

10. Screening for Prostate Cancer

RECOMMENDATION

Routine screening for prostate cancer with digital rectal examinations, serum tumor markers (e.g., prostate-specific antigen), or transrectal ultrasound is not recommended.

Burden of Suffering

Prostate cancer is the most common noncutaneous cancer in American men.¹ After lung cancer, it accounts for more cancer deaths in men than any other single cancer site. Prostate cancer accounted for an estimated 244,000 new cases and 40,400 deaths in the U.S. in 1995.¹ Risk increases with age, beginning at age 50, and is also higher among African American men. Because it is more common in older men, prostate cancer ranks 21st among cancers in years of potential life lost.² The age-adjusted death rate from prostate cancer increased by over 20% between 1973 and 1991.³ The lifetime risk of dying from prostate cancer is 3.4% for American men.³ The reported incidence of prostate cancer has increased in recent years by 6% per year, a trend attributed to increased early detection efforts.⁴ Because local extension beyond the capsule of the prostate rarely produces symptoms, about one to two thirds of patients already have local extracapsular extension or distant metastases at the time of diagnosis.⁵ Ten-year survival rates are 75% when the cancer is confined to the prostate, 55% for those with regional extension, and 15% for those with distant metastases.⁶ The potential morbidity associated with progression of prostate cancer is also substantial, including urinary tract obstruction, bone pain, and other sequelae of metastatic disease.

Accuracy of Screening Tests

The principal screening tests for prostate cancer are the digital rectal examination (DRE), serum tumor markers (e.g., prostate-specific antigen [PSA]), and transrectal ultrasound (TRUS). The reference standard for these tests is pathologic confirmation of malignant disease in tissue obtained by biopsy or surgical resection. The sensitivity and specificity of screening tests for prostate cancer cannot be determined with certainty, however, because biopsies are generally not performed on patients with negative screening test results. False-negative results are unrecognized un-

less biopsies are performed for other reasons (e.g., abnormal results on another screening test, tissue obtained from transurethral prostatic resection). The resulting incomplete information about the number of true- and false-negative results makes it impossible to properly calculate sensitivity and specificity. Only the positive predictive value (PPV)—the probability of cancer when the test is positive—can be calculated with any confidence.

Even the PPV is subject to uncertainty because of the inaccuracies of the usual reference standard. Needle biopsy, the typical reference standard used for calculating sensitivity and specificity, has limited sensitivity. One study suggested that as many as 19% of patients with an initially negative needle biopsy (but abnormal screening test results) had evidence of cancer on a second biopsy.⁷ Moreover, studies vary in the extent to which the gland is sampled during needle biopsy. Recent studies, in which larger numbers of samples are obtained from multiple sections of the gland, provide a different reference standard than the more limited needle biopsies performed in older studies. These methodologic problems account for the large variation in the reported sensitivity, specificity, and PPV of prostate cancer screening tests and the current controversy over their true values.

DRE is the oldest screening test for prostate cancer. Its sensitivity is limited, however, because the examining finger can palpate only the posterior and lateral aspects of the gland. Studies suggest that 25–35% of tumors occur in portions of the prostate not accessible to the examining finger.⁸ In addition, Stage A tumors, by definition, are nonpalpable. Most recent studies report that DRE has a sensitivity of 55–68% in detecting prostate cancer in asymptomatic men,^{9,10} but values as low as 18–22% have also been reported in studies using different screening protocols.^{11,12} The DRE also has limited specificity, producing a large proportion of false-positive results. The reported PPV in asymptomatic men is 6–33%^{10,13–15} but appears to be somewhat higher when performed by urologists rather than by general practitioners.¹⁶

Elevations in certain serum tumor markers (e.g., PSA and prostatic acid phosphatase) provide another means of screening for prostate cancer. In screening studies, a PSA value greater than 4 ng/dL has a reported sensitivity of over 80% in detecting prostate cancer in asymptomatic men,¹⁰ although a sensitivity as low as 29% has also been reported in studies using different screening protocols.¹¹ Prostatic acid phosphatase has a much lower sensitivity (12–20% for Stage A and B disease) and PPV (below 5%) than PSA,¹⁷ and its role in screening has largely been replaced by PSA. PSA elevations are not specific for prostate cancer. Benign prostatic conditions such as hypertrophy and prostatitis can produce false-positive results; about 25% of men with benign prostatic hypertrophy (BPH) and no malignancy have an elevated PSA level.¹⁸

In most screening studies involving asymptomatic men, the reported

PPV of PSA in detecting prostate cancer is 28–35%.^{10,19–21} In many instances, however, other screening tests (e.g., DRE) are also positive. The PPV of PSA when DRE is negative appears to be about 20%.²² It is unclear whether the same PPV applies when screening is performed in the general population. Participants in most screening studies are either patients seen in urology clinics or volunteers recruited from the community through advertising. Studies suggest that such volunteers have different characteristics than the general population.²³ For example, in one screening study, 53% of the volunteers had one or more symptoms of prostatism.¹⁰ Since PPV is a function of the prevalence of disease, routine PSA testing of the general population, if it had a lower prevalence of prostate cancer than volunteers, would generate a higher proportion of false-positive results than has been reported in the literature. A significant difference in prevalence in the two populations has not, however, been demonstrated.

Several techniques have been proposed to enhance the specificity and PPV of the PSA test. The serum concentration of PSA appears to be influenced by tumor volume, and some investigators have suggested that PSA density (the PSA concentration divided by the gland volume as measured by TRUS) may help differentiate benign from malignant disease.^{24–26} According to these studies, a PSA density greater than 0.15 ng/mL may be more predictive of cancer. Other studies suggest that the rate of change (PSA velocity), rather than the actual PSA level, is a better predictor of the presence of prostate cancer. An increase of 0.75 ng/mL or higher per year has a reported specificity of 90% and 100% in distinguishing prostate cancer from BPH and normal glands, respectively.²⁷ PSA values tend to increase with age, and investigators have therefore proposed age-adjusted PSA reference ranges.^{28,29} Current evidence is inadequate to determine the relative superiority of any of these measures or to prove conclusively that any is superior to absolute values of PSA.³⁰ The most effective method to increase the PPV of PSA screening is to combine it with other screening tests. In a large screening study, the combination of an elevated PSA and abnormal DRE achieved a PPV of 49%. Even with this improved accuracy, however, combined DRE and PSA screening led to the performance of needle biopsies on 18% of the screened population,¹⁰ raising important public policy issues (see below).

A large proportion of cancers detected by PSA screening may be latent cancers, indolent tumors that are unlikely to produce clinical symptoms or affect survival. Autopsy studies indicate that histologic evidence of prostate cancer is present in about 30% of men over age 50. The reported prevalence of prostate cancer in men without previously known prostate cancer during their lifetimes is 10–42% at age 50–59, 17–38% at age 60–69, 25–66% at age 70–79, and 18–100% at age 80 and older.^{31–37} Recent autopsy studies have even found evidence of carcinoma in 30% of men aged 30–49.³⁸ Although patients who undergo autopsy may not be entirely rep-

representative of the general population, these prevalence rates, combined with census data,³⁹ suggest that millions of American men have prostate cancer. Fewer than 40,000 men in the U.S. die each year from prostate cancer, however, suggesting that only a subset of cancers in the population are clinically significant. Natural history studies indicate that most prostate cancers grow slowly over a period of many years.⁴⁰ Thus, many men with early prostate cancer (especially older men) will die of other causes (e.g., coronary artery disease) before their cancer becomes clinically apparent. Because a means of distinguishing definitively between indolent and progressive cancers is not yet available, widespread screening is likely to detect a large proportion of cancers whose effect on future morbidity and mortality is uncertain.

Recent screening studies have suggested, however, that cancers detected by PSA screening may be of greater clinical importance than latent cancers found on autopsy. Studies of asymptomatic patients with nonpalpable cancers detected through PSA screening have reported extracapsular extension, poorly differentiated cell types, tumor volumes exceeding 3 mL, and metastases in 31–38% of cancers that were pathologically staged.^{20,41–43} In a retrospective review of radical prostatectomies performed on patients with nonpalpable prostate cancer detected by PSA screening, 65% had a volume greater than 1 mL, and surgical margins were positive in 26% of cases.⁴⁴ In a similar series, the mean tumor volume was 7.4 mL and 30% of the tumors had penetrated the capsule.⁴⁵

The sensitivity of PSA for clinically important cancers was examined in a recent nested case-control study among 22,000 healthy physicians participating in a long-term clinical trial.⁴⁶ Archived blood samples collected at enrollment were compared for 366 men who were diagnosed clinically with prostate cancer during a 10-year follow-up period and 1,098 matched controls without cancer. PSA was elevated (>4 ng/mL) in 46% of the men who subsequently developed prostate cancer and 9% of the control group (i.e., sensitivity 46%, specificity of 91%). For cancers diagnosed within the first 4 years of follow-up, the sensitivity of PSA was 87% for aggressive cancers but only 53% for nonaggressive cancers (i.e., small, well-differentiated tumors), suggesting that PSA is more sensitive for clinically important disease. Given the low incidence of aggressive prostate cancer in this study (1% over 10 years), the reported specificity of 91% would generate a PPV (10–15%) that is lower than that reported from studies using routine biopsies (28–35%).¹⁰ Furthermore, this study could not address the central question of whether PSA would have identified aggressive cancers at a potentially curable stage.

TRUS is a third means of screening for prostate cancer, but its performance characteristics limit its usefulness as a screening test. In most studies, TRUS has a reported sensitivity of 57–68% in detecting prostate cancer

in asymptomatic men.^{9,10} Because TRUS cannot distinguish between benign and malignant nodules, its PPV is lower than PSA. Although a PPV as high as 31% has been reported for TRUS,⁴⁷ its reported PPV when other screening tests are normal is only 5–9%.^{15,19} Even when cancers are detected, the size of tumors is often underestimated by TRUS. The discomfort and cost of the procedure further limit its role in screening.

Effectiveness of Early Detection

There is currently no evidence that screening for prostate cancer results in reduced morbidity or mortality, in part because few studies have prospectively examined the health outcomes of screening. A case-control study found little evidence that DRE screening prevents metastatic disease; the relative risk of metastatic prostate cancer for men with one or more screening DREs compared with men with none was 0.9 (95% confidence interval, 0.5–1.7).⁴⁸ A cohort study also reported little benefit from DRE screening,⁴⁹ but its methodologic design has been criticized. Randomized controlled trials of DRE and PSA screening, which are expected to provide more meaningful evidence than is currently available, are currently under way in the U.S. and Europe.⁵⁰ The results of these studies, however, will not be available for over a decade. Therefore, recommendations for the next 10 years will depend on indirect evidence for or against effectiveness.

Indirect evidence that early detection of prostate cancer improves outcome is limited. Survival appears to be longer for persons with early-stage disease; 5-year survival is 87% for Stage A (nonpalpable) tumors, 81% for Stage B (palpable, organ-confined cancer), 64% for Stage C (local extracapsular penetration), and 30% for Stage D (metastatic).⁵ Due to recent screening efforts, prostate cancer is now increasingly diagnosed at a less advanced stage. As with survival advantages observed with other cancers, however, it is not known to what extent lead-time and length biases account for differences in observed survival rates (see Chapter ii). The frequently indolent nature of prostate cancer makes length bias a particular problem in interpreting stage-specific survival data. Successful treatment of indolent tumors may give a false impression that “cure” was due to treatment. Prostate cancers detected through screening are more likely to be organ-confined than cancers detected by other means.²⁰ Proponents of radical prostatectomy often argue that such cancers are potentially curable by removing the gland. As already noted, however, current evidence is inadequate to determine with certainty whether these organ-confined tumors are destined to progress or affect longevity; thus the need for treatment is often unclear.

Even if the need for treatment is accepted, the effectiveness of available treatments is unproven. Stage C and Stage D disease are often incurable, and the efficacy of treatment for Stage B prostate cancer is uncertain. Cur-

rently available evidence about the effectiveness of radical prostatectomy, radiation therapy, and hormonal treatment derives largely from case-series reports without internal controls, usually involving carefully selected patients and surrogate outcome measures for monitoring progression (e.g., PSA levels).^{51–55} Although men treated for organ-confined prostate cancer have a normal life expectancy, it is not clear how much their prognosis owes to treatment. The only randomized controlled trial of prostate cancer treatment, which compared radical prostatectomy with expectant management, reported no difference in cumulative survival rates over 15 years, but the study was conducted in the 1970s and suffered from several design flaws.^{56,57} Randomized controlled trials to evaluate the effectiveness of current therapies for early disease are being launched in the U.S. and Europe, but results are not expected for 10–15 years.^{58,59}

Some observational studies suggest that survival for early-stage prostate cancer may be good even without treatment. A Swedish population-based cohort study of men with early-stage, initially untreated prostate cancer found that, after 12.5 years, 10% had died of prostate cancer and 56% had died of other causes. The 10-year disease-specific survival rate (adjusted for deaths from other causes) for the study population was 85%. Cancer-related morbidity was significant, however. Over one third of the cancers progressed through regional extension, and 17% metastasized. The patient's age and the tumor stage did not significantly influence survival rates, but tumor grade (degree of differentiation) did affect survival; the 5-year survival rate was only 29% for poorly differentiated tumors.^{59–61} Critics of the study have argued that the high survival rates were due to the relatively large proportion of older men and of tumors detected incidentally during transurethral prostatic resection, and that Swedish data are not generalizable to the U.S.^{22,62} Other studies have reported similar results; in one series of selected men with well- and moderately differentiated cancer and extracapsular (nonmetastatic) extension, 5- and 9-year survival rates were 88% and 70%, respectively, without treatment.⁶³ Reported 10-year disease-specific survival for expectant management of palpable but clinically localized prostate cancer is 84–96%.^{64–66} Finally, it is unclear whether reported survival rates in these studies, in which many cancers were detected without screening, are generalizable to screen-detected cancers.

Reviewers have attempted to compare the efficacy of treatment and watchful waiting by pooling the results of uncontrolled studies. An analysis of six studies concluded that conservative management of clinically localized prostate cancer (delayed hormone therapy but no surgical or radiation therapy) was associated with a 10-year disease-specific survival rate of 87% for men with well- or moderately differentiated tumors and 34% for poorly differentiated tumors.⁶⁷ The assumptions used in the model are not universally accepted, however.^{68,69} A structured literature

review concluded that the median annual rates of metastatic disease and prostate cancer mortality were 1.7% and 0.9%, respectively, without treatment.⁷⁰ This study was criticized for including a large proportion of patients with well-differentiated tumors and those receiving early androgen deprivation therapy.⁷¹ Another review concluded that the annual rates for metastasis and mortality were higher (2.5% and 1.7%, respectively), but the review was limited to patients with palpable clinically localized cancers and excluded studies of cancers found incidentally at prostatectomy. In this population, disease-specific survival was estimated to be 83% for deferred treatment, 93% for radical prostatectomy, and 74% for external radiation therapy.⁷² Thus, the effectiveness of treatment when compared with watchful waiting remains uncertain.

Uncertainties about the effectiveness of treatment are important because of its potentially serious complications. Needle biopsy, the diagnostic procedure performed on about 20% of men screened with DRE and PSA,¹⁰ is generally safe but results in infection in 0.3–5% of patients, septicemia in 0.6% of patients, and significant bleeding in 0.1% of patients.^{19,73–75} The potential adverse effects of radical prostatectomy are more substantial. Although urologists at specialized centers report operative mortality rates of 0.2–0.3%,^{55,76} published rates in clinical studies and national databases range between 0.7% and 2%.^{6,70,77–79} An examination of Medicare claims files estimated that the 30-day mortality rate was 0.5%.⁸⁰ The reported incidence of impotence varies between 20% and 85%,^{11,51,70,79,81,82} depending on definitions for impotence and whether bilateral nerve-sparing techniques are used. Other complications of prostatectomy include incontinence (2–27%), urethral stricture (10–18%), thromboembolism (10%), and permanent rectal injuries (3%).^{11,51,70,77,83–87} A study of Medicare patients who underwent radical prostatectomy in the late 1980s reported a 30-day operative mortality rate of 1% and a 4–5% incidence of perioperative cardiopulmonary complications. Over 30% wore pads to control wetting, 6% underwent corrective surgery for incontinence, and 2% required the use of an indwelling catheter. Over 60% reported partial erections and 15% underwent treatment for sexual dysfunction; 20% had dilatations or surgical procedure for strictures.⁸⁸ Studies of generally healthy and younger patients who have undergone radical prostatectomy in recent years have noted considerably fewer complications.⁵⁵

Complications of radiation therapy include death (about 0.2–0.5%), acute gastrointestinal and genitourinary complications (8–43%), chronic complications requiring surgery or prolonged hospitalization (2%), impotence (40–67%), urethral stricture (3–8%), and incontinence (1–2%).⁸⁹ Three-dimensional conformal radiotherapy, a recently introduced technique for more precise, high-dose treatment, is reported to produce acute and chronic gastrointestinal or genitourinary complications in 55–76%

and 11–12% of patients, respectively.⁹⁰ Complication rates in studies of radiation therapy cannot be compared with confidence to reported complication rates for surgery because of differences in study designs and patient populations.

Recent decision analyses have combined current estimates of the benefits and harms to predict whether early treatment improves survival. A frequently cited decision analysis for men aged 60–75 concluded that, in most cases of clinically localized prostate cancer, neither surgery nor radiation therapy significantly improved life expectancy.⁹¹ According to the model, treatment generally results in less than 1 year of improvement in quality-adjusted survival. In men over age 70, the analysis suggested that treatment was more harmful than watchful waiting. The study has been criticized because the subjects consisted largely of older men with low-volume, low-grade tumors and because the probability estimates used in the model may be incorrect.^{71,92} Defenders of the study note that the data were adjusted for age and tumor grade (but not stage). Retrospective quality-of-life analyses have reported similar findings, noting that men who have undergone radical prostatectomy or radiation therapy for localized prostate cancer generally report lower quality of life due to impaired sexual, urinary, and bowel function than untreated men, even after controlling for the sexual and urinary dysfunction that is common in this age group.⁹³

Other decision analyses have examined whether screening itself improves survival. Although older analyses suggested a modest benefit from screening,^{94,95} more recent models have reached more pessimistic conclusions when quality-of-life adjustments are incorporated. One analysis concluded that screening and treatment result in an average loss of 3.5 quality-adjusted months of life.⁹⁶ Another decision analysis concluded that one-time screening of men aged 50–70 with either DRE or PSA would increase life expectancy by 0–0.2 days and 0.6–1.6 days, respectively, but quality-adjusted life would be decreased by 1.8–7.1 days and 2.1–9.5 days, respectively, per patient screened.⁹⁷ The assumptions and calculations used in this model have also been criticized.⁹⁸ A recent analysis of annual screening after age 50 concluded that screening would result in an average loss of 0.7 quality-adjusted life-years per patient screened.^{98a}

Recommendations of Other Groups

The American Cancer Society⁹⁹ recommends an annual DRE for both prostate and colorectal cancer, beginning at age 40. It recommends that the annual examination of men age 50 and older should include a serum PSA measurement and that PSA screening should begin at age 40 for African American men and those with a family history of prostate cancer.¹⁰⁰ Similar recommendations have been issued by the American Uro-

logical Association¹⁰¹ and the American College of Radiology.¹⁰² In 1994, the Food and Drug Administration expanded the licensure for the PSA test to include screening.¹⁰³ The Canadian Task Force on the Periodic Health Examination (CTF) recommended against the routine use of PSA or TRUS as part of the periodic health examination; while recognizing the limitations of DRE, they concluded that the evidence was not sufficient to recommend that physicians discontinue use of DRE in men aged 50–70.¹⁰⁴ A 1995 report by the Office of Technology Assessment concluded that research to date had not determined whether or not systematic early screening for prostate cancer with PSA or DRE would save lives, and that the choice to have screening or forego it would depend on patient values.¹⁰⁵ The recommendations of the American College of Physicians and American Academy of Family Physicians are currently under review. In 1992, the American Urological Association concluded that the value of TRUS as an independent screening procedure has not been established and should be reserved for patients with an abnormal DRE or PSA.¹⁰⁶

Discussion

In summary, prostate cancer is a serious public health problem in the United States, accounting for 35,000–40,000 deaths each year and substantial morbidity from disease progression and metastatic complications. Autopsy studies indicate, however, that these cases arise from a much larger population of latent prostate cancers that are present in over nine million American men. Although screening tests such as PSA have adequate sensitivity to detect clinically important cancers at an early stage, they are also likely to detect a large number of cancers of uncertain clinical significance. The natural history of prostate cancer is currently too poorly understood to determine with certainty which cancers are destined to produce clinical symptoms or affect survival, which cancers will grow aggressively, and which will remain latent. Prostate cancer has a complex biology with many unanswered questions about heterogeneity, tumor-host interactions, and prognostic stratification.

More fundamentally, there is no evidence to determine whether or not early detection and treatment improve survival. For men with well- and moderately differentiated disease, treatment appears to offer little benefit over expectant management, whereas the most aggressive tumors may have spread beyond the prostate by the time they are detected by screening. Observed survival advantages for men with early-stage disease may be due to length bias and other statistical artifacts rather than an actual improvement in clinical outcome. Although it is possible that treatment is beneficial for an unknown proportion of men with early prostate cancer, definitive evidence regarding effectiveness will not be available for over a

decade, when ongoing randomized controlled trials are completed. In the interim years, during which thousands of deaths from prostate cancer are predicted, screening might be justified for its potential benefit were it not for its potential harms. Widespread screening will subject many men to anxiety from abnormal test results and the discomfort of prostate biopsies; aggressive treatment for screen-detected cancers will expose thousands of men to the risks of incontinence, impotence, death, and other sequelae without clear evidence of benefit. Decision-analysis models suggest that the negative impact of these complications on quality of life may outweigh the potential benefits of treatment, but the designs and assumptions of these models are controversial. The absence of proof that screening can reduce mortality from prostate cancer, together with the clear potential that screening will increase treatment-related morbidity, argues against a policy of routine screening in asymptomatic men.

The economic implications of widespread prostate screening, although not a principal argument against its appropriateness, also warrant attention. A full discussion of the cost effectiveness of prostate screening is beyond the scope of this chapter. Moreover, cost effectiveness cannot be properly determined without evidence of clinical effectiveness. Nonetheless, it is clear that routine screening of the 28 million American men over age 50,³⁹ as recommended by some groups, would be costly. Researchers have predicted that the first year of mass screening would cost the country \$12–28 billion.^{6,11} This investment might be worthwhile if the morbidity and mortality of prostate cancer could be reduced through early detection—given certain assumptions, prostate cancer screening might even achieve cost-benefit ratios comparable to breast cancer screening¹⁰⁷—but there is currently little evidence to support these assumptions. The costs of this form of screening, with its emphasis on older men, is likely to increase in the future with the advancing age of the United States population; the number of American men over age 55 is expected to nearly double in the next 30 years, from 23 million men in 1994 to 44 million by 2020.³⁹

There is some evidence that the recent increase in prostate screening may be generating a poorly controlled expansion in the performance of radical prostatectomies, creating an unnecessary iatrogenic morbidity in a growing population of surgical patients. The rising incidence of prostate cancer due to increased screening has been accompanied by a tripling in rates for radical prostatectomy in the U.S.⁴ If early detection and treatment are effective, they are most likely to benefit men under age 70 rather than older men. As already noted, 10-year survival for early-stage prostate cancer approaches 90%. Thus, most men over age 70, who face a life expectancy of just over 10 years, are more likely to die of other causes than of prostate cancer. Subjecting these men to the risks of biopsy and treat-

ment is often unwarranted, and many proponents of prostate screening therefore recommend against screening after age 70. Nonetheless, studies indicate that radical prostatectomy rates for men aged 70–79 increased 4-fold in 1984–1990, and the trend appears to be continuing in this decade. Population-based rates for prostatectomy in men aged 70–79, many of whom are unlikely to benefit from the procedure, appear to be the same as in men aged 60–69.⁷⁸ According to an American College of Surgeons survey, one out of three men undergoing radical prostatectomy in 1990 was age 70 or older.⁷⁹

The lack of evidence regarding the benefits of prostate screening and the considerable risks of adverse effects make it important for clinicians to inform patients who express an interest in screening about the consequences of testing before they consent to screening. Although such counseling is proper for all forms of screening, the need for informed consent is especially important for prostate cancer screening because of current uncertainty about its effectiveness and because the proper choice for an individual is highly dependent on personal preferences. Screening is more likely to be chosen by men with strong fears of prostate cancer and by those who can accept the risks of incontinence, impotence, and other treatment complications. Screening is less likely to be chosen by men who are skeptical of the risks of cancer and the effectiveness of treatment and who have strong fears that treatment complications will jeopardize their quality of life.

CLINICAL INTERVENTION

Routine screening for prostate cancer with DRE, serum tumor markers (e.g., PSA), or TRUS is not recommended (“D” recommendation). Patients who request screening should be given objective information about the potential benefits and harms of early detection and treatment. Patient education materials that review this information are available.¹⁰⁸ If screening is to be performed, the best-evaluated approach is to screen with DRE and PSA and to limit screening to men with a life expectancy greater than 10 years. There is currently insufficient evidence to determine the need and optimal interval for repeat screening or whether PSA thresholds must be adjusted for density, velocity, or age.

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