerve-sparing surgery is performed with the assistance of a robotic, computer-controlled device, to help reduce the risk of adverse events. According to the pathologic evaluation, the tumor is an adenocarcinoma that has extended beyond the capsule of the gland but has not involved the seminal vesicles.

Staging studies, including an MRI of the pelvis and abdomen and a bone scan, confirm the extent of the tumor and demonstrate lack of lymph node involvement or distant metastasis (T3a, N0, M0). Because of the T3a finding, a course of external-beam radiation therapy to the local site is prescribed.

At the three-month follow-up visit, the PSA level has increased to 20 ng/mL, and a bone scan demonstrates multiple skeletal lesions, primarily in the ribs, pelvis, and skull, none of which had been seen on the previous scan. Due to the rapid progression of disease and the metastatic lesions, the patient's survival is estimated to be less than three years.

After a discussion with his surgeon, oncologist, and urologist, the patient decides to forego ADT, choosing instead to enroll in a clinical trial for treatment consisting of chemotherapy with docetaxel in combination with the angiogenesis inhibitor bevacizumab over a course of several months. The treatment causes some nausea, malaise, and hair loss, but the patient tolerates the effects well. The primary bothersome adverse effect is oral ulcers, which require topical treatment. The PSA level drops steadily during follow-up, reaching a level of 0.4 ng/mL after approximately six months of treatment.

Patient A continues to feel well after two years of follow-up, and the PSA level has remained at 0.2 ng/mL or less. Incontinence that was present after the surgery has ended, but erectile dysfunction remains, despite the use of medications.

DISEASES AND CONDITIONS OF THE TESTES

Testicular conditions are fairly uncommon but are more prevalent among younger men than older men [164; 165]. As with conditions of the prostate, testicular conditions may be associated with similar symptoms, creating a challenge for accurate diagnosis. When evaluating a man who has acute scrotal pain, a primary objective is to distinguish benign conditions from those requiring immediate intervention and from testicular cancer.

TESTICULAR TORSION

Testicular torsion occurs in approximately one in 4,000 male individuals younger than 25 years of age each year [164]. In 90% of cases, intravaginal torsion is caused by a congenital malformation of the processus vaginalis [164]. Predisposing factors include increased testicular volume, testicles with horizontal lie, history of cryptorchidism, and a spermatic cord with a long intrascrotal portion [166]. Surgery to repair the torsion is necessary to save the testicle; thus, early diagnosis is critical [164; 165].

The most common misdiagnosis of testicular torsion is epididymitis [164; 167]. The first step should be to determine the onset of pain, as testicular torsion is associated with pain of sudden onset; in contrast, the onset of pain is insidious in epididymitis and other conditions [164; 165]. The physical examination also plays an important role in distinguishing testicular torsion from epididymitis. A key distinction is the absence of the cremasteric reflex in testicular torsion, which has been found to have a sensitivity of at least 99% in two studies of boys [167; 168]. To elicit this reflex, the medial thigh is stroked or pinched, which causes contraction of the cremaster muscle and elevation of the testis. If the testicle moves at least 0.5 cm, the reflex is positive [164]. Other distinguishing features include the area of tenderness, appearance of the scrotum, and testicular lie (***Table 9***) [164; 165; 167; 168].

If the diagnosis of testicular torsion is still in question after physical examination or if the onset of pain was 6 to 12 hours previously, color Doppler ultrasonography should be carried out [164; 165]. This imaging study has been found to have a sensitivity of 88% and a specificity of 90% in detecting testicular torsion in boys [169]. Decreased or absent blood flow and rotation of the spermatic cord on the affected side are indicators of testicular torsion [164; 166]. Scintigraphy with technetium 99m pertechnetate has a higher sensitivity, but this modality is not as readily available as ultrasonography in some institutions [164; 170].

DISTINGUISHING BETWEEN TESTICULAR TORSION AND EPIDIDYMITIS		
Sign/Symptom	**Testicular Torsion**	**Epididymitis**
Onset of pain	Sudden (<12 hours)	Insidious
Cremasteric reflex	Absent	Present
Tenderness	Diffuse; spermatic cord	Epididymal area
Appearance of scrotum	Usually normal	Edematous, "orange peel" appearance
Testicular lie	High	Normal
Source: [164; 165; 167; 168]		*Table 9*

A diagnosis of testicular torsion, whether highly suspected or definitive, requires immediate surgical intervention, and a surgical consultation should be obtained [164; 165]. The success rate for manual detorsion has been low (approximately 26%), so this procedure should be avoided as an alternative to surgical treatment [164; 171].

EPIDIDYMITIS

Inflammation of the epididymis affects a small proportion of men. Few epidemiologic studies are available, but the prevalence has been estimated to be approximately 0.29% to 0.9% and is the same across racial/ethnic populations [172]. Acute epididymitis is usually caused by bacterial infection, and the source of the infection varies. For men who are younger than 35 years of age and sexually active, the source is most commonly an STI. The most frequently identified micro-organisms are *C. trachomatis* and *Neisseria gonorrhoeae* [57; 173]. The diagnosis and treatment of epididymitis caused by STIs are discussed later in this course.

Among men who are older than 40 years of age, epididymitis is usually associated with bacterial infection of the urinary tract. Epididymitis has also been reported as a side effect of the drug amiodarone, used for ventricular arrhythmias [174]. A review of the literature indicated that the time to onset of the condition ranged from 4 to 71 months and developed at a daily dose of 200 to 800 mg [174; 175]. In many cases, there is no known etiology [176]. When pain, swelling, and/or inflammation persist for more than three months, the condition is considered to be chronic.

Men with acute epididymitis usually present with unilateral pain and tenderness in the testicle [173]. Additional symptoms include dysuria, urinary frequency or urgency, and symptoms related to the source of infection (e.g., fever, chills, or pain). Urinalysis and urine culture should be done to determine the presence of infection [175; 176].

Obtaining a careful history is an important first step in the diagnosis of epididymitis. The practitioner should ask about the sexual history; surgical history, especially in the scrotal area; the location, severity, and frequency of pain; and the presence and duration of symptoms [176]. When symptoms have been present for three months or longer, the Chronic Epididymitis Symptom Index can help determine the impact of symptoms on the quality of life [176].

As stated previously, several findings on physical examination can distinguish epididymitis from testicular torsion [164; 165; 167; 168]. The physical examination should also include evaluation of the abdomen, especially to check for tenderness in the flank and bladder distention, and the inguinal regions [165]. Examination of the scrotum should be carried out bilaterally, assessing the degree of swelling, presence of erythema, and differences in size [165].

Acute infectious epididymitis is treated by addressing the underlying infection, and antibiotics should be chosen according to the causal micro-organism. Symptomatic relief for both infectious and noninfectious epididymitis can be achieved with bed rest, scrotal support and elevation, ice packs, and anti-

inflammatory agents or analgesics. If tenderness or swelling persists after treatment with antibiotics or if a mass becomes palpable, further evaluation should be carried out to rule out testicular cancer [173; 177]. Watchful waiting is suggested for chronic epididymitis [176].

Consultation with a urologist may be appropriate for men with complications or with chronic epididymitis [173]. Scrotal exploration may be necessary if abscess, testicular infarction, or pyocele develops. Epididymectomy has been used to treat chronic epididymitis, but the outcomes have varied widely [176].

VARICOCELE

A varicocele is a dilated, tortuous inflammation of the veins of the spermatic cord above the testicle. A prevailing thought has been that the superior mesenteric artery compresses the left renal vein over the aorta, also known as the "nutcracker effect" [178]. This theory has been confirmed by studies that have shown that varicoceles are less common in obese men [178; 179]. It has also been suggested that the condition is caused by damage to the contractile mechanism of the smooth muscle organization of spermatic veins [180]. As a result of anatomic differences, the condition is more common in the left testicle, but advances in imaging have led to reports of high rates of bilaterality [181]. Varicocele can cause discomfort in the scrotal area, but usually the condition is asymptomatic [165].

The frequency of varicocele among adolescents and young adults is approximately 15% to 20%, and the rate is higher among men who have some level of infertility, with reports of 77% and 81% in some studies [181; 182]. A study of older men (mean age: 60.7 years) demonstrated a prevalence of 42% [183].

Varicoceles vary in size, and large ones can be identified through physical examination alone. Varicoceles can have an adverse effect on spermatogenesis, and infertility has been associated with varicoceles that can be palpated [182]. The most significant finding is a feeling of a "bag of worms" when the scrotum is palpated [165; 182]. The varicocele may disappear or be substantially reduced when the patient is recumbent [182]. Smaller varicoceles can be detected by asking the patient to perform the Valsalva maneuver in the standing position [182]. In older men (at least 60 years of age), varicoceles have been associated with significantly smaller and soft testes [183]. Color Doppler ultrasonography is the diagnostic procedure of choice when the findings of the clinical examination are inconclusive [182].

The treatment of varicocele depends on several factors, including the age of the patient, the size of the varicocele, the results of semen analyses, and the patient's desire for fertility [182]. Varicoceles in adolescents and young adults have been associated with significant loss of testicular volume and growth arrest of the testes, the risk of which increases with the size of the varicocele [184; 185]. These individuals should be monitored with physical examination and semen analyses to detect changes in testicular function, as earlier treatment will increase the likelihood of recovering normal spermatogenetic function [182; 186]. Advances in minimally invasive procedures and surgeries have led to significant strides in the management of symptomatic varicoceles [187]. Many experts agree that indications for surgical intervention in adolescents are pain, large varicoceles, hypotrophy of the involved testicle, bilateral varicocele, intratesticular varicocele, and abnormal semen parameters on serial evaluation. The ideal method for treating adolescent varicocele has not been clearly established, but the main task is to decrease the number of recurrences and complications while retaining optimum testicular function. Because of this, many surgeons respect the attitude "catch-up growth" [188]. Treatment approaches and outcomes of therapy are discussed more fully in the section on infertility.

The European Association of Urology recommends treating varicoceles in men with a clinical varicocele, oligospermia, and otherwise unexplained infertility in the couple.

(https://uroweb.org/wp-content/uploads/EAU-Guidelines-Male-Infertility-2016-2.pdf. Last accessed June 12, 2019.)

Strength of Recommendation/Level of Evidence: A/1a (Consistent systematic reviews of randomized controlled trials)

TESTICULAR CANCER

Testicular cancers are primarily germ cell tumors and are classified as seminomas and nonseminomas, the latter type being more clinically aggressive [177]. Testicular cancer is rare, accounting for approximately 1% of all malignant tumors [177]. However, the worldwide incidence of this type of cancer has been increasing in the past six decades [177]. As with other testicular conditions, this cancer is most common among male individuals 20 to 34 years of age [177; 189]. Early detection results in a cure rate of approximately 95% [177].

Prevalence

As noted, testicular cancer is rare. In 2019, there will be an estimated 9,560 new cases of testicular cancer diagnosed in the United States and an estimated 410 deaths [190]. According to 1975–2016 SEER data, the prevalence is highest among non-Hispanic white men (7.5 per 100,000), followed by American Indian/Alaska Native and Hispanic men (5.2 per 100,000), Asian/Pacific Islander men (2.2 per 100,000), and black men (1.6 per 100,000) [191].

Etiology

Among the several risk factors for testicular cancer, the primary one is cryptorchidism, which can increase the risk 11-fold [177]. Other risk factors include a family history of the disease, testicular dysgenesis, and Klinefelter syndrome [177]. A history of cancer in one testicle confers an increased risk (2% to 5%) of cancer in the contralateral testicle over the 25 years following diagnosis [192].

Screening

The USPSTF does not recommend routine screening for testicular cancer—by either clinician examination or self-examination—for asymptomatic adolescent and adult male individuals, as there is no evidence that screening reduces mortality [193]. The USPSTF notes that instead of screening, men should be advised to report testicular problems promptly, as cure rates are high for any stage of testicular cancer [193].

The Scottish Intercollegiate Guidelines Network recommends that patients with suspected testicular malignancy (i.e., a lump in the testis, doubtful epididymo-orchitis or orchitis, not resolving within two to three weeks) should be referred urgently for urologic assessment.

(https://www.sign.ac.uk/assets/sign124.pdf. Last accessed December 11, 2018.)

Level of Evidence: D (Evidence from non-analytic studies or expert opinion)

Diagnosis

Most often, testicular cancer presents as discomfort or swelling in the testicles that is suggestive of epididymitis or orchitis [177]. Physical examination will demonstrate a palpable mass [177]. Occasionally, the patient may note tender or swollen breasts or loss of sex drive.

According to the NCCN guideline for the treatment of testicular cancer, testicular ultrasonography is optional if a diagnosis is obvious from the physical examination, but the guideline notes that this diagnostic test is usually done to define the lesion [177]. Both the NCCN and ASCO recommend measuring serum levels of alpha-fetoprotein (AFP), human chorionic gonadotropin (beta-hCG), and lactate dehydrogenase (LDH) to help determine if the testicular mass is a germ cell tumor and, if so, whether it is a seminoma or a nonseminoma [177; 194]. A nonseminoma is associated with an elevated AFP level; in contrast, an elevated level of beta-hCG, with a normal AFP level, usually indicates a seminoma [177].

Additional evaluation should include a chest x-ray and CT of the abdomen and pelvis to determine if lymph nodes are involved [177]. If metastatic disease is suspected, further imaging studies, such as bone scan, magnetic resonance imaging, or positron emission tomography, may be necessary. Open biopsy is not usually performed [177].

Treatment Options

Men with suspected testicular cancer should be referred to an oncologist who will discuss treatment options, which include orchiectomy and radiation therapy or chemotherapy, depending on the type of tumor and the stage of disease. Lymph node dissection may also be necessary for metastatic disease. The possibility of sperm banking should be discussed before any type of treatment is initiated [177].

Treatment options for early stage seminoma (stage I, confined to the testicle and epididymis) are active surveillance (preferred), single-agent carboplatin (one or two cycles), or radiation therapy [177].

Radiation therapy is recommended for stage II seminoma (involvement of nearby lymph nodes), with the treated area extended to include the ipsilateral iliac lymph nodes [177]. If radiation is contraindicated, chemotherapy with three cycles of bleomycin, etoposide, and cisplatin (BEP) or four cycles of etoposide and cisplatin (EP) is recommended. If chemotherapy is given, both regimens are recommended [177]. Chemotherapy with EP or BEP is recommended for stage III seminoma (involvement of distant lymph nodes and/or viscera) [177].

Treatment options for nonseminoma include surveillance, chemotherapy, and retroperitoneal lymph node dissection [177]. Selecting the appropriate therapy involves consideration of many factors, including the extent of disease in the lymph nodes, the levels of serum tumor markers before and during treatment, radiographic findings, and the commitment of the patient to adhere to surveillance protocols that involve frequent blood work and CT [177]. Chemotherapy involves either EP or BEP [177].

The cure rates for testicular cancer are high, even when cancer is at an advanced stage at the time of diagnosis [177]. The overall five-year survival for testicular cancer (all stages) is 95.2% [190].

Follow-Up

Men who have been treated for testicular cancer should be followed up at regular intervals to monitor for signs of recurrence. Follow-up visits typically include a history and physical examination and serum tumor markers. The ASCO guideline on the serum tumor markers for male individuals with germ cell tumors notes that there is insufficient evidence to determine whether monitoring tumor markers improves survival or health outcomes but nonetheless recommends measuring AFP and beta-hCG levels during each surveillance visit, and the NCCN also recommends an LDH as part of surveillance [194]. Evidence is also lacking regarding optimal surveillance intervals, and the intervals vary according to diagnosis (seminoma or nonseminoma) and stage of disease [177]. In general, the recommended intervals are every two months in the first year, every three months in the second year, every six months in the third and fourth years, and annually thereafter [177]. It is recommended that surveillance continue for at least 10 years [177; 194]. Chest x-ray and computed tomography of the abdomen and pelvis are recommended at greater intervals [177].

The follow-up evaluation plays an important role in assessing for the long-term effects of treatment. The primary effect of chemotherapy is oligospermia, but sperm production can be recovered [195; 196]. A population-based study found that 70% of testicular cancer survivors fathered children [197]. Secondary acute leukemias have been reported to develop after chemotherapy and radiation therapy, and other consequences of platinum-based chemotherapy include hearing deficits and impaired renal function [198; 199]. Melanomas and cancers at many sites have been associated with radiation therapy, occurring 10 years or more after treatment [198]. Lastly, the risk of cardiac events has been increased for testicular cancer survivors who had been treated with radiation therapy and/or chemotherapy [200].

MALE BREAST CANCER

Breast cancer in men is rare; an estimated 2,670 new cases were diagnosed in the United States in 2019, and an estimated 500 men died of the disease [16]. These figures represent less than 1% of all breast cancer diagnosed in this country. Although the numbers are low, the prevalence has increased 26% since the early 1980s, prompting increased attention and highlighting the need to emphasize to men—and their healthcare providers—that breast cancer is not confined to women [201]. The lack of awareness of the disease has led to a longer time between the development of symptoms and diagnosis and to a later age (mean age: 67 years) and stage of disease at the time of diagnosis compared with women [201; 202].

Male breast cancer has not been extensively studied, and research is difficult because of the small numbers of men with the disease. Reviews of the literature have been helpful in identifying risk factors, clinical and pathologic characteristics, and the role of genetics [201; 202; 203]. Studies have shown that male breast cancer differs from female breast cancer in many ways. For example, some risk factors unique to men include the following [203]:

- Undescended testes
- Orchiectomy
- Infertility
- Gynecomastia
- Mastitis
- Breast trauma
- Infertility
- Klinefelter syndrome
- Radiation to the chest wall

BRCA2 mutation is found in approximately 4% to 16% of men with breast cancer [203].

A painless subareolar lump or swelling is the most common presenting symptom, occurring in approximately 85% of men with breast cancer [201; 204]. Other common symptoms are nipple retraction, localized pain, or nipple ulceration, bleeding, or discharge. About 1% to 2% of men will have no symptoms [201; 204]. In diagnosing male breast cancer, the primary consideration is to distinguish cancer from gynecomastia, which is present in about 30% of healthy men [202].

The approach to the diagnostic evaluation of male breast cancer is the same as for female breast cancer. A history and physical examination will help determine potential risk factors and identify the clinical features. Mammography has good sensitivity and specificity, and ultrasonography may be useful, especially for detecting involvement of the lymph nodes [202]. Biopsy is essential for elucidating the pathologic characteristics. In male breast cancers, the overexpression of estrogen receptor and progesterone receptors is likely [203; 205].

As noted, data on male breast cancer are limited, and recommendations for treatment have been extrapolated from the literature on female breast cancer and from small series of men with the disease. Modified radical mastectomy is used most often, with lumpectomy rarely performed [203]. Sentinel node biopsy has also been effective in men [206; 207]. Adjuvant radiation therapy has been associated with a lower local recurrence rate and a higher survival rate [202; 203]. Adjuvant chemotherapy has been carried out according to guidelines for women at high risk for recurrence. Adjuvant hormone therapy has a clear role in the treatment of men with hormone receptor-positive cancer, with reductions in recurrence and death [204; 208]. In addition, tamoxifen has led to a 50% response rate for metastatic breast cancer [202].

Five-year survival rates for men with breast cancer have been reported to be between 40% and 65% [201; 202]. In one retrospective study, the median survival was 87 months (83 months for men with invasive disease) [203]. Older age, higher stage of disease, and increasing tumor size have been associated with shorter survival [203]. The risk of second cancers (breast and nonbreast) appears to be high [209].

MALE SEXUAL HEALTH

Sexual dysfunction affects more than a quarter of men, yet attention to sexual health is low because of the lack of validated evidence-based guidelines for diagnosis and treatment as well as men's hesitancy to discuss sexual health issues with their primary healthcare providers [210; 211]. Clinicians should include questions about sexual function in routine health evaluations and foster an environment of trust and open dialogue to help elicit information on sexual health from their male patients.

Issues related to sexual health change over the course of a man's lifetime. Early ejaculation is of concern to men across the ages, erectile dysfunction and late-onset hypogonadism are of special concern to older men, and infertility and STIs are more common issues among younger men.

PREMATURE EJACULATION

As defined by the AUA, premature ejaculation is "ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners" [212]. This definition and others have not been evidence based, however, and the International Society of Sexual Medicine charged a panel of experts with developing an evidence-based definition. According to this definition, premature ejaculation is "a male sexual dysfunction characterized by ejaculation which always or nearly always occurs prior to or within about one minute of vaginal penetration, and the inability to delay ejaculation on all or nearly all vaginal penetrations, and negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy" [213]. The definition is limited to men with lifelong premature ejaculation who have vaginal intercourse. Some have called for the condition to be called "early" ejaculation as a more accurate description of the condition [214].

Premature ejaculation is thought to be the most common sexual disorder among men, and the condition is associated with a high rate of psychosocial distress and has a substantial impact on men's relationships with their partners [215; 216].

Prevalence

The reported prevalence of premature ejaculation in the United States has varied widely, ranging from 5% to 40%, depending primarily on the definition [210; 212]. The highest prevalence is found among men who are 60 years or age or older [214].

Diagnosis

No diagnostic criteria have been established for premature ejaculation, and an AUA guideline recommends that the condition be diagnosed on the basis of the sexual history alone; laboratory studies or physiologic testing is needed only if the history or physical examination suggests a complex cause [212]. Among the details to be elicited from the history are [212]:

- Frequency and duration of premature ejaculation
- Relationship of premature ejaculation to specific partners
- Degree of stimulus resulting in premature ejaculation
- Nature and frequency of sexual activity (foreplay, masturbation, intercourse, use of visual cues)
- Impact of premature ejaculation on sexual activity
- Types and quality of personal relationships and quality of life
- Aggravating or alleviating factors
- Relationship to drug use or misuse

The patient's partner may be helpful in providing a description of the problem, and care should be taken to distinguish premature ejaculation from erectile dysfunction [212]. The AUA recommends that, for men with concomitant premature ejaculation and erectile dysfunction, erectile dysfunction should be treated first [212].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Male Training Center for Family Planning and Reproductive Health, asking men about problems with sexual function is particularly important to identify underlying cardiovascular disease among men who present with symptoms of sexual dysfunction routinely starting at 25 years of age. Specific questions include if the man is experiencing sexual dysfunction such as inability to obtain and maintain an adequate erection for satisfactory sexual activity (impotence, erectile dysfunction), premature or delayed ejaculation, loss of libido, painful intercourse, and also priapism, a prolonged painful erection not associated with sexual desire.

(https://www.guidelinecentral.com/summaries/preventive-male-sexual-and-reproductive-health-care-recommendations-for-clinical-practice. Last accessed June 12, 2019.)

Level of Evidence: Expert Opinion/Consensus Statement

Treatment Options

The treatment approaches for premature ejaculation include psychologic, behavioral, and pharmacologic therapies, and the risks and benefits of all options should be discussed with the patient and, when possible, his partner [212]. Behavioral therapy was once considered to be the standard therapy, but studies have shown that the best approach may involve a combination of therapies to address the limitations of each approach as well as the multimodal causes of premature ejaculation [210; 217; 218].

No medication has been approved for the treatment of premature ejaculation, leaving the pharmacologic treatment to involve the off-label use of serotonin reuptake inhibitors or topical anesthetics [210; 212; 218; 219]. The nonselective serotonin reuptake inhibitor clomipramine and the selective serotonin reuptake inhibitors fluoxetine, paroxetine, and sertraline are recommended by the AUA as treatment to prolong the latency of ejaculation [212]. The doses studied have varied, and dosing is prescribed as either continuous (daily regimen) or situational (taken only before sexual activity); the optimal duration of therapy has not been determined (***Table 10***) [212]. The side effects of these drugs have not been evaluated outside the depression setting, but the effects appear to be similar for men who are not using the drug for depression, with the most common effects being nausea, dry mouth, and drowsiness [212].

Treatment with topical lidocaine/prilocaine has also been shown to be effective in increasing the latency of ejaculation and is another option recommended by the AUA [212; 220; 221]. The drug is typically applied 20 to 30 minutes before sexual activity; earlier application (30 to 45 minutes prior to sexual activity) has led to numbness of the penis and loss of erection in a substantial number of men [221]. Topical treatment avoids adverse events associated with systemic therapy [222]. In 2016, the European Union approved a topical eutectic lidocaine/prilocaine metered-dose spray (Fortacin) for use in the treatment of primary premature ejaculation [223; 224]. The spray has not been approved for this use in the United States [225].

One drug, dapoxetine, a short-acting selective serotonin reuptake inhibitor, is the first drug developed specifically for premature ejaculation, and it has been approved for use in several European countries, but not in the United States or Canada [222]. Several studies and systematic reviews have shown dapoxetine to substantially improve (compared with placebo) intravaginal ejaculatory latency time, perceived control, and patient-reported global impression of change and decrease related personal distress and difficulty [222; 226; 227; 228]. However, the agent is characterized by discontinuation rates of up to 90%, primarily due to side effects, cost issues, efficacy below expectations, and the need for scheduling sexual intercourse [224]. The most common side effects have been nausea, dizziness, diarrhea, insomnia, and headache.

Psychologic and behavioral therapies are valuable components of treatment [210; 217; 218]. Relationship counseling and sex therapy can help facilitate communication between the patient and his partner and ease tension surrounding sexual activity.

AUA RECOMMENDED PHARMACOLOGIC THERAPY OPTIONS FOR PREMATURE EJACULATION		
Agent	**Daily Dose[a]**	**Pre-Intercourse Dose**
Nonselective serotonin reuptake inhibitor		
Clomipramine (Anafranil)	25–50 mg	25 mg (4 to 24 hours prior to sexual activity)
Selective serotonin reuptake inhibitors		
Fluoxetine (Prozac)	5–20 mg	—
Paroxetine (Paxil)	10 mg, 20 mg, or 40 mg	20 mg (3 to 4 hours prior to sexual activity)
Sertraline (Zoloft)	25–200 mg	50 mg (4 to 8 hours prior to sexual activity)
Topical agent		
Lidocaine/prilocaine cream (EMLA cream)	—	Lidocaine 2.5%/prilocaine 2.5% (20 to 30 minutes prior to sexual activity)
[a]The lowest dose should be used when beginning therapy, with upward titration based on response.		
Source: [212]		*Table 10*

Psychologic and behavioral therapies should focus on gaining confidence, learning control techniques, lessening performance anxiety, overcoming barriers to intimacy, achieving pleasure, and gaining satisfaction [210; 217].

ERECTILE DYSFUNCTION

Erectile dysfunction is primarily a vascular disorder, but hormonal, neurologic, and psychologic factors are also involved. Approximately 70% of cases of erectile dysfunction are organic and not of psychologic origin [229]. The condition is defined as an inability to maintain an erection sufficient for sexual intercourse [230]. The term erectile dysfunction has come to replace "impotence" to more accurately describe a condition that is not associated with a loss of sexual desire or problems with ejaculation or orgasm [230].

Prevalence

Erectile dysfunction is estimated to affect more than 150 million men worldwide [231]. The prevalence has ranged from 10% to 30% among men 40 to 49 years of age and from 25% to 76% among men older than 70 years of age [232; 233; 234]. Ethnicity has also been a factor, with a higher rate for black men and a lower rate for Hispanic men compared with white men [232]. However, another study showed that Hispanic men were more likely to report erectile dysfunction [234].

Erectile dysfunction has been reported to be more common among men with comorbidities, and the strongest associations have been found for metabolic syndrome, cardiovascular disease, and diabetes [214; 234; 235]. Among men with no known cardiovascular disease, erectile dysfunction has preceded coronary artery disease, stroke, and peripheral artery disease by an average of three years (range: two to five years) [236]. In addition, a meta-analysis (14 cohort studies; 92,757 men) showed that erectile dysfunction was an independent risk factor for cardiovascular and cerebrovascular events [237]. Other risk factors for erectile dysfunction include hormone disorders, neurologic conditions, psychologic disorders, history of surgery or radiation in the pelvic region, use of illicit drugs, and some prescription drugs (most notably, antihypertension agents) [238]. Encouraging men with these risk factors to modify their lifestyle and/or treating comorbidities may help reduce the risk of erectile dysfunction [239].

Diagnosis

A detailed medical history is integral to diagnosing erectile dysfunction, as the history may elucidate an underlying cause. It is important to also document a psychosocial and sexual history to evaluate the potential of other related or contributing factors [230]. The physical examination should involve assessment of the abdomen, genitals, and pulses in the lower extremity [230].

Treatment Options

Erectile dysfunction is best managed with a combination approach [235]. Because of the strong relationship between erectile dysfunction and modifiable risk factors, lifestyle changes should be a first-line approach to managing the condition. The importance of achieving or maintaining a healthy body mass index, increasing exercise, and smoking cessation should be emphasized, especially given the relationship between erectile dysfunction and cardiovascular disease.

Both the AUA and the ACP recommend oral phosphodiesterase-5 inhibitors as first-line pharmacotherapy for erectile dysfunction in men for whom this class of drugs is not contraindicated [230; 231]. Three drugs in the class have been approved for use in the treatment of erectile dysfunction: sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra). Sildenafil and vardenafil differ from tadalafil with respect to the time to maximum serum level (1 hour vs. 2 hours) and serum half-life (4 hours vs. 18 hours) [230]. Furthermore, the duration of action is longest for tadalafil (up to 36 hours) [240].

The ACP's systematic review demonstrated that each of the three drugs substantially improves erectile function and successful sexual intercourse compared with placebo [231]. The ACP also noted that there was insufficient evidence to recommend one drug over another and suggested that the choice be made according to the preferences of an individual patient with respect to ease of use, cost, and the adverse effects profile [231]. Since the publication of that guideline, a meta-analysis has shown that tadalafil is the most effective agent, followed by vardenafil, with no major differences in the safety profile of any of the phosphodiesterase-5 inhibitors [241].

The side effects of all three drugs are similar, with headache, dyspepsia, facial flushing, nasal congestion, and visual disturbances being the most common events [230; 240; 242]. The FDA has issued two mandates to revise labeling of these agents. In 2005, the agency required the labels for all three of the drugs to reflect the possibility of sudden vision loss after taking the drugs for a period of time [243]. The alert was associated with several case reports that suggested a temporal association between use of one of the drugs and nonarteritic anterior ischemic optical neuropathy (NAION), a cause of irreversible vision loss [243]. However, subsequent studies showed that the risk of NAION was similar among men who were and were not taking a phosphodiesterase-5 inhibitor [244; 245]. Still, some researchers have suggested that an examination of the fundus be performed on men who may be at higher risk for NAION before a phosphodiesterase-5 inhibitor is prescribed [243].

In 2007, the FDA mandated changes to the labels of phosphodiasterase-5 inhibitors to more prominently display warnings about the potential for sudden hearing loss [246]. A cross-sectional population-based study of more than 11,000 men subsequently demonstrated a higher likelihood of self-reported hearing loss associated with use of any phosphodiasterase-5 inhibitor (odds ratio: 2.23), but the association was significant only for sildenafil [247].

Use of a phosphodiesterase-5 inhibitor is contraindicated in several situations. They should not be taken by men who take organic nitrates (nitroglycerin) or nitrites (amyl nitrite) [248; 249]. Vardenafil should not be used for men with a history of prolonged QT interval (or who take medication to prolong the QT interval) [230]. The use of a phosphodiesterase-5 inhibitor concomitantly with an alpha-blocker for lower urinary tract symptoms may lead to increased systemic vasodilation [230].

Men who are being treated with a phosphodiesterase-5 inhibitor should be followed up closely to monitor efficacy and side effects. Attention to changes in health status and other medications is essential to avoid drug interactions. Clinicians should emphasize the importance of men providing information about treatment with a phosphodiesterase-5 inhibitor in case of a cardiovascular emergency [230].

When treatment with a phosphodiesterase-5 inhibitor is ineffective, the clinician should discuss the risks and benefits of other options. The likelihood of another medication being effective is unclear [230]. Other, more invasive approaches may be successful but are associated with risks. For example, alprostadil may be given as an intraurethral suppository, but it should initially be given under close medical supervision because of a risk of syncope [230]. Intracavernous injection of a vasoactive drug is associated with the highest potential for priapism, and clinicians should ensure that men understand the correct technique and the importance of seeking medical intervention for a prolonged erection [230]. Vacuum constriction devices are associated with low patient acceptability, and only devices with a vacuum limiter should be recommended, in order to avoid high negative pressures [230]. The risks associated with penile prostheses include mechanical failure, erosion, and infection [230]. The AUA guideline does not recommend the use of trazodone, testosterone therapy (for men with normal serum levels), or yohimbine and other herbal therapies [230].

Psychosocial therapy is an important component of treatment for erectile dysfunction. A meta-analysis showed that group psychotherapy in combination with sildenafil significantly improved erectile function and successful sexual intercourse compared with sildenafil alone [250].

LATE-ONSET HYPOGONADISM

In both men and women, levels of sex hormones decline with age. However, the ways in which these levels change and the symptoms associated with the decline differ greatly between men and women. There is no well-defined equivalent of menopause in men, although the phrase "andropause" is used frequently to refer to decreased testosterone and resulting symptoms. Other phrases, most notably androgen deficiency syndrome and late-onset hypogonadism, may be more accurate descriptors of the process. By any name, the condition is a complex of symptoms that includes loss of sexual satisfaction and overall well-being [251]. The condition is related to lower testosterone levels, which begin to decrease 1% to 2% each year beginning at 30 years of age [252].

Late-onset hypogonadism is distinct from hypogonadism in younger male individuals. For boys and young men, hypogonadism is related to testicular failure and is usually associated with a congenital abnormality, most often Klinefelter syndrome [251]. In older men with hypogonadism, testosterone levels are rarely as low as the levels in young men with primary hypogonadism [251].

Several important questions about late-onset hypogonadism remain unanswered [252; 253]:

- It is unclear whether the symptoms are caused by a reduction in testosterone or are a result of the normal physiologic process of aging.
- There is no consistent level of testosterone to define hypogonadism, and there is confusion about what testosterone levels should be measured.
- There is ongoing debate about the risk-benefit ratio of testosterone therapy for older men.

SYMPTOMS AND SIGNS SUGGESTIVE OF TESTOSTERONE DEFICIENCY IN MEN	
Specific	Incomplete or delayed sexual development, eunuchoidism Loss of body (axillary and pubic) hair, reduced shaving Very small (especially <5 mL) or shrinking testes
Suggestive	Reduced sexual desire (libido) and activity Decreased spontaneous erections Breast discomfort, gynecomastia Inability to father children, low or zero sperm count Height loss, low trauma fracture, low bone mineral density Hot flushes, sweats
Nonspecific	Decreased energy, motivation, initiative, and self-confidence Feelings of sadness or being "blue," depressed mood, dysthymia Poor concentration and memory Sleep disturbance, increased sleepiness Mild unexplained anemia (normochromic, normocytic, in the female range) Reduced muscle bulk and strength Increased body fat, body mass index

Source: [Modified, with permission, from Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018;103(5):1715-1744.] *Table 11*

Prevalence

There is a wide range in the reported prevalence of late-onset hypogonadism. In a population-based observational study, symptomatic androgen deficiency was found in nearly 6% of men 30 to 79 years of age, whereas in the Hypogonadism in Males (HIM) study, the prevalence was nearly 39% among men 45 years of age and older visiting primary care practices [254; 255]. The prevalence increases substantially with age and is similar across racial/ethnic populations [254; 255].

Diagnosis

A diagnosis of late-onset hypogonadism requires both documentation of relevant symptoms and measurement of testosterone levels. The condition is associated with a variety of physiologic, psychologic, cognitive, and sexual symptoms; some signs and symptoms are more specific than others, and no combination of symptoms is typical (***Table 11***) [252; 255].

Diagnosing late-onset hypogonadism is challenging because many signs and symptoms are associated with the normal process of aging or can be attributed to coexisting conditions. Two questionnaires that can help to identify late-onset hypogonadism are the Androgen Deficiency in Aging Males (ADAM) questionnaire and the Aging Males' Symptoms (AMS) scale [256; 257; 258; 259; 260]. The ADAM questionnaire consists of 10 questions, and the condition is defined by a positive response to two specific questions: "Do you have a decrease in libido (sex drive)?" and "Are your erections less strong?" or to any three of the other questions [256]. The AMS scale asks men to provide a score of 1 to 5 to each of 17 somatic, psychologic, and sexual symptoms. The ADAM questionnaire has been validated against testosterone levels, whereas the AMS scale was designed to evaluate the quality of life and has not been correlated to testosterone levels [261]. Both have excellent specificity but poor sensitivity [251].

POTENTIAL BENEFITS AND RISKS OF TESTOSTERONE THERAPY	
Benefits	**Potential Risks**
Improvement in sexual desire and function	Stimulation of growth of prostate cancer
Increase in bone mineral density	Worsening of symptoms related to benign prostatic hypertrophy
Improvements in mood, energy, and quality of life	Liver toxicity and liver tumor
Change in body composition and improvement in muscle mass and strength	Gynecomastia
Improvement in cognitive function	Erythrocytosis Testicular atrophy and infertility Skin diseases Sleep apnea
Source: [262]	*Table 12*

In its updated practice guidelines on the treatment of androgen deficiency, the Endocrine Society recommends making a diagnosis of hypogonadism "in men with symptoms and signs of testosterone deficiency and unequivocally and consistently low serum testosterone and/or free testosterone concentrations (when indicated)" [252]. The testosterone level fluctuates from day to day and throughout the day, with peak serum concentrations in the morning. Therefore, clinicians should measure total testosterone concentrations on two separate mornings when the patient is fasting [252].

Treatment Options

The increase in treatment with testosterone has been tremendous. Although there are benefits of testosterone therapy, there are also many potential risks (***Table 12***), and the risk-benefit ratio for men with late-onset hypogonadism has not been clearly defined [255; 256; 261]. Because of questions about the benefits and harms of testosterone, the Endocrine Society is specific in its recommendations for testosterone therapy (***Table 13***) and recommends against a general policy of offering testosterone therapy to all older men with low testosterone levels [252].

Testosterone replacement is available in several forms, including oral agents, injectable formulations, transdermal gels and patches, and buccal tablets [252; 263]. In general, a decision on the type of therapy should be made according to the patient's preference, with consideration of several factors, including pharmacokinetics, cost, ease of use, and side effect profile [252; 263].

Follow-Up

Close follow-up is essential for men being treated with testosterone replacement. The clinical response and side effects should be monitored at intervals of three to six months [252]. The treatment target should be a testosterone level in the middle of the normal range [252]. Follow-up should include evaluation of the prostate, through determination of PSA levels and DRE at three to six months for men 40 years of age and older who have a baseline PSA greater than 0.6 ng/mL. In addition, a hematocrit level should be determined at three to six months and then annually; treatment should be discontinued if the hematocrit is greater than 54%.

RECOMMENDATIONS OF THE ENDOCRINE SOCIETY REGARDING TESTOSTERONE THERAPY FOR ADULT MEN WITH HYPOGONADISM	
Diagnosis and evaluation	*Recommendations* Make a diagnosis of hypogonadism only in men with symptoms and signs consistent with testosterone deficiency and unequivocally and consistently low serum testosterone levels and/or free testosterone concentrations (when indicated). Confirm diagnosis by repeating measurement of fasting morning total testosterone. Measure serum luteinizing hormone and follicle-stimulating hormone levels to distinguish between primary (testicular) and secondary (pituitary-hypothalamic) hypogonadism. *Suggestions* Perform further evaluation to identify the etiology of hypothalamic, pituitary, and/or testicular dysfunction in men with hypogonadism. Measure serum testosterone level in men who have specific clinical signs and symptoms and consider measuring serum testosterone level in men who report less specific signs and symptoms. Measure morning total testosterone level by a reliable assay as the initial diagnostic test. Measure free or bioavailable testosterone level, using an accurate and reliable assay, in men in whom total testosterone concentrations are near the lower limit of the normal range and in whom alterations of sex hormone-binding globulin are suspected. Do not evaluate androgen deficiency during an acute or subacute illness. Measure bone mineral density with use of dual-energy x-ray absorptiometry scanning in men with severe androgen deficiency or low trauma fracture.
Treatment	*Recommendations* Use testosterone therapy for men with hypogonadism to induce and maintain secondary sex characteristics and correct symptoms of testosterone deficiency. Do not use testosterone therapy for men planning fertility in the near term or in men with breast or prostate cancer. Do not use testosterone therapy without further urologic evaluation in men with palpable prostate nodule or induration or a prostate-specific antigen (PSA) level of 3 or 4 ng/mL in men at high risk of prostate cancer (e.g., black race, first-degree relative with prostate cancer). Do not use testosterone therapy for men with a hematocrit greater than 50%, untreated severe obstructive sleep apnea, severe lower urinary tract symptoms, or uncontrolled or poorly controlled heart failure, or in men with type 2 diabetes (as a means of glycemic control) who have low testosterone concentrations. *Suggestions* Initiate testosterone therapy with any of the following regimens, chosen on the basis of an individual man's preference, consideration of pharmacokinetics, treatment burden, and cost: • Testosterone enanthate or cypionate: 75–100 mg IM weekly, or 150–200 mg IM every two weeks • Testosterone patch (nongenital): 5 mg, one or two applied nightly over the skin of the back, thigh, or upper arm (away from pressure areas) • Testosterone gel (1%): 5–10 g applied daily over a covered area of nongenital skin • Testosterone bioadhesive buccal tablet: 30 mg applied to buccal mucosa every 12 hours • Testosterone pellets: SC every three to six months (dose and regimen vary with the formulation used) • Oral testosterone undecanoate, injectable testosterone undecanoate, testosterone-in-adhesive matrix patch, and testosterone pellets, where available Consider short-term testosterone therapy in men with HIV, low testosterone concentrations, and weight loss (when other causes of weight loss have been excluded) to induce and maintain body weight and lean mass gain. Do not routinely prescribe testosterone therapy to all men 65 years of age or older with low testosterone concentrations. Offer testosterone therapy on an individualized basis after discussing the risks/benefits with the patient.
Monitoring	*Recommendations* Evaluate the patient three to six months after the initiation of treatment and then annually. Determine hematocrit at baseline, at three to six months, and then annually. (Stop therapy if the hematocrit is higher than 54%.) Evaluate the patient for signs and symptoms of formulation-specific adverse events at each visit. Obtain a urologic consultation if there is any of the following: • Increase in serum or plasma PSA level >1.4 ng/mL within any 12-month period of testosterone treatment • PSA velocity >0.4 ng/mL/yr using the PSA level after 6 months of testosterone therapy as the reference (PSA velocity should be used only if there are longitudinal PSA data for more than two years.) • Detection of a prostatic abnormality on digital rectal examination • AUA/IPSS score >19 *Suggestions* Monitor testosterone levels three to six months after initiation of testosterone therapy, with an aim of achieving serum testosterone levels during treatment in the mid-normal range. (For men receiving testosterone enanthate or cypionate, the aim should be a testosterone level between 350 and 600 ng/dL at one week after the injection.) Repeat bone mineral density of the lumbar spine, femoral neck, and hip after one to two years of testosterone therapy in hypogonadal men with osteoporosis or low trauma fracture.
Screening	*Recommendation* Do not screen for hypogonadism in the general population.

Source: [252] *Table 13*

MALE INFERTILITY

Infertility is clinically defined as the inability to conceive after one year of unprotected intercourse [264]. Male infertility affects nearly 15% of couples; a male factor is the only cause in approximately 20% of infertile couples and is a contributing factor in another 20% to 40% [264]. Fertility declines with age, and research has shown that men older than 35 years of age are twice as likely to be infertile as men younger than 25 years of age [265; 266]. Approximately 15% of infertile men have azoospermia, the complete absence of sperm in the ejaculate [267].

Etiology

More than half of male infertility or subfertility is potentially correctable; often, the cause is unknown. The causes, both correctable and uncorrectable, include [264; 268]:

- Varicocele
- Obstruction of a duct (epididymal, vasal, or ejaculatory)
- Ejaculatory dysfunction
- Testicular atrophy
- Hypogonadotropic hypogonadism
- Infection
- Side effects of medication
- Environmental toxins
- Bilateral cryptorchidism
- Genetic abnormality (Y chromosome microdeletion)
- Congenital absence of vas deferens

Diagnosis

According to the AUA best practice statement on male infertility, the minimal evaluation of male infertility should include a complete medical and reproductive history, physical examination by a urologist or reproductive specialist, and at least two semen analyses [264]. It is important not to rely solely on semen analysis, as an underlying medical or genetic cause of infertility may be missed [268]. Other tests may be necessary, depending on the findings of this initial evaluation. For example, if azoospermia is demonstrated or there are signs suggestive of specific endocrinopathy, testosterone and follicle-stimulating hormone levels should be determined [267].

The medical history can help to detect an underlying cause of infertility. Factors that can affect fertility include [268]:

- Kallmann, Young, or Kartagener syndrome
- Pituitary disease
- Previous testicular disorders
- History of inguinal, scrotal, or retroperitoneal surgery
- Anticancer chemotherapy

The reproductive history should address the following issues: frequency and timing of intercourse, duration of fertility, use of lubricants, and sexual history (including STIs) [264; 267; 268].

Physical examination may identify a varicocele, the most common cause of infertility [165; 182]. Other findings on physical examination that may suggest a cause of infertility include small testes (less than 4 cm in greatest dimension or less than 20 cm^3), signs of ductal obstruction (induration or engorgement of the vas deferens or epididymis), and abnormal distribution of hair and fat, which may indicate endocrinopathy [268].

As noted, the semen analysis should be carried out on at least two specimens, obtained at least one month apart [264]. The specimens should be collected after two to three days of abstinence. The World Health Organization (WHO) first established reference values for semen analysis in 1987 and published its fifth update in 2010 [269]. In the 2010 WHO manual, the criteria for semen analysis on male infertility are [269; 270]:

- Semen volume: 1.5 mL
- Total sperm number: 39 million/ejaculate
- Sperm concentration: 15 million/mL

- Vitality: 58% live
- Total motility (progressive + nonprogressive): 40%
- Morphologically normal forms: 4.0%

The updated criteria met with controversy, with some noting that the new reference values would lead to fewer men being classified as infertile based on semen analysis alone [271; 272]. Such reclassification has an effect on diagnosis, patient referral, and indications for assisted reproductive technologies [272].

Treatment Options

Treatment options are available for correctable causes of infertility. Varicoceles can be repaired through open or laparoscopic surgery or by percutaneous embolization [182]. Surgical treatment leads to elimination of the varicocele in 90% of men, with improvement in the semen quality, production of testosterone, and rates of subsequent pregnancy [182; 273]. For men with infertility related to obstruction, microsurgical reconstruction of the obstructed duct has led to the appearance of sperm in the ejaculate and higher rates of subsequent pregnancy [267]. Several techniques for retrieving sperm are also available. Options for reproductive assistance and adoption should be explored for men who have uncorrectable infertility. Genetic counseling should be offered to men with nonobstructive azoospermia due to primary testicular failure [267].

The National Collaborating Centre for Women's and Children's Health recommends that men be informed that there is an association between elevated scrotal temperature and reduced semen quality, but that it is uncertain whether wearing loose-fitting underwear improves fertility.

(https://www.nice.org.uk/guidance/cg156. Last accessed June 12, 2019.)

Level of Evidence: Expert Opinion/Consensus Statement

SEXUALLY TRANSMITTED INFECTIONS

STIs are a serious public health concern, with nearly 20 million new infections each year [274]. The actual number of STIs is thought to be much greater, as the infections are both underdiagnosed and under-reported. In addition to the substantial morbidity associated with STIs, the financial cost is tremendous; nearly $16 billion was spent in 2008 on direct medical costs associated with the eight major STIs (chlamydia, gonorrhea, hepatitis B virus, HIV, human papillomavirus [HPV], herpes simplex virus type 2 [HSV-2], trichomoniasis, and syphilis) [275]. The vast majority of the costs were attributable to HIV ($12.6 billion), followed by HSV-2 ($540.7 million), chlamydia ($516.7 million), and gonorrhea ($162.1 million) [275].

The discussion here is confined to STIs with the greatest effect on men: chlamydia, gonorrhea, syphilis, HSV-2, and HPV [57]. Although HSV-2 and HPV infections are more common among women than men, the infections have serious implications for men. For example, nearly one-third of the 22,000 HPV-associated cancers that occur each year in the United States develop in men [276]. Infection with HSV-2 increases the risk for HIV, which is particularly important for black men, who are at greater risk for both HSV-2 and HIV [277].

Despite the availability of comprehensive guidelines for the testing and treatment of STIs, studies have shown poor compliance; in one study, fewer than one-third of individuals with an STI seen in an emergency department received recommended antibiotic treatment, and compliance with history-taking, diagnostic testing, and counseling ranged from 14% to 79% [278]. In addition, improvements in rates of HPV vaccination are needed [279].

RATE OF COMMON SEXUALLY TRANSMITTED INFECTIONS (STIs) AMONG MEN ACCORDING TO RACE/ETHNICITY, 2017							
STI	Prevalence (per 100,000)						
	All Men	Black (Non-Hispanic)	American Indian/ Alaskan Native	Hispanic	White (Non-Hispanic)	Asian	Native Hawaiian/ Other Pacific Islander
Chlamydia	363.1	1175.8	781.2	404.1	211.3	129.6	715.4
Gonorrhea	202.5	548.1	301.9	113.7	66.4	34.7	187.8
Syphilis (primary and secondary)	16.9	24.2	11.1	11.8	5.4	4.4	13.9
Source: [57]							*Table 14*

Prevalence of STIs

The prevalence of STIs according to gender vary with infection; chlamydia, HSV-2, and HPV occur more often among female than male individuals; gonorrhea occurs at similar rates among female and male individuals; and syphilis occurs more often among male than female individuals [57; 277; 280]. Overall, almost two-thirds of all STIs occur in individuals 15 to 24 years of age [57]. Among men, most STIs are far more prevalent in the non-Hispanic black population than in other ethnic/racial populations and are least prevalent in the Asian population (***Table 14***) [57; 277; 281].

Chlamydia

More than 1.7 million cases of chlamydia were reported to the CDC in 2017, the largest number of cases of any condition reported to the CDC [57]. The 2017 rate (528.8 per 100,000) represents an increase of 6.9% over the 2016 rate [57]. Chlamydial infection occurs more than twice as commonly in women than men, but the increase in the number of infections has been greater in men. During 2016–2017 alone, the rate among men increased 10.5%; however, during 2013–2017, rates of reported cases among men increased 39.3% (compared with an 11.1% increase among women) [57].

Gonorrhea

The rate of gonorrhea, the second most commonly reported notifiable disease in the United States, reached an historic low of 98.1 cases per 100,000 in 2009. The rate increased to 171.9 cases per 100,000 in 2017 [57]. The rate of gonorrhea among men (202.5 cases per 100,000) was higher than the rate among women (141.8 cases per 100,000). During 2013–2017, the rate among men increased 86.3%, while it increased 39.4% among women in the same time period [57].

Syphilis

In 2000–2001, the rate of syphilis (primary and secondary) was 2.1 cases per 100,000; however, the rate has increased almost every year since that time. In 2017, a total of 30,644 cases were reported, and the national rate had increased to 9.5 cases per 100,000, the highest rate since 1993 [57]. During 2000–2016, the rise in the rate was primarily attributable to men; however, during 2015–2016, the rate increased both among men (14.7%) and among women (35.7%) [57]. Young men who have sex with men have accounted for an increasing number of syphilis cases in the United States, and the number of reported cases is highest for that population. In 2017, men accounted for 87.7% of all cases of syphilis, and of those, 57.9% were MSM [57].

HSV-2

At least 50 million people in the United States are infected with HSV-2, but the infection has not been diagnosed in most infected people [173]. According to data from the National Health and Nutrition Examination Survey (NHANES), the seroprevalence of HSV-2 decreased slightly from 18.0% in 1999–2000 to 12.1% in 2015–2016 [57; 277]. The seroprevalence is more than twice as high among female individuals (33.9%) than among male individuals (14.5%) [57]. Among those who tested positively for HSV-2, 87% did not know they were infected [57]. As with other STIs, HSV-2 infection is more common among non-Hispanic black men than other racial/ethnic populations [57].

HPV

Data on HPV infection in men are limited. According to a data brief published by the National Center for Health Statistics (NCHS), during 2011–2014, the seroprevalence of any HPV was 7.3% among adults 18 to 69 years of age, with 11.5% among men and 3.3% among women [282]. In the HIM study, an ongoing prospective cohort study of the natural history of HPV in men (from the United States, Mexico, and Brazil), the overall prevalence of HPV infection was 65.2%, with the highest rates among white and black men (71.5% and 66.2%, respectively) and the lowest, among Asian/Pacific Islander men (42.2%) [281; 283].

Prevention, Control, and Screening

Prevention and control are keys to lowering the prevalence of STIs, and the primary preventive strategies are limiting the number of sexual partners, abstinence, the use of condoms and barriers, and, in the case of HPV, with vaccination [173; 276]. The importance of abstaining from sexual activity should be emphasized to individuals with a confirmed STI [173].

Control of STIs involves the identification of asymptomatic individuals and of symptomatic individuals who may not seek health care; effective diagnosis and treatment; and the evaluation, treatment, and counseling of sex partners of infected individuals [173]. The CDC encourages clinicians to promote prevention with patient-centered education that focuses on risk reduction measures directed at an individual patient's personal risk [173]. Obtaining a thorough sexual history is an essential component of prevention, and the CDC suggests asking questions related to [173]:

- Partners (gender and number)
- Protection (from STIs)
- Practices (types of sexual activity)
- Past history of STIs (patient and partners)
- Prevention (of pregnancy)
- Use of injected drugs (patient and partners)
- Exchange of money for sex (patient and partners)
- Other sexual practices

Clinicians should use simple, direct language when asking these questions and exhibit respect, compassion, and a nonjudgmental attitude [173]. Organizations such as the National Network of STI/HIV Prevention Training Centers, a CDC-funded group, can help clinicians enhance their skills in counseling individuals about prevention. Resources can be found on the organization's website, available at https://nnptc.org/nnptc-resources.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The U.S. Preventive Services Task Force recommends intensive behavioral counseling for all sexually active adolescents and for adults who are at increased risk for sexually transmitted infections (STIs).

(http://annals.org/aim/fullarticle/1906847. Last accessed June 12, 2019.)

Strength of Recommendation: B (There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.)

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS FOR SCREENING FOR SEXUALLY TRANSMITTED INFECTIONS (STIs) IN MALE INDIVIDUALS	
STI	**Recommendation**
Chlamydia	Insufficient evidence to recommend for or against screening in men
Gonorrhea	Insufficient evidence to recommend for or against screening in men
Syphilis	Strongly recommend screening for individuals at increased risk
Genital herpes	No screening for asymptomatic adults and adolescents
Source: [284]	*Table 15*

Recommendations for screening vary according to risk and the type of STI (***Table 15***) [284]. The USPSTF also recommends high-intensity behavioral counseling for all sexually active adolescents and for adults at increased risk for STIs and HIV [284]. The USPSTF has not issued recommendations for screening for HPV, but in 2011, the Advisory Committee on Immunization Practices (ACIP) recommended HPV vaccination for male individuals [276]. The ACIP recommends routine use of quadrivalent HPV vaccine for boys 11 or 12 years of age and for male individuals 13 to 21 years of age who have not initiated or completed the three-dose series [276; 286]. In 2014, a 9-valent vaccine was approved by the FDA for boys 9 to 15 years of age [285]. The ACIP also notes that men 22 to 26 years of age may also be vaccinated [276; 286]. In addition, hepatitis B vaccination is recommended for any patient who is being evaluated for an STI [173].

Diagnosis

The symptoms of STIs vary and are often similar to symptoms associated with other conditions of the urogenital tract, and some infected individuals may be asymptomatic.

Infection with chlamydia is often asymptomatic [173]. Diagnosis can be made by testing of a urethral or rectal swab or a urine specimen [173]. Nucleic acid amplification tests are the most sensitive tests and can be used for urine specimens [173].

Primary syphilis usually presents as a solitary chancre that develops at the site of infection approximately three weeks after exposure to the spirochete *Treponema pallidum* [287]. The chancre is typically painless and must be distinguished from other genital lesions, such as genital herpes, venereal warts, chancroid, and lymphogranuloma venereum (caused by *C. trachomatis*) [287].

Dark-field microscopy to detect *T. pallidum* is the optimum method of diagnosing syphilis. Although no such detection tests are commercially available, some laboratories provide locally developed and validated polymerized chain reaction (PCR) tests for the detection of *T. pallidum* [173]. A presumptive diagnosis of syphilis can be made with two types of serologic tests: nontreponemal tests (Venereal Disease Research Laboratory [VDRL] and rapid plasma regain [RPR] tests) and treponemal tests (such as fluorescent treponemal antibody absorbed [FTA-ABS] tests or the *T. pallidum* passive particle agglutination [TP-PA] assay) [173]. The CDC notes that using only one type of serologic test is insufficient for a diagnosis [173].

Gonococcal infection, which is caused by *Neisseria gonorrhoeae* (a gram-negative diplococcus), can lead to either urethritis or epididymitis [288]. Urethritis is accompanied by such symptoms as purulent discharge from the penis, dysuria, or erythema at the meatus [288]. Epididymitis caused by gonococcal infection is usually associated with unilateral testicular pain and no other symptoms [288]. Disseminated infection is rare (1% to 3%) [289]. A diagnosis of gonorrhea is confirmed by culture of a urethral specimen for *N. gonorrhoeae* on a Gram stain or by nucleic acid amplification testing done on a urine sample [173; 288]. Both techniques have similar sensitivity and specificity [173].

The CDC recommends that all individuals who are evaluated for gonorrhea should also be evaluated for chlamydia, syphilis, and HIV infection [173]. In one study of more than 3,800 men and women, approximately 10% to 30% of individuals with gonorrhea had concomitant infection with chlamydia [290]. The typical lesions of genital HSV-2 in men appear on or around the penis and are first noted as either a single or multiple erythematosus macular lesion(s). However, these lesions are absent in many infected individuals [173]. Viral culture is the preferred test for the diagnosis of HSV-2, but it requires two to seven days for results. The sensitivity of viral culture depends on the quality of the sample and the time at which the sample is obtained; sensitivity declines as the lesion begins to heal. A PCR test is available and is suggested by the CDC for analysis of cerebrospinal fluid when central nervous system disease is suspected [173]. Type-specific serologic tests are available as laboratory assays and point-of-care tests [173]. These tests have varying degrees of sensitivity for the detection of the HSV-2 antibody (80% to 90%) and specificity of at least 96% [173].

Treatment Options

The treatment of STIs has four main goals [173]:

- Eradicate infection
- Alleviate symptoms and signs
- Decrease complications (infertility, chronic pain, dissemination of disease)
- Prevent transmission

The CDC has developed comprehensive guidelines for the treatment of STIs, which it updated in 2015 (***Table 16*** and ***Table 17***) [173]. For chlamydia, gonorrhea, or syphilis, single-dose regimens generally offer an advantage for the treatment of individuals with poor healthcare-seeking or compliance behaviors [173]. The CDC notes that for the treatment of syphilis, neither combinations of benzathine penicillin and procaine penicillin nor oral penicillin preparations are considered appropriate and emphasizes the importance of distinguishing the standard benzathine penicillin product widely used in the United States (Bicillin L-A) from the combination benzathine-procaine penicillin (Bicillin C-R); the latter is not appropriate for the treatment of syphilis [173].

In addition to antibiotic treatment, bed rest, scrotal elevation, and analgesics can help to alleviate symptoms such as fever and local inflammation, which are primarily associated with gonorrhea. Beginning treatment as early as possible decreases the likelihood of complications and spread of infection, especially in the case of syphilis [173]. To prevent the transmission of infection, a patient with a confirmed or suspected STI should be told to avoid sexual contact until therapy is completed and he (and/or his partner) no longer has symptoms [173]. The need for sexual partners to be evaluated for treatment should also be emphasized. State and local health departments may provide assistance in arranging for the evaluation and treatment of sex partners of infected men.

HSV-2

The antiviral medications used to treat HSV-2 can only partially control the signs and symptoms of infection; they cannot eradicate the virus or reduce the risk, frequency, or severity of recurrence after the treatment course has been completed [173]. Men with HSV-2 infection should be given medication for episodic treatment of recurrent infection; treatment should begin within one day after the onset of a lesion [173]. If recurrences are frequent (six or more within a year), long-term suppression therapy may be appropriate; such therapy has been shown to reduce the frequency of recurrence by 70% to 80% [173].

Follow-Up

Peterman et al. found a 14.7% rate of reinfection among men during the first year after treatment for an STI [291]. An unexpected finding in the study was the high percentage (66%) of asymptomatic infections. The authors suggested that treated individuals be rescreened at three months. The CDC recommends follow-up with clinical examination and serologic evaluation at 6 and 12 months after treatment [173].

TREATMENT OF CHLAMYDIA, SYPHILIS, AND GONORRHEA AS RECOMMENDED BY THE CENTERS FOR DISEASE CONTROL AND PREVENTION

Infection	Recommended Treatment	Notes
Chlamydia	Azithromycin 1 g PO (single dose) OR Doxycycline 100 mg PO, twice daily for seven days ALTERNATIVES Erythromycin base 500 mg PO 4 times daily for seven days OR Erythromycin ethylsuccinate 800 mg PO four times daily for seven days OR Levofloxacin 500 mg PO once daily for seven days OR Ofloxacin 300 mg PO twice daily for seven days	Azithromycin and doxycycline offer similar efficacy. Alternative regimens do not offer any advantage in terms of dosing or cost.
Gonorrhea	Ceftriaxone 250 mg IM (single dose) PLUS Azithromycin 1 g PO (single dose) OR Doxycycline 100 mg PO twice daily for seven days	Alternative, if ceftriaxone is not available: Cefixime 400 mg PO (single dose) PLUS Azithromycin 1 g PO (single dose) OR Doxycycline 100 mg PO twice daily for seven days Alternative, if patient has severe allergy to cephalosporins: Azithromycin 2 g PO (single dose) and test-of-cure in one week
Primary and secondary syphilis	Benzathine penicillin G 2.4 million units IM (single dose)	Additional doses do not enhance efficacy. For patients allergic to penicillin, alternative regimens include doxycycline (100 mg PO, twice daily for 14 days) or tetracycline (500 mg PO, four times daily for 15 days)

Source: [173] *Table 16*

TREATMENT OF HSV-2 AS RECOMMENDED BY THE CENTERS FOR DISEASE CONTROL AND PREVENTION

Drug	Treatment Dosage		
	Initial Infection	Recurrent Infection	Long-Term Suppression
Acyclovir	400 mg three times daily for 7 to 10 days OR 200 mg, five times daily for 7 to 10 days	400 mg three times daily for 5 days OR 800 mg, two times daily for 5 days OR 800 mg, three times daily for 5 days	400 mg twice daily
Famciclovir	250 mg, three times daily for 7 to 10 days	125 mg two times daily for 5 days OR 1.0 g two times (single day)	250 mg twice daily
Valacyclovir	1 g two times daily for 7 to 10 days	500 mg two times daily for 3 days OR 1.0 g once daily for 5 days	500–1,000 mg once daily

Source: [173] *Table 17*

All states require that cases of chlamydia, gonorrhea, syphilis, HIV, and acquired immune deficiency syndrome (AIDS) be reported to local health authorities [173]. Clinicians should seek advice from state or local health departments if reporting requirements are unclear [173].

HEALTH ISSUES FOR MEN WHO HAVE SEX WITH MEN

It is difficult to determine an accurate percentage of MSM in the overall population because of the under-reporting of sexual behavior, but surveys indicate that this group of men represents at least 4% and up to approximately 16% of the population seen by any given healthcare professional [58; 292; 293]. The population that includes MSM (made up of gay, bisexual, and transgender individuals) has been identified as one of the six most underserved groups in the United States, yet medical training and standard resources for healthcare providers lack information on addressing the routine health concerns of this population [292; 294]. MSM have specific healthcare needs that clinicians must understand in order to provide appropriate, comprehensive care.

Perhaps the most important health risk for MSM is their avoidance of routine health care [293]. MSM do not seek routine health care for a variety of reasons. They may have difficulty coming to terms with their sexual identity, fear being judged by healthcare professionals, or be embarrassed to discuss their sexual behavior. In addition, many MSM do not recognize their health risks or their need for screening and preventive health care [58; 294]. Health risks also may not be recognized by MSM who do seek health care, and they may not be forthcoming about sexual behavior [294; 295]. A study has indicated that less than 20% of MSM had discussed their risk of HIV infection with their healthcare provider [296].

Creating a welcoming clinical environment is the first step in fostering an open dialogue between healthcare providers and MSM [240; 295]. Among the factors that contribute to such an environment are educational materials about specific healthcare needs for gay and lesbian individuals, a posted statement of nondiscriminatory care, and forms that contain more inclusive choices and gender-neutral language [240; 295]. In addition, healthcare professionals and office personnel should maintain a nonhomophobic attitude, communicate clearly and sensitively using gender-neutral terms, and recognize how their own attitudes affect clinical judgments [293; 297]. Confidentiality is an important issue for MSM, and healthcare personnel should assure the patient that some information could be kept out of the medical record [240].

Comprehensive health care for MSM must focus on the population's disproportionate risks for several conditions, including STIs, anal and other types of cancer, substance misuse, eating disorders, suicide, and victimization [294]. Thus, it is essential for clinicians to address several issues with MSM [58; 173; 292; 298]:

- Use of safe sexual practices
- Screening and immunization for hepatitis A and B viruses
- Testing and consideration of pre-exposure prophylaxis for HIV infection
- Routine screening for STIs
- Routine screening for anal HPV-related neoplasia
- Potential risk for specific cancers (testicular, Hodgkin lymphoma, Kaposi sarcoma)
- Assessment of substance misuse (tobacco, alcohol, cocaine, methamphetamine)
- Nutrition and exercise
- Evaluation of psychologic well-being and mental health
- Screening for violence

Health risks should be addressed at the patient's first visit and each subsequent visit [58]. An algorithm has been developed to help guide recommended screening for MSM (***Figure 3***) [58]. In addition, because of an increased risk of HPV-related cancer, the ACIP now recommends HPV vaccination for MSM up to 26 years of age if they did not receive the vaccine when they were younger [276].

According to the CDC, pre-exposure prophylaxis is recommended as one prevention option for sexually active adult MSM at substantial risk of HIV acquisition. (https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.pdf. Last accessed June 12, 2019.)

Level of Evidence: IA (One or more well-executed randomized controlled trials)

Sensitivity should be used in obtaining the medical and sexual history, and the sexual history should be placed in context by emphasizing that an understanding of sexual behaviors is essential to evaluating risks and providing optimal care. It should also be noted that a sexual history is an important component in the care of all patients, regardless of their sexual orientation or behaviors. Because of the various stages a man may be in with respect to his sexual identity, care should be taken to distinguish sexual behavior from sexual identity [295; 297].

It is also vital to have resources readily available to provide to MSM as needed. Such resources include information on STI clinics, substance misuse facilities, services for victims of abuse, and referrals for counseling. The Gay and Lesbian Medical Association (GLMA) has developed resources to help clinicians provide appropriate care to gay, lesbian, bisexual, and transgender individuals. The GLMA was has also a guideline for the care of this population, and the brochure (available at http://www.glma.org) includes a variety of additional resources [295].

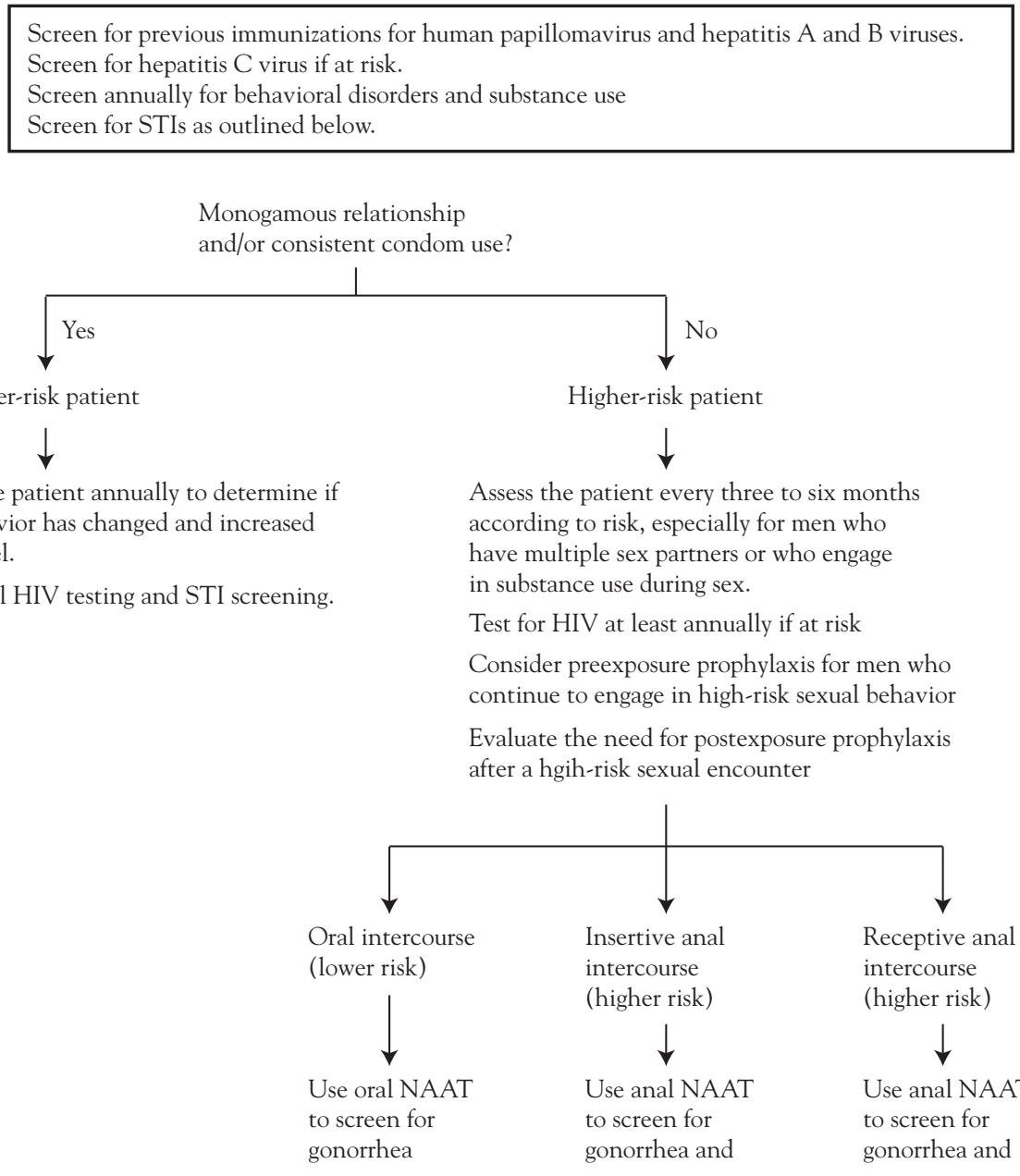
PSYCHOSOCIAL WELL-BEING OF MEN

Psychosocial well-being is important to men, and many conditions or situations can disrupt the sense of well-being. Among the more common factors that can have a negative effect on well-being for both sexes are everyday stressors (positive as well as negative), personal conflicts, traumatic events, and depression. In general, men lack the social support and interpersonal relationships that help women to cope with stresses [299]. Because of this, men differ in their ability to handle stress, with many men resorting to anger, violence, and substance misuse to deal with stress or depression [28; 300]. As a result, stress/anger, substance misuse, and depression are among the psychosocial conditions with the most serious health implications for men. Most men will not seek help for psychosocial disorders and may not recognize the symptoms of depression [45; 300; 301]. Thus, it is important for healthcare providers to address psychosocial well-being and potential threats to well-being as part of routine health evaluations of men.

STRESS/ANGER

Stress and anger have long been associated with negative health consequences. Most of the earlier research focused on the effects of stress and hostility on coronary heart disease, and additional research has found a link between hostility and a more rapid decline in lung function in older men [302; 303; 304]. Appropriate expression of anger has been suggested as a way to improve health, and controlling anger has been shown to promote well-being in older individuals [305].

ALGORITHM FOR SCREENING MEN WHO HAVE SEX WITH MEN



NAAT = nucleic acid amplification testing.

Source: Reprinted with permission from Preventive health care for men who have sex with men. June 15, 2015, Vol. 91, No. 12, American Family Physician. Copyright © 2015 American Academy of Family Physicians. All rights reserved. *Figure 3*

Safety is also of concern, as anger has been associated with an increased incidence of injuries and violence. In one study, higher levels of anger (at a given moment) were associated with an increased risk of injury, especially in men [306]. In that study, nearly 32% of individuals who had been injured reported having some degree of irritability before the injury. Men are the usual perpetrators of intimate partner violence causing injury, and these men tend to be younger (18 to 35 years of age), to be from a racial/ethnic minority population, and to have low socioeconomic status [307; 308]. Substance misuse and unemployment are also associated with such violence [307]. However, identifying a perpetrator of intimate partner violence in a clinical setting is difficult [308]. It is important to remember that men can also be victims of intimate partner violence, and this is especially true for MSM [309].

Although the USPSTF found insufficient evidence for or against routine screening for intimate partner violence (including child abuse and elder abuse), a survey of patients within a private family practice network showed that 97% of respondents believed that physicians should ask patients about family stress and conflict [310; 311]. The survey sample included women who had been physically hurt by intimate partner violence as well as men who had admitted perpetrating such injury. These findings support early studies that indicated patient preference for clinicians to ask questions about physical and sexual abuse [312]. The American Academy of Family Physicians (AAFP) notes that family physicians can provide early intervention in family violence through routine screening and the identification of abuse and that physicians should be alert for the presence of family violence in virtually every patient encounter [313]. It seems reasonable and appropriate for clinicians to include within routine health assessments of men questions about feelings of anger and frustration and urges to strike family members [307; 309]. Suggestions for strategies that focus on anger management and conflict resolution may be helpful, especially for adolescents and young men [309].

SUBSTANCE MISUSE

As noted, substance misuse is higher among men than among women in all age categories, and men are more likely to have psychosocial problems related to the misuse [28; 307]. Although the rate of alcohol misuse is highest among younger men, men older than 65 years of age are of special concern because they are much more likely than women to be "problem" drinkers and to misuse a wide range of illicit as well as prescription drugs [307]. As the general population ages, the misuse of illicit drugs is expected to increase [314]. Adding to this problem is the low rate of screening for alcohol misuse in the older population and the secrecy of many men about drug use [314; 315].

Additional concerns are the use of anabolic steroids among adolescents and young adult men and the use of methamphetamine among MSM. Use of anabolic steroids begins during the teenage years in approximately 25% of cases, and about 10% of all users are teenagers [316]. The prevalence of methamphetamine use among MSM is approximately 10% to 20%, a rate that is 10 times higher than that in the general population [317].

Several professional organizations, including the USPSTF, recommend screening and behavioral counseling intervention to reduce alcohol misuse [318]. However, reported rates of screening have been low [319]. Several screening instruments have been developed, and they vary in the number of questions, the populations for which they are best suited, and their usefulness in specific situations; no one tool is perfect [320; 321; 322; 323]. The CAGE questionnaire, which includes four questions, is best for detecting alcohol dependency and is easy and quick to perform [320; 321]. However, the test may not detect low, but risky, levels of drinking [307; 324]. The Alcohol Use Disorders Identification Test (AUDIT) is the most accurate for detecting problem drinking [319; 322].

Screening in the older population is especially important, as low levels of alcohol use can cause morbidity due to age-related physiologic changes, comorbidities, and the use of prescription medications [325]. Screening tools developed specifically for older individuals should be used, such as the geriatric version of the Michigan Alcohol Screening Test (MAST) or the Alcohol-Related Problems Survey (ARPS) [325; 326; 327]. Clinicians should also ask specific questions about drug use.

A medical history is also helpful, and a family history of alcoholism is a risk factor [319]. Clues to a problem with alcohol can be provided by such symptoms as amnesic episodes, mood swings, chronic fatigue, gastrointestinal symptoms, anxiety, and excessive sweating [319]. Several physical findings can suggest that a patient has a problem with alcohol or drugs, including [319; 324]:

- Mild tremor
- Unsteady gait
- Tachycardia
- Odor of alcohol or marijuana
- Enlarged, tender liver
- Nasal irritation (cocaine use)
- Conjunctival irritation (marijuana use)
- Excessive use of aftershave or mouthwash
- Signs of chronic obstructive pulmonary disease, hepatitis B or C, or HIV infection

Signs that should raise a "red flag" about substance misuse are frequent absences from work or school, history of frequent trauma or accidental injuries, depression or anxiety, other substance misuse, labile hypertension, sexual dysfunction, sleep disorders, poor nutrition, gastrointestinal symptoms, and interpersonal conflicts [307; 319; 324].

Clinicians should provide brief interventions, such as short counseling strategies, for men who are identified to have at-risk drinking. These interventions have been shown to be effective [284; 319; 324]. Alcoholism and drug addiction are best treated by an addiction medicine specialist or through an inpatient or outpatient program [324]. Primary care providers should have referrals for counseling and treatment readily available, as well as resources on support groups, such as Alcoholics Anonymous and Narcotics Anonymous.

To help healthcare professionals carry out the appropriate diagnosis and treatment of patients with alcohol problems, the National Institutes on Alcoholism and Alcohol Abuse (NIAAA) developed the publication *Helping Patients Who Drink Too Much: A Clinician's Guide*, which features an updated guideline on screening and brief intervention. The most recent edition is available on the NIAAA website at https://www.niaaa.nih.gov/guide.

DEPRESSION

Depression is often regarded as a "woman's disease" because it is diagnosed more frequently in women than men. However, researchers and the health community at large now realize that depression is of serious concern in men and is underdiagnosed [28; 328]. According to data from 2017, the prevalence of depression was 5.3% among men and 8.7% among women [329].

Despite the lower rates of depression in men compared with women, the rate of completed suicide is nearly four times higher for men (21.9 vs. 6.3 per 100,000) [25]. Suicide is a leading cause of death for men in many age groups and across all racial/ethnic populations, except for the black population [25].

The underdiagnosis of depression in men involves clinician-related and patient-related factors. Clinicians' lack of appropriate training and discomfort with dealing with depression contribute to a low rate of diagnosis, estimated to be about 50% [3; 330]. In addition, no screening instrument for suicide risk has been shown to reliably detect suicide risk in primary care populations [331]. This is unfortunate, as primary care providers appear to be in a position to intervene. As many as 83% of people who died by suicide had contact with their primary care physician in the year before death, with approximately 20% seeing their physician one day before death [330; 332]. In addition, 50% to 66% of individuals who committed suicide saw

their primary care physician within one month of their death, with 10% to 40% committing suicide within one week of the visit [331]. Thus, better recognition of depression and suicide risk by primary care providers may help reduce suicide rates.

Many patient-related factors in the underdiagnosis of depression are primarily related to gender issues, including [28; 300; 328; 330; 333; 334]:

- Reluctance of men to seek help
- Lack of men's recognition of the symptoms of depression
- Hesitancy of men to express emotions
- Tendency for men to see depression as a weakness
- Men's misconceptions about mental illness and its treatment

Diagnosis

Because men are less likely to express their emotions, they may recognize and discuss only the physical symptoms of depression, making diagnosis a challenge [300; 301; 333]. A carefully taken history can elicit information about risk factors, which include a family history of depression, the use of some medications (beta blockers, histamine H2-receptor antagonists, benzodiazepines, and methyldopa), chronic illness or other comorbidity, lack of social support, recent life stressor, and single marital status [307; 335]. Substance misuse frequently occurs concomitantly with depression, more often in men than women, but the direction of the causal relationship is not clear [300; 335].

Many of the symptoms of depression reported by women are the same for men: depressed mood, changes in appetite and sleep habits, problems with concentration, and an inability to find pleasure in once pleasurable activities [300]. It has been proposed that the symptoms of depression in men represent a male depressive syndrome, characterized by such symptoms as irritability, acting-out, aggression, low tolerance of stress, low impulse control, tendency to blame others, and a greater willingness to take risk [28; 300; 330; 333]. Men with depression may thus present with a very different symptom profile [328].

Identification of suicide risk is an essential component of the evaluation of a man with depression. Many of the risk factors for suicide are similar to those for depression; when the circumstances surrounding completed suicides were reviewed, the following were found to be factors [25]:

- Loss of a partner (through death or other means)
- Loss of job
- History of mental illness
- Depressed mood
- Previous suicide attempts
- Physical health problems
- Intimate partner problem
- Preceding or impending crisis (within two weeks)
- Financial problem

Clinicians should ask questions to determine the duration of symptoms and explore possible triggers of depression [328]. Because of their lack of experience with discussing emotions, many men may be uncomfortable with open-ended questions such as, "How do you feel?"; rather, discussing emotions in situational contexts can help men better express what they are feeling and why [333]. It may also be helpful to de-emphasize the negative connotation of depression and frame questions within the overall context of health and well-being [314].

Treatment Options

The treatment approach will depend on the severity of symptoms and the patient's preference. In general, a combination of psychotherapy and pharmacologic management provides the best results for most men [328; 335]. Potential psychotherapy approaches include cognitive behavior therapy and interpersonal psychotherapy [300; 307; 328]. First-line pharmacologic treatment involves the use of selective serotonin reuptake inhibitors, such as paroxetine, sertraline, and fluoxetine [307].

This treatment approach has efficacy rates of 30% to 70% [328]. Clinicians should emphasize the importance of taking the medication as prescribed, as it may be two to four weeks before a benefit is evident [328]. Depression that is associated with chronic illness is often seen as an inevitable consequence of the disease, but the depression should be treated. Frequently, the treatment improves the overall outcome [335].

FOSTERING ENHANCED HEALTH BEHAVIORS IN MEN

The strong association between lifestyle choices and men's morbidity and mortality clearly demonstrates the need to foster healthier behaviors among men. Creating a better understanding of the importance of health care requires broad-scale campaigns to heighten awareness of the need for routine and preventive health care and to encourage men to schedule physician visits. Also needed are efforts at the community and practice levels to enhance health-seeking behavior and improve men's understanding of their health. The efficacy of all of these efforts depends on addressing the unique features of the masculine gender identity.

LARGE-SCALE CAMPAIGNS

The Men's Health Network has established National Men's Health Week as the week leading up to Father's Day each June [336]. Highlights of the Week include health fairs, screening, and distribution of educational materials in workplaces and elsewhere in the community. Other Men's Health Network campaigns "speak" to men, with names such as "Men at Work" and "Time Out for Men's Health" maintenance schedule [336].

Some have suggested that large-scale campaigns that feature well-respected athletes and actors can increase appeal to men [45]. However, others have cautioned that, while celebrity endorsement of screening may have a positive effect on men, such campaigns may not target the right audience or address all the pertinent facts [337].

The optimal educational campaigns are those that target men and attempt to challenge men's perceptions of health and the need for preventive care. For example, to heighten awareness about depression in men, the National Institute of Mental Health launched the "Real Men, Real Depression" campaign and produced an accompanying booklet "Men and Depression" [335]. Both the campaign and the booklet feature quotes and vignettes from men who have been treated for depression.

Analysis of data about men who lack a usual source of care indicates that such men are more apt to be younger, Hispanic, single (never married or divorced), without insurance, and living in the southern or western parts of the United States or in urban areas [39]. Education about the importance of health care should be provided through public service announcements, media, schools, and workplaces as appropriate to target these groups of men [39]. Given men's propensity to see a physician only when they are sick or have symptoms, educational messages should emphasize the importance of preventive visits and discourage symptoms as a motivator for seeking health care [338]. Resources should also be culturally appropriate for diseases and conditions that disproportionately affect men of certain races and ethnicities.

As a result of men's reluctance to seek help, educational strategies that provide anonymity may be particularly well-suited for them [45; 339]. Print resources should be distributed through a variety of venues that men frequent, such as the workplace, schools, religious organizations, sports arenas, men's organizations or clubs, pubs, supermarkets, car and motorbike dealerships, and barbershops [45; 339; 340]. In addition, digital media may be effective, especially for younger men. A study showed that 90-second educational video clips on men's health, sent by e-mail, were well-received [341].

Many community-based educational programs targeting men have been successful, especially among men in racial/ethnic minority populations. For example, a culturally tailored, language-concordant navigator program was successful at improving rates of colorectal cancer screening at a healthcare center serving a low-income, ethnically and linguistically diverse community [342]. The Black Barbershop Health Outreach Program (BBHOP) has been an effective program for promoting cardiovascular health, and the program can be used as a model for other health topics [343]. Another barbershop-based program involves training barbers to educate their clients about prostate cancer [344]. Focus groups of men from churches of a variety of denominations have indicated that church-based education may also be effective [35; 345].

PRACTICE-LEVEL STRATEGIES

Men are more likely to use healthcare services that are quick and easy; consequently, making physician visits more convenient may increase the number of men who seek health care [339; 346]. Evening office hours and walk-in appointments may be helpful in addressing this problem, and male-specific group appointments have been effective in enhancing men's education on health issues, with high satisfaction reported by participants [347]. In addition, nontraditional settings for healthcare services have been suggested, such as within workplaces and near sports venues, shopping centers, and men's organizations [45; 339].

Men who are most likely to seek preventive care are those who live with a spouse or partner [348]. In addition, men have been shown to have strong feelings about women as the arbiters of health for the entire family and are likely to be influenced to seek health care by a member of the opposite sex; this is especially true for men in racial/ethnic minority populations [35; 40; 43; 45]. Given these findings, healthcare providers should talk to their female patients to emphasize the importance of encouraging the men in their families to seek routine health care. Additionally, all interactions with male patients should be used to promote routine health assessments. Men who seek help for acute problems should be reminded of the need for screening and be counseled about risk factors [45; 349]. A subsequent visit should be encouraged, and this message may be reinforced by providing a take-home reminder or by scheduling an appointment while the patient is in the office [45].

As noted earlier, fostering open communication in a nonjudgmental environment is essential. Clinicians should take care to raise health issues with their male patients and to overcome some masculine traits in communication, such as a reluctance to ask questions [240]. Asking open-ended questions may be helpful in some cases, and providing a questionnaire before the visit may foster discussion [45]. Assumptions about a man's willingness to share information should be avoided, as men have been more forthcoming when they receive cues that they are expected to provide valuable information [350]. Lastly, men often have a need to feel empowered, and shared decision making is important [351].

Decision aids are available in a variety of formats and literacy levels, and they may be useful in helping men make informed decisions about care [119; 129; 130; 131]. Also, clinicians should review decision aids and educational resources carefully before using them to ensure that the information is comprehensive and accurate [129]. Resources should be available about the risks involved with not wearing a safety belt or motorcycle helmet, driving while intoxicated, speeding, handling firearms, stress/anger management, and safety issues in the home and at work.

Clinicians can help ensure that their patients receive reliable online information by posting the addresses of authoritative websites in their office, in print resources, and within the community (***Table 18***). Healthcare providers should be familiar with established guidelines for screening among men in various age categories and should emphasize the relative benefits and disadvantages of screening (***Table 19***). The Electronic Preventive Services Selector (ePSS) is an application for mobile devices that provides USPSTF information on screening and counseling, as well as preventive medication services. The AUA offers the Men's Health Checklist, a compact, downloadable reference for coordinating care of men; it is available at https://www.auanet.org/publications/mens-health-checklist.

Routine health assessments should include screening and counseling about lifestyle factors that have an impact on health, such as substance misuse, diet, exercise, safe sex practices, and sun protection. Education about sun protection and self-examination for moles is especially important given the increase in the lifetime risk for melanoma among men [24]. At each routine visit, healthcare providers should assess each male patient's individual lifestyle, psychosocial, and occupational risks. The high rate of unintentional injury as a cause of death for men calls for increased attention to safety issues.

CONCLUSION

In response to high morbidity and mortality rates among men over the past decade, researchers have focused increased attention on men's health issues. Many factors contribute to health-related gender disparities, but male gender identity is thought to have the most significant impact. The characteristics of the traditional male role (self-reliance, independence, and maintenance of a strong image) cause men to seek health care much less often than women, especially for preventive care. As a result, disease in men may remain undiagnosed until more advanced stages. A tendency for risky behavior, another aspect of the traditional male role, also has a significant effect on men's mortality, as evidenced by unintentional injury being the third leading cause of death among all men. Such behaviors as substance misuse and non-use of protective devices (safety belts, helmets) begin in adolescence and continue into adulthood; across all age-groups, the rates of these behaviors are higher for male individuals than for female individuals. These behaviors are strongly associated with both chronic diseases and all-cause mortality in men.

Prostate cancer is a major concern for many men, and the issues of prostate cancer screening and treatment options are complex and confusing for patients as well as healthcare professionals. Informed decision making is also an important aspect of many benign conditions, such as prostatitis, BPH, premature ejaculation, erectile dysfunction, and late-onset hypogonadism. These conditions have a substantial effect on the quality of life for men, yet men are reluctant to initiate conversations on these topics because of embarrassment and a hesitancy to express feelings and symptoms. It is important to create an environment of open dialogue and ask questions to help men discuss these topics.

The psychosocial well-being of men is important for overall health. Alcohol misuse and depression have both been underdiagnosed in men, especially older men, and clinicians should remain diligent in screening for these disorders in their male patients.

Improvement of men's health relies on men gaining a greater understanding of their risk factors and becoming more involved in the health issues that affect them. Healthcare professionals have a critical role in helping to develop strategies to enhance men's utilization of healthcare resources and in encouraging their male patients to engage in screening and preventive care and to adopt healthy behaviors. Health assessments and screening should be carried out according to established guidelines, with consideration given to each individual patient's specific risks.

ONLINE HEALTH RESOURCES FOR MEN
General
American Heart Association *Information on cardiovascular disease, diabetes, cerebrovascular disease; tools for healthy lifestyle habits (diet, exercise, smoking) ("Getting Healthy" section).* https://www.heart.org
Centers for Disease Control and Prevention National Men's Health Week *Area devoted to men's health issues.* https://www.cdc.gov/family/nmhw
Men's Health Network *Site devoted to men's health issues. Publishes Blueprint for Men's Health: A Guide to a Healthy Lifestyle.* http://www.menshealthnetwork.org
Cancer
American Cancer Society *Cancer prevention and early detection worksheet for men—a tool to help men identify risks and understand preventive measures and early detection strategies for prostate cancer and lung cancer; includes links to information on various types of cancer. Information on prevention, screening, diagnosis, and treatment of all types of cancer.* https://www.cancer.org
National Cancer Institute *Information on prevention, screening, diagnosis, and treatment of all types of cancer.* https://www.cancer.gov
National Comprehensive Cancer Network *Patient guides (based on evidence-based guidelines) on the treatment of a variety of cancers.* https://www.nccn.org/patients
Smoking Cessation
Centers for Disease Control and Prevention Smoking and Tobacco Use https://www.cdc.gov/tobacco
National Cancer Institute https://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco
Genitourinary Disorders
Urology Care Foundation, The Official Foundation of the American Urological Association *Information on benign prostatic hypertrophy, prostate cancer, erectile dysfunction, and other urologic conditions.* https://www.urologyhealth.org
Depression
National Institute of Mental Health *Articles on depression in men, as well as personal stories of men with depression.* https://www.nimh.nih.gov/health/topics/depression
Alcohol and Drug Use
National Institute on Alcohol Abuse and Alcoholism *Research-based information on drinking its effect on health.* https://www.niaaa.nih.gov/alcohol-health
National Institute on Drug Abuse *Easy-to-read information about drugs, addiction, and recovery.* https://easyread.drugabuse.gov
Sexually Transmitted Infections
Centers for Disease Control and Prevention Sexually Transmitted Diseases https://www.cdc.gov/std
Source: Compiled by Author — *Table 18*

RECOMMENDATIONS AND SUGGESTIONS FOR HEALTH ASSESSMENTS, SCREENING, AND COUNSELING FOR MEN			
Intervention	**Suggested Frequency**	**Relevant Ages (Years)**	**Recommending Body/Source**
Routine physical examination (with determination of height, weight, and body mass index)	Every 3 to 5 years Every 1 to 2 years Yearly	18 to 39 40 to 49 50 and older	
Blood pressure screening	Every 1 to 2 years, depending on blood pressure	Beginning at 18	USPSTF
Cholesterol level/lipid profile	At least every 5 years	Beginning at 40 (earlier if at increased risk)	USPSTF
Diabetes (type 2) screening	Every 3 years	All men with blood pressure >135/80 mm Hg	USPSTF
Cancer-related check-up (for cancer of the thyroid, testicles, lymph nodes, oral cavity, and skin)	At each routine examination	Beginning at 20	ACS
Assessment, Counseling, and Behavioral Interventions as Appropriate			
Tobacco use	At each routine examination	All men	USPSTF
Alcohol use	At each routine examination	All men	USPSTF
Drug (illicit) use	At each routine examination	All men	ASAM
Depression	At each routine examination, when staff-assisted depression care supports are in place	All men	USPSTF
Counseling			
Healthy diet	At each routine examination	Men with risk factors for cardiovascular disease and diet-related chronic diseases	USPSTF
Exercise	At each routine examination	All men	AAFP, AMA, AHA, CDC
Sun avoidance and use of sunscreen	At each routine examination	All men	ACS, AAD, NIH Consensus Panel
Aspirin prophylaxis for cardiovascular disease and colorectal cancer	At each routine examination	50 to 59, with 10% or greater 10-year CVD risk and 10-year life expectancy	USPSTF
Self-examination for melanoma	At each routine examination	All men	ACS
Avoidance of sexually transmitted infections	At each routine examination	All sexually active men at increased risk	CDC
Risk of HIV infection	At each routine examination	All men who have sex with men	USPSTF
Risk for hepatitis A and B	At each routine examination	All men who have sex with men and others at high risk	
Sexual health	At each routine examination	All men	
Risks and benefits of prostate cancer screening	See Table 6		

Table 19 continues on next page.

RECOMMENDATIONS AND SUGGESTIONS FOR HEALTH ASSESSMENTS, SCREENING, AND COUNSELING FOR MEN *(Continued)*			
Intervention	**Suggested Frequency**	**Relevant Ages (Years)**	**Recommending Body/Source**
Screening			
Colorectal cancer	Every 5 to 10 years	50 to 75	USPSTF
Osteoporosis	At each routine examination	By 65	ACP
HIV	Not established (encourage men to be tested)	15 to 65 (younger and older men at increased risk)	USPSTF
Visual acuity (comprehensive eye examination)	Every 1 to 2 years	Beginning at 65	AAO
Abdominal aortic aneurysm (ultrasonography)	Once	65 to 75 (men who have ever smoked)	USPSTF
Immunizations			
Tetanus, diphtheria, pertussis (Td/Tdap)	Once (Tdap), with booster (Td) every 10 years	All men	ACIP
Influenza vaccine	Yearly	All men	ACIP
Pneumococcal vaccine	Once	65 and older (1 dose) 19 to 64 if risk factors present (1 or 2 doses)	ACIP
Hepatitis A	Once	All men, if risk factors are present (2 or 3 doses, depending on vaccine)	ACIP
Hepatitis B	Once	All men, if risk factors present (3 doses)	ACIP
Human papillomavirus (HPV)	Once	19 to 21 (3 doses) 22 to 26, if at increased risk (3 doses)	ACIP
Zoster (shingles)	Once	60 and older	ACIP
Haemophilus influenzae type b (Hib)	Once	All men, if risk factors present (1 or 3 doses depending on indication)	ACIP
Source: [58; 284; 298; 352]			*Table 19*

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