Screening for Prostate Cancer: A Review of the Evidence for the U.S. Preventive Services Task Force

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Background: Screening can detect prostate cancer at earlier, asymptomatic stages, when treatments might be more effective.

Purpose: To update the 2002 and 2008 U.S. Preventive Services Task Force evidence reviews on screening and treatments for prostate cancer.

Data Sources: MEDLINE (2002 to July 2011) and the Cochrane Library Database (through second quarter of 2011).

Study Selection: Randomized trials of prostate-specific antigen–based screening, randomized trials and cohort studies of prostatectomy or radiation therapy versus watchful waiting, and large observational studies of perioperative harms.

Data Extraction: Investigators abstracted and checked study details and quality using predefined criteria.

Data Synthesis: Of 5 screening trials, the 2 largest and highest-quality studies reported conflicting results. One found that screening was associated with reduced prostate cancer–specific mortality compared with no screening in a subgroup of men aged 55 to 69 years after 9 years (relative risk, 0.80 [95% CI, 0.65 to 0.98]; absolute risk reduction, 0.07 percentage point). The other found no statistically significant effect after 10 years (relative risk, 1.1 [CI, 0.80 to 1.5]). After 3 or 4 screening rounds, 12% to 13% of screened men had false-positive results. Serious infections or urine retention occurred after 0.5% to 1.0% of prostate biopsies. There were 3 randomized trials and 23 cohort studies of treatments. One good-quality trial found that prostatectomy for localized prostate cancer decreased risk for prostate cancer–specific mortality compared with watchful waiting through 13 years of follow-up (relative risk, 0.62 [CI, 0.44 to 0.87]; absolute risk reduction, 6.1%). Benefits seemed to be limited to men younger than 65 years. Treating approximately 3 men with prostatectomy or 7 men with radiation therapy instead of watchful waiting would each result in 1 additional case of erectile dysfunction. Treating approximately 5 men with prostatectomy would result in 1 additional case of urinary incontinence. Prostatectomy was associated with perioperative death (about 0.5%) and cardiovascular events (0.6% to 3%), and radiation therapy was associated with bowel dysfunction.

Limitations: Only English-language articles were included. Few studies evaluated newer therapies.

Conclusion: Prostate-specific antigen–based screening results in small or no reduction in prostate cancer–specific mortality and is associated with harms related to subsequent evaluation and treatments, some of which may be unnecessary.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2011;155:762-771. www.annals.org
For author affiliations, see end of text.
This article was published at www.annals.org on 7 October 2011.

Editor's Note: *The related draft recommendation statement was available for public comment at www.uspreventiveservicestaskforce.org. The USPSTF will consider all submitted comments when it finalizes its recommendation. To sign up for notification about the posting of draft recommendation statements, please visit the USPSTF Web site.*

Prostate cancer is the most commonly diagnosed cancer in U.S. men (1–3). Prostate-specific antigen (PSA)–based screening can detect prostate cancer at earlier, asymptomatic stages, when treatments might be more effective.

See also:

Print
Editors' Notes 763

Web-Only
Appendix Tables
Appendix Figures
Conversion of graphics into slides

The U.S. Preventive Services Task Force (USPSTF) last reviewed the evidence on prostate cancer screening (4) and issued recommendations in 2008 (5). Since then, large trials of prostate cancer screening have been published (6, 7). Benefits and harms of treatments for prostate cancer were last reviewed by the USPSTF in 2002 (8). This article summarizes 2 recent reviews commissioned by the USPSTF to synthesize the current evidence on screening (9) and treatments (10) for localized prostate cancer.

Methods

Scope of the Review

We followed a standardized protocol and developed an analytic framework that focused on the following key questions:

1. Does PSA-based screening decrease prostate cancer–specific or all-cause mortality?

2. What are the harms of PSA-based screening for prostate cancer?

3. What are the benefits of treatment of early-stage or screening-detected prostate cancer?

4. What are the harms of treatment of early-stage or screening-detected prostate cancer?

Detailed methods and data for the review, including search strategies, multiple evidence tables with quality ratings of individual studies, and pooled analyses of some harms data, are available in the full report (10). Also of note, androgen deprivation therapy, cryotherapy, and high-intensity focused ultrasonography are reviewed in the full report (10) but are not presented in this article.

Data Sources and Searches

We searched Ovid MEDLINE from 2002 to July 2011, PubMed from 2007 to July 2011, and the Cochrane Library Database through the second quarter of 2011 and reviewed reference lists to identify relevant articles published in English.

Study Selection

At least 2 reviewers independently evaluated each study to determine inclusion eligibility. We restricted inclusion to published studies. We included randomized trials of screening for prostate cancer in asymptomatic men (including those with chronic, mild lower urinary tract symptoms) that incorporated 1 or more PSA measurements, with or without additional methods, such as digital rectal examination, and reported all-cause or prostate cancer–specific mortality or harms associated with screening. We also included randomized trials and cohort studies of men with screening-detected prostate cancer that compared radical prostatectomy or radiation therapy (the most common primary treatments for localized prostate cancer [11, 12]) with watchful waiting and reported all-cause mortality, prostate cancer–specific mortality, or prespecified harms (quality of life or functional status, urinary incontinence, bowel dysfunction, erectile dysfunction, psychological effects, and surgical complications). We included studies of clinically localized (T1 or T2) prostate cancer because more than 90% of screening-detected prostate cancers are localized (6, 7, 13). We included only studies that reported risk estimates for mortality adjusted at a minimum for age at diagnosis and tumor grade (no study reported adjusted risk estimates for treatment harms). We also included large (>1000 participants) uncontrolled observational studies of perioperative mortality and surgical complications.

We classified "no treatment," "observation," or "deferred treatment" as watchful waiting because patients probably received at least watchful waiting. We also grouped watchful waiting with active surveillance because studies of active surveillance provided insufficient information to determine whether more active follow-up actually occurred (14), and older studies used these terms interchangeably.

Context

Examining the tradeoffs between potential benefits and harms of prostate cancer screening is a hot topic.

Contribution

This updated systematic review for the U.S. Preventive Services Task Force found the following: screening based on prostate-specific antigen led to detection of more cases of prostate cancer, small to no reduction in prostate cancer–specific mortality after about 10 years, and several potential harms related to false-positive test results and subsequent evaluations and therapies.

Caution

Evidence regarding the mortality-associated benefits of screening conflicted.

Implication

The clinical benefits of screening for prostate cancer remain uncertain. Consequences include evaluations and treatments that have associated complications and that may be unnecessary.

—The Editors

Data Extraction and Quality Assessment

One investigator abstracted details on the patient population, study design, analysis, duration of follow-up, and results. A second investigator reviewed data abstraction for accuracy. Two investigators independently applied criteria developed by the USPSTF (15) to rate the quality of each study as good, fair, or poor. Discrepancies were resolved through a consensus process.

Data Synthesis and Analysis

We assessed the aggregate internal validity (quality) of the body of evidence for each key question (good, fair, and poor) by using methods developed by the USPSTF on the basis of the number, quality, and size of studies; consistency of results between studies; and directness of evidence (15). We synthesized results of treatment studies descriptively, using medians and ranges, because few randomized, controlled trials (RCTs) were available and studies varied in the populations and interventions evaluated, methodologic quality, duration of follow-up, and other factors. We stratified results according to study type and qualitatively assessed the effects of study quality, duration of follow-up, year of publication, and mean age on results.

Role of the Funding Source

This study was funded by the Agency for Healthcare Research and Quality (AHRQ) under a contract to support the work of the USPSTF. Staff at AHRQ and USPSTF members helped develop the scope of this work and reviewed draft manuscripts. The draft systematic reviews were reviewed by external peer reviewers not affiliated with the USPSTF, then revised for the final version. Approval from AHRQ was required before this manuscript could be

submitted for publication, but the authors are solely responsible for the content and the decision to submit.

RESULTS

Appendix Figures 1 and 2 (available at www.annals.org) show the results of the search and study selection process.

We identified 2 fair-quality (6, 7) and 3 poor-quality (16–20) randomized trials of PSA-based screening (**Appendix Table 1**, available at www.annals.org). We also included a report describing results from a single center (21) participating in a fair-quality trial (7). Sample sizes ranged from 9026 to 182 160 and maximum follow-up from 11 to 20 years (median, 6 to 14 years).

We identified 11 studies (2 RCTs [22–29] and 9 cohort studies [30–38]) on benefits of prostate cancer treatments and 16 studies (2 RCTs [39–42] and 14 cohort studies [43–58]) on harms (**Appendix Table 2**, available at www.annals.org). Sample sizes ranged from 72 to 44 630 and duration of follow-up from 1 to 23 years. Four studies were rated good quality (23, 42, 52, 56, 58), 1 poor quality (29), and the remainder fair quality. Frequent methodologic shortcomings were failure to describe loss to follow-up (6 cohort studies and all 3 RCTs met this criterion) and inadequate blinding of outcome assessors (no cohort studies and 1 RCT met this criterion). Only 2 studies (33, 40) clearly described the control group intervention (**Appendix Table 2**). We also included 6 observational studies (59–64) of surgical complications after prostatectomy.

Key Question 1: Does PSA-Based Screening Decrease Prostate Cancer–Specific or All-Cause Mortality?

The fair-quality U.S. Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial randomly assigned 76 693 men between 55 and 74 years of age to annual PSA screening in combination with digital rectal examination versus usual care (6). After 7 years' (complete) follow-up, screening was associated with increased prostate cancer incidence (relative risk [RR], 1.2 [95% CI, 1.2 to 1.3]) but no effect on prostate cancer–specific (RR 1.1 [CI, 0.75 to 1.7]) or all-cause (RR, 0.98 [CI, 0.92 to 1.0]) mortality. Similar results were observed after 10 years (67% of sample; RR, 1.1 [CI, 0.80 to 1.5]). Up to 52% of men assigned to usual care underwent a PSA test at some point during the trial, and 44% of trial participants had undergone PSA screening before entry.

The fair-quality European Randomized Study of Screening for Prostate Cancer (ERSPC) randomly assigned 182 000 men aged 50 to 74 years from 7 countries to PSA testing every 2 to 7 years (depending on center and year) or to usual care (7). Data from 2 other study centers were excluded for reasons not specified in the study protocol. Levels of PSA for diagnostic evaluation ranged from 2.5 to 4.0 μg/L (1 center used 10 μg/L for several years). Recruitment and randomization procedures and age eligibility also varied. After a median of 9 years, prostate cancer incidence was higher in the screened group (net increase, 34 per 1000 men), but there was no statistically significant difference in prostate cancer–specific mortality (RR, 0.85 [CI, 0.73 to 1.0]). A prespecified subgroup analysis of 162 243 men aged 55 to 69 years found that screening was associated with reduced prostate cancer–specific mortality (RR, 0.80 [CI, 0.65 to 0.98]; absolute risk reduction, 0.07 percentage point), for an estimated 1410 men invited to screening and 48 treated to prevent 1 prostate cancer–specific death.

After publication of the main ERSPC results, 1 participating center (Göteborg, Sweden) reported results separately (21). It found PSA screening (threshold, 2.5 to 3.0 μg/L) every 2 years in 20 000 men age 50 to 64 years to be associated with increased prostate cancer incidence (hazard ratio [HR], 1.6 [CI, 1.5 to 1.8]) and decreased risk for prostate cancer–specific mortality (RR, 0.56 [CI, 0.39 to 0.82]; absolute risk reduction, 0.34 percentage point) after a median of 14 years. Outcomes for 60% of participants were included in the main ERSPC report (7). Although no other center separately reported results, only exclusion of the Swedish center data from the overall ERSPC analysis resulted in loss of the statistically significant effect of screening on prostate cancer–specific mortality (RR, 0.84 [CI, 0.70 to 1.01]), suggesting better results than the other centers (7).

Three poor-quality trials (number of men invited to screening ranged from 1494 to 31 333) found no difference between screening-invited and control groups in prostate cancer–specific mortality risk (16, 17, 20). Two of the trials (17, 19) were included in the 2008 USPSTF review (4); results after 5 years' additional follow-up are now available from 1 of the trials (20). Methodological shortcomings in these trials included failure to describe adequate randomization or allocation concealment methods, poorly described loss to follow-up, and unclear masking of outcomes assessors. One trial used a high PSA cut point (10 μg/L) (16).

Key Question 2: What Are the Harms of PSA-Based Screening for Prostate Cancer?

Direct harms of PSA-based screening were reported in the ERSPC and PLCO trials (6, 7). The Finnish center of the ERSPC trial found that 12% of men received at least 1 false-positive result after 3 rounds of PSA testing (cutoff, 4.0 μg/L) (65). For the entire ERPSC trial, 76% of prostate biopsies for an elevated PSA level identified no cancer (7). In the PLCO trial, the cumulative risk for at least 1 false-positive result was 13% after 4 PSA tests (cutoff, 4.0 μg/L), with a 5.5% risk for undergoing at least 1 biopsy due to a false-positive test result (66).

Physical harms of screening in the PLCO trial included bleeding or pain from digital rectal examination (0.3 event per 10 000 men screened); bruising or fainting due to venipuncture (26 events per 10 000 men screened);

and biopsy complications, such as infection, bleeding, and urinary difficulties (68 events per 10 000 evaluations) (6). The Rotterdam, Netherlands, center of the ERSPC trial reported that among 5802 biopsies performed, 200 men (3.5%) developed fever, 20 (0.4%) experienced urine retention, and 27 (0.5%) required hospitalization for signs of prostatitis or urosepsis (67).

None of the RCTs of PSA-based screening provided information on potential psychological harms, such as anxiety, or adverse effects on health-related quality of life. The 2008 USPSTF review found evidence that false-positive PSA test results are associated with adverse psychological effects but could not estimate their magnitude (4).

Key Question 3: What Are the Benefits of Treatment of Early-Stage or Screening-Detected Prostate Cancer?

Prostatectomy

Prostatectomy was compared with watchful waiting in 1 good-quality RCT ($n = 695$) of men with localized (stage T1b, T1c, or T2) prostate cancer (**Appendix Table 3**, available at www.annals.org) (22–24, 28). It did not specifically enroll men with screening-detected prostate cancer, and about 75% of cancers were palpable (stage T2). By comparison, 36% of localized cancers in the ERSPC screening trial were stage T2 (7). The 2002 USPSTF review included results through 6 years of follow-up (28). Data now available through 15 years showed a sustained decrease in risk for prostate cancer–specific mortality (15% vs. 21%; RR, 0.62 [CI, 0.44 to 0.87]; absolute difference, 6.1 percentage points [CI, 0.2 to 12 percentage points]) and all-cause mortality (RR, 0.75 [CI, 0.61 to 0.92]; absolute difference, 6.6 percentage points [CI, −1.3 to 14 percentage points]) (23). In subgroup analyses, benefits were restricted to men younger than 65 years of age (RR, 0.49 [CI, 0.31 to 0.79] for prostate cancer–specific mortality; RR, 0.52 [CI, 0.37 to 0.73] for all-cause mortality). A small ($n = 142$), poor-quality RCT found no difference between prostatectomy and no prostatectomy for localized prostate cancer on overall survival through 23 years (29). It did not report prostate cancer–specific mortality.

Eight cohort studies (median $n = 2264$ [range, 316 to 25 900]) with a duration of follow-up ranging from 4 to 13 years consistently found prostatectomy for localized prostate cancer to be associated with decreased risk for all-cause mortality (6 studies; median adjusted HR, 0.46 [range, 0.32 to 0.67] [31, 33–37]) and prostate cancer–specific mortality (5 studies; median adjusted HR, 0.32 [range, 0.25 to 0.50] [30, 33, 35, 36, 38]) compared with watchful waiting (**Appendix Table 3**). The largest was a fair-quality, propensity-adjusted analysis of data from the U.S. Surveillance, Epidemiology and End Results (SEER) program ($n = 25\,900$) of men 65 to 80 years of age that found decreased risk for all-cause mortality after 12 years (adjusted HR, 0.50 [CI, 0.66 to 0.72]) (37). A large ($n = 22\,385$), fair-quality Swedish cohort study also found prostatectomy to be associated with decreased risk for all-cause mortality after 4 years of follow-up, after adjustment for age, Gleason score, and PSA level (adjusted HR, 0.41 [CI, 0.36 to 0.48]) (31).

Radiation Therapy

No RCTs compared radiation therapy versus watchful waiting. Five cohort studies (median $n = 3441$ [range, 334 to 30 857]) with follow-up ranging from 4 to 13 years consistently found that radiation therapy (external-beam radiation therapy [EBRT] or unspecified modality) for localized prostate cancer was associated with decreased risk for all-cause mortality (5 studies; median adjusted HR, 0.68 [range, 0.62 to 0.81] [31, 35–38]) and prostate cancer–specific mortality (5 studies; median adjusted HR, 0.66 [range, 0.63 to 0.70]) compared with watchful waiting (**Appendix Table 3**) (30, 35–38). The largest study, a previously described analysis of SEER data, found radiation therapy to be associated with decreased propensity-adjusted risk for all-cause mortality (adjusted HR, 0.81 [CI, 0.78 to 0.85]) (37). A large Swedish cohort study (also described earlier) found radiation therapy to be associated with decreased risk for all-cause mortality (adjusted HR, 0.62 [CI, 0.54 to 0.71]) (31).

Key Question 4: What Are the Harms of Treatment of Early-Stage or Screening-Detected Prostate Cancer?

Prostatectomy

Urinary Incontinence and Erectile Dysfunction. Prostatectomy was associated with increased risk for urinary incontinence compared with watchful waiting in 1 RCT (RR, 2.3 [CI, 1.6 to 3.2]) (41) and 4 cohort studies (median RR, 4.0 [range, 2.0 to 11]) (**Appendix Table 4**, available at www.annals.org) (47, 49, 53, 56). In the RCT, the absolute increase in risk for urinary incontinence with surgery was 28 percentage points (49% vs. 21%) (41). In the cohort studies, the median rate of urinary incontinence with watchful waiting was 6% (range, 3% to 10%), with prostatectomy associated with a median increase in absolute risk of 18 percentage points (range, 8 to 40 percentage points) (47, 49, 53, 56).

Prostatectomy was also associated with an increased risk for erectile dysfunction compared with watchful waiting in 1 RCT (RR, 1.8 [CI, 1.5 to 2.2]) (41) and 5 cohort studies (median RR, 1.5 [range, 1.3 to 2.1]) (**Appendix Table 4**) (47, 49, 53, 54, 56). In the RCT, the absolute increase in risk for erectile dysfunction with surgery was 36 percentage points (81% vs. 45%) (41). In the cohort studies, the median rate of erectile dysfunction with watchful waiting was 52% (range, 26% to 68%), with prostatectomy associated with a median increase in absolute risk of 26 percentage points (range, 21 to 29 percentage points) (47, 49, 53, 54, 56).

Differences in study quality, duration of follow-up, or year of publication did not seem to explain differences in estimates across studies. The studies provided few details

about the specific surgical procedures evaluated, although open retropubic radical prostatectomy was the dominant procedure when most of the studies were conducted (68). One observational study stratified estimates for erectile dysfunction and urinary incontinence by use of a nerve-sparing (n = 494; 68% and 9.4%, respectively) versus a non–nerve-sparing (n = 476; 87% and 15%, respectively) technique (56).

Consistent with the studies reporting dichotomous outcomes, 8 cohort studies that evaluated urinary and sexual function outcomes by using continuous scales found that prostatectomy was associated with worse outcomes compared with watchful waiting (**Appendix Table 4** [43, 46, 48, 51, 53, 55–57]).

Quality of Life. Eight studies reported generic quality of life (43, 46, 48, 50, 51, 53, 55, 56). Two studies reported very similar Short-Form 36 (SF-36) physical and mental component summary scores after prostatectomy and watchful waiting (**Appendix Table 5,** available at www.annals.org) (43, 56). On specific SF-36 subscales, prostatectomy was associated with better physical function (6 studies; median difference, 8 points [range, 2 to 16 points]) (43, 46, 48, 51, 53, 55) and emotional role function subscale scores (7 studies; median difference, 8 points [range, −5 to 13 points]) (43, 46, 48, 50, 51, 53, 55), with small or no clear differences on other SF-36 subscales.

Surgical Complications. The largest (n = 101 604) study of short-term (≤30-day) complications after prostatectomy reported a 30-day perioperative mortality rate of 0.5% in Medicare claimants (60); 3 other large observational studies reported similar findings (59, 61, 62). Advanced age and increased number of serious comorbid conditions were associated with higher perioperative mortality, although absolute rates were less than 1% even in men at higher risk. In the Medicare database study, perioperative rates of serious cardiovascular events were 3% and rates of vascular events (including pulmonary embolism and deep venous thrombosis) were 2% (60). In 2 other studies (n = 1243 [63] and 11 010 [59]), rates of cardiovascular events were 0.6% and 3% and rates of vascular events 1% and 2%, respectively. Serious rectal or ureteral injury due to surgery ranged from 0.3% to 0.6% (60, 63).

Other Harms. Five studies (reported in 6 publications) found no clear differences between prostatectomy and watchful waiting in risk for bowel dysfunction (41, 42, 46, 47, 49, 56). One RCT found no difference between prostatectomy and watchful waiting in risk for high levels of anxiety, depression, or worry after 4 years (42).

Radiation Therapy

Urinary Incontinence and Erectile Dysfunction. Radiation therapy was associated with increased risk for urinary incontinence compared with watchful waiting in 1 small RCT, but the estimate was very imprecise (RR, 8.3 [CI, 1.1 to 63]) because of small numbers of events (1 in the watchful waiting group) (**Appendix Table 4**) (39). There was no clear increase in risk in 4 (total n = 1910) cohort studies (median RR, 1.1 [range, 0.71 to 2.0]) (47, 49, 53, 56).

Radiation therapy was associated with increased risk for erectile dysfunction compared with watchful waiting in 6 cohort studies, with similar estimates across studies (median RR, 1.3 [range, 1.1 to 1.5]) (**Appendix Table 4**) (47, 49, 53, 54, 56, 58). Rates of erectile dysfunction ranged from 26% to 68% (median, 50%) with watchful waiting; radiation therapy was associated with a median increase in pooled absolute risk of 14 percentage points (range, 7 to 22 percentage points).

Five of the six studies did not provide details about the type of radiation therapy (for example, EBRT versus brachytherapy) or dosing regimen. One good-quality cohort study reported a 7.0% rate of urinary incontinence after high-dose brachytherapy (n = 47), 5.4% after low-dose brachytherapy (n = 58), and 2.7% after EBRT (n = 123) (56). Rates of erectile dysfunction were 72%, 36%, and 68%, respectively.

Consistent with the studies reporting dichotomous outcomes, 10 studies found radiation therapy to be associated with worse sexual function compared with watchful waiting on the basis of continuous scales, although no clear differences were seen in sexual bother scores and measures of urinary function (**Appendix Table 4**) (40, 43, 46, 48, 51, 53, 55–58).

Quality of Life. Ten studies reported generic quality of life (40, 43, 46, 48, 50, 51, 53, 55, 56, 58). Three studies found no differences between radiation therapy and watchful waiting in SF-36 physical (median difference, 0 points [range, −3 to 0 points]) or mental (median difference, 0 points [range, −2 to 1 point]) component summary scores (**Appendix Table 4**) (43, 56, 58). Results favored watchful waiting on the physical role function subscale (7 studies; median difference, −9 points [range, −22 to 1 point]) (43, 46, 48, 51, 53, 55, 58), with no clear differences on other SF-36 subscales.

Other Harms. Six cohort studies consistently found radiation therapy to be associated with worse Prostate Cancer Index bowel bother (median difference, −6 points [range, −10 to −2 points]) and function (median difference, −8 points [range, −15 to −3 points) than watchful waiting (43, 48, 51, 53, 56, 58). In studies that evaluated bowel function serially, effects seemed to be most pronounced in the first few months after radiation therapy and gradually improved (40, 46, 51, 57). This might help explain the inconsistent results among studies that reported dichotomous outcomes. Although 1 study found radiation therapy associated with substantially increased risk for bowel urgency after 2 years (3.2% vs. 0.4%; RR, 7.5 [CI 1.0 to 56]) (47), 2 studies with longer duration of follow-up (5.6 [49] and 3 years [56]) found no increased risk.

One cohort study reported similar effects of EBRT and brachytherapy on Prostate Cancer Index bowel func-

tion and bother (43). Another study found low-dose brachytherapy to be associated with smaller effects on bowel bother (about 3-point change from baseline) compared with high-dose brachytherapy (9-point change) or EBRT (8-point change) (56).

No study reported effects of radiation therapy versus watchful waiting on anxiety or depression.

Discussion

The **Table** shows our summary of the evidence. Screening based on PSA identifies additional cases of prostate cancer, but most trials found no statistically significant effect on prostate cancer–specific mortality. Recent meta-analyses of randomized trials included in this review found no pooled effect of screening on prostate cancer–specific mortality (69, 70). However, the 2 largest and highest-quality trials reported conflicting results (6, 7). The ERSPC trial found PSA screening every 2 to 7 years to be associated with a 20% relative reduction in risk for death from prostate cancer in a prespecified subgroup of men aged 55 to 69 years (7), whereas the PLCO trial found no effect (6). High rates of previous PSA screening and contamination in the control group of the PLCO trial may have reduced its ability to detect benefits, although these factors do not explain the trend toward increased risk for prostate cancer–specific mortality in the screened group. The proportion of men in the PLCO trial who initially chose active surveillance or expectant management instead of curative treatment was lower than in the ERSPC trial (10% vs. 19%), and the PLCO trial evaluated a shorter screening interval (annual vs. every 2 to 7 years), suggesting that more conservative screening and treatment strategies might be more effective than more aggressive ones. Chance could also explain the apparent discrepancy between the 2 trials because the risk estimate CIs overlapped. Additional follow-up might help resolve the discrepancy, given the long lead time (10 to 15 years) that may be necessary to fully understand the effect of PSA-based screening.

Treatment studies can help inform screening decisions by providing information about potential benefits of interventions once prostate cancer is detected. However, only 1 good-quality randomized trial compared an active treatment for localized prostate cancer with watchful waiting (23). It found that prostatectomy was associated with decreased risk for all-cause and prostate cancer–specific mortality after 15 years of follow-up, although benefits seemed to be limited to younger men on the basis of subgroup analyses. Because the RCT did not enroll men specifically with screening-detected prostate cancer, its applicability to screening is uncertain. Although cohort studies consistently found prostatectomy and radiation therapy to be associated with decreased risk for all-cause and prostate cancer–specific mortality compared with watchful waiting, estimates are susceptible to residual confounding, even after statistical adjustment.

Screening is associated with potential harms, including serious infections or urine retention in about 1 of 200 men who undergo prostate biopsy as a result of an abnormal screening result. False-positive screening results occurred in 12% to 13% of men randomly assigned to PSA-based screening (65, 66), with 1 trial reporting no prostate cancers in three quarters of screening-triggered biopsies (7). Screening also is likely to result in overdiagnosis because of the detection of low-risk cancers that would not have caused morbidity or death during a man's lifetime, and overtreatment of such cancers, which exposes men to unnecessary harms (71). Over three quarters of men with localized prostate cancer (about 90% of screening-detected cancers are localized) undergo prostatectomy or radiation therapy (11, 12). On the basis of data from the ERSPC trial, the rate of overdiagnosis with screening was estimated to be as high as 50% (72), and 48 men received treatment for every prostate cancer–specific death prevented (7). Treating approximately 3 men with prostatectomy or 7 with radiation therapy instead of watchful waiting would each result in 1 additional case of erectile dysfunction, and treating approximately 5 men with prostatectomy instead of watchful waiting would result in 1 additional case of urinary incontinence. Prostatectomy and radiation therapy were not associated with worse outcomes on most measures related to general health-related quality of life compared with watchful waiting, suggesting that negative effects related to specific harms may be offset by positive effects (perhaps related to less worry about untreated prostate cancer). Prostatectomy was also associated with perioperative (30-day) mortality (about 0.5%) and cardiovascular events (0.6% to 3%), and radiation therapy was associated with bowel dysfunction.

The evidence on treatment-related harms reviewed for this report seemed to be most applicable to open retropubic radical prostatectomy and EBRT, although details of specific surgical techniques or radiation therapy techniques and dosing regimens were frequently lacking. We found little evidence with which to evaluate newer techniques for prostatectomy (including nerve-sparing approaches that use laparoscopy, either robotic-assisted or freehand) compared with watchful waiting, but found no pattern suggesting that more recent studies reported different risk estimates than older studies. Limited data suggest that low-dose brachytherapy may be associated with fewer harms than high-dose brachytherapy or EBRT (56). A potential harm of radiation therapy not addressed in this review is secondary posttreatment carcinogenic effects (73, 74).

Other treatments used for localized prostate cancer are reviewed in the full report, available on the USPSTF Web site (10). Although androgen deprivation is the next most commonly used therapy for localized prostate cancer after prostatectomy and radiation therapy (11), it is comparatively uncommon and is not recommended as primary therapy (75, 76) because of evidence suggesting ineffectiveness (32), as well as an association with important adverse

Table. Summary of Evidence

Studies (*n*), and Overall Quality	Limitations	Consistency	Applicability to Screening Population	Summary of Findings
KQ 1. Does PSA-based screening decrease prostate cancer–specific or all-cause mortality?				
5 RCTs Overall quality: fair	Only 2 fair-quality RCTs; 1 additional fair-quality report from a center participating in 1 of the RCTs with substantial population overlap	Low (inconsistent results between highest-quality trials)	Some screening practices (interval and PSA thresholds) were different from typical U.S. practice	PSA-based screening identifies more prostate cancers, but most trials found no effect on risk for death from prostate cancer. However, the 2 largest and highest-quality trials reported conflicting results. The ERSPC trial found PSA screening every 2–7 y to be associated with decreased risk for death from prostate cancer in a prespecified subgroup of men aged 55–69 y after 9 y (RR, 0.80 [95% CI, 0.65–0.98]; absolute risk reduction, 0.07 percentage point), but the PLCO trial found no effect after 10 y (RR, 1.1 [CI, 0.80–1.5]). The PLCO trial had a relatively high rate of previous PSA testing (44%) and contamination in the control group (50% received ≥1 PSA test). The ERSPC trial varied in recruitment and randomization procedures, screening intervals, and PSA cut points among study centers. There were greater use of active treatments and more frequent screening intervals in the PLCO trial than the ERSPC trial. A fair-quality study from 1 center participating in the ERSPC trial reported better results than the overall ERSPC analysis, with substantial overlap in patient populations. Three poor-quality screening trials did not find PSA-based screening associated with decreased risk for death from prostate cancer.
KQ 2. What are the harms of PSA-based screening for prostate cancer?				
2 RCTs Overall quality: fair	Randomized evidence available only from 2 fair-quality trials	High	Some screening practices (interval and PSA thresholds) differed from typical U.S. practice	Reports from 2 fair-quality trials found false-positive rates of 12%–13% after 3–4 rounds of PSA-based screening, and 1 trial found that 76% of prostate biopsies identified no cancer. Serious infections or urine retention occurred after 0.5%–1.0% of prostate biopsies. Evidence was insufficient to estimate the magnitude of psychological harms associated with false-positive PSA test results.
KQ 3. What are the benefits of treatment of early-stage or screening-detected prostate cancer?				
Prostatectomy				
10 studies: 2 RCTs, 8 cohort studies Overall quality: fair	Only 1 RCT	High	Prostate cancers in the RCT were primarily clinically detected rather than screening-detected, and there was a high proportion of stage T2 cancers; limited information was provided on specific surgical techniques evaluated	Prostatectomy was associated with decreased risk for prostate cancer–specific mortality (RR, 0.62 [CI, 0.44–0.87]; absolute difference, 6.1 percentage points [CI, 0.2–12 percentage points]) and all-cause mortality (RR, 0.75 [CI, 0.61–0.92]; absolute difference, 6.6 percentage points [CI, −1.3 to 14 percentage points]) compared with watchful waiting after 15 y of follow-up in 1 good-quality RCT. Subgroup analysis suggests benefits are limited to men aged <65 y. Observational studies also found prostatectomy to be associated with decreased risk for death from prostate cancer (6 studies; median adjusted HR, 0.46 [range, 0.32–0.67]) and all-cause mortality (5 studies; median adjusted HR, 0.32 [range, 0.25–0.50]) after 4–13 y of follow-up compared with watchful waiting.
Radiation therapy				
5 cohort studies Overall quality: fair	No RCTs	High	Limited information provided on specific radiation therapy techniques and regimens evaluated	Radiation therapy was associated with decreased risk for prostate cancer–specific mortality (5 studies; median adjusted HR, 0.66 [range, 0.63–0.70]) and all-cause mortality (5 studies; median adjusted HR, 0.68 [range, 0.62–0.81]) after 4–13 y of follow-up compared with watchful waiting.
KQ 4. What are the harms of treatment of early-stage or screening-detected prostate cancer?				
Prostatectomy				
18 studies: 1 RCT; 11 cohort studies; 6 uncontrolled observational studies Overall quality: fair	Only 1 RCT of fair quality, unadjusted risk estimates for presence of urinary incontinence or erectile dysfunction from cohort studies	Moderate	Limited information provided on specific surgical techniques evaluated	Prostatectomy was associated with increased risk for urinary incontinence compared with watchful waiting in 1 RCT (RR, 2.3 [CI, 1.6–3.2]; risk difference, 28%) and 4 cohort studies (median RR, 4.0 [range, 2.0–11]; median risk difference, 18 percentage points [range, 8–40 percentage points]). On the basis of large databases and surgical series, prostatectomy was associated with risk for perioperative death (about 0.5%) and cardiovascular events (0.6%–3%). Prostatectomy was not associated with worse outcomes on SF-36 summary component scores and most SF-36 subscales.
Radiation therapy				
14 studies: 1 RCT; 13 cohort studies Overall quality: fair	Only 2 RCTs, unadjusted risk estimates for presence of urinary incontinence or erectile dysfunction from cohort studies	Moderate	Limited information provided on specific radiation therapy techniques and regimens evaluated	Radiation therapy was associated with increased risk for erectile dysfunction compared with watchful waiting in 6 cohort studies (median RR, 1.3 [range, 1.1–1.5]). Risk for urinary incontinence was increased in 1 RCT with a very imprecise estimate (RR, 8.3 [CI, 1.1–63]), but not in 4 cohort studies (median RR, 1.1 [range, 0.71–2.0]). Radiation therapy was also associated with an increased risk for bowel dysfunction, which appeared to improve over time. Radiation therapy was not associated with worse outcomes on SF-36 summary component scores and most SF-36 subscales.

ERSPC = European Randomized Study of Screening for Prostate Cancer; HR = hazard ratio; KQ = key question; PLCO = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; PSA = prostate-specific antigen; RCT = randomized, controlled trial; RR = relative risk; SF-36 = Short-Form 36.

events, such as coronary heart disease, myocardial infarction, diabetes, and fractures, when given for more advanced prostate cancer (77–79).

Our study has limitations. We excluded non–English-language articles, which could result in language bias, although we identified no non–English-language studies that would have met inclusion criteria. We included cohort studies of treatments, which are more susceptible to bias and confounding than well-conducted randomized trials. However, confounding by indication may be less of an issue in studies that evaluate harms (80), and analyses stratified by study design did not suggest differential estimates. If patients are selected for a specific prostate cancer treatment in part because of a lower perceived risk for harms, the likely effect on observational studies would be to underestimate risks. For mortality outcomes, which may be more susceptible to confounding by indication, we included only studies that performed statistical adjustment. Finally, studies did not distinguish well between active surveillance and watchful waiting. Active surveillance might be associated with more harms (due to repeated biopsies or subsequent interventions) than watchful waiting, and studies with well-described active surveillance interventions that are consistent with current definitions for this therapy are needed (14).

In summary, PSA-based screening is associated with detection of more prostate cancers; small to no reduction in prostate cancer–specific mortality after about 10 years; and harms related to false-positive test results, subsequent evaluation, and therapy, including overdiagnosis and overtreatment. If screening is effective, optimal screening intervals and PSA thresholds remain uncertain. The ERSPC trial evaluated longer screening intervals (2 to 7 years) and in some centers lower PSA thresholds (2.5 to 4.0 μg/L) as compared with typical U.S. practice (6). When available, results from the Prostate Cancer Intervention Versus Observation Trial, which compared prostatectomy with watchful waiting for screening-detected cancer, may help clarify which patients would benefit from prostatectomy or other active treatments, potentially reducing harms from unnecessary treatment (81).

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Acknowledgment: The authors thank Mary Barton, MD, MPP, and U.S. Preventive Services Task Force Leads Ned Calonge, MD, MPH, Michael LeFevre, MD, MSPH, Rosanne Leipzig, MD, PhD, and Timothy Wilt, MD, MPH for their contributions to this report.

Grant Support: By the Agency for Healthcare Research and Quality (contract number HHSA-290-2007-10057-I-EPC3, Task Order 3).

Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M11-1085.

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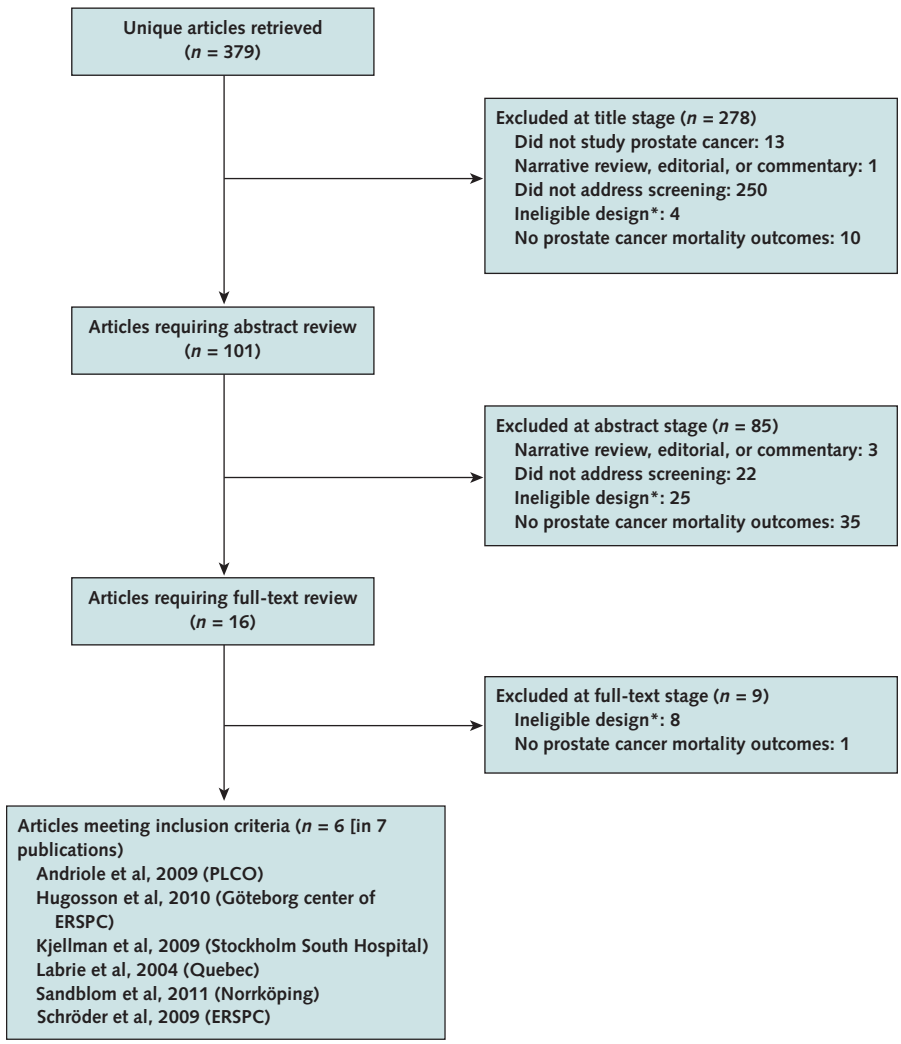
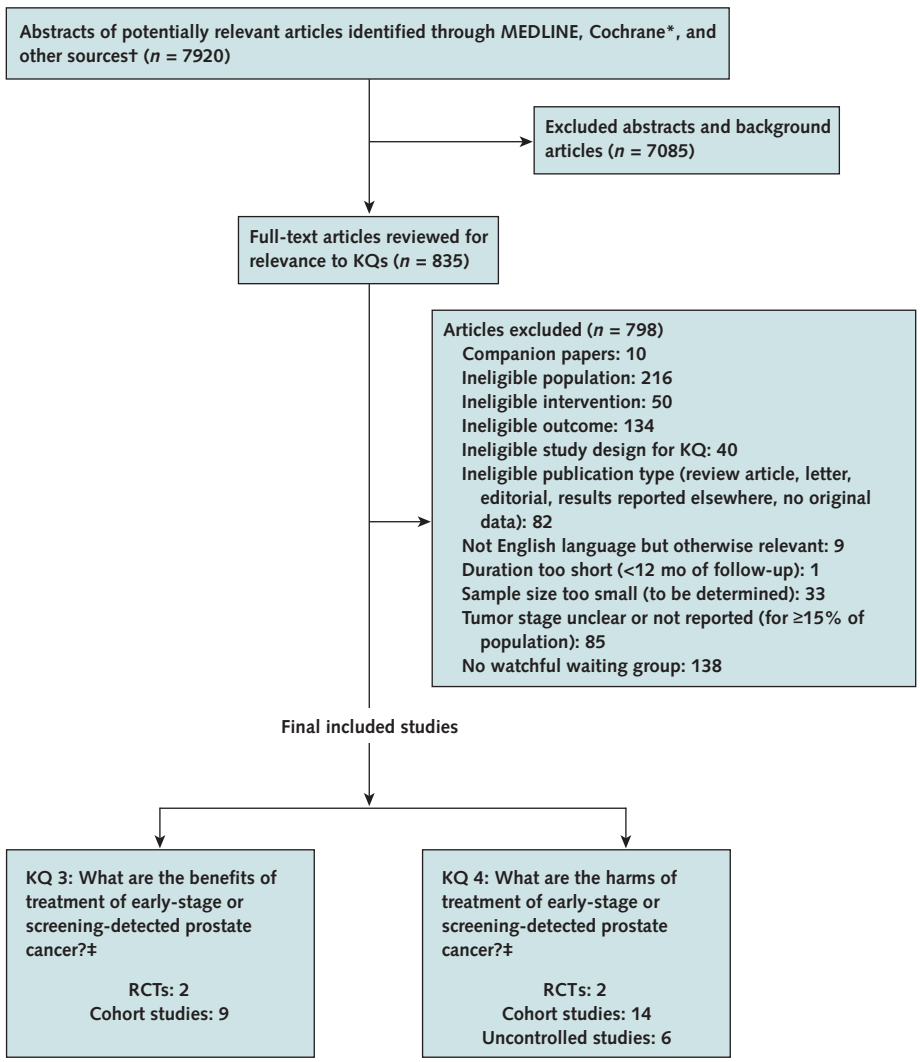
Appendix Figure 1. **Summary of literature search and selection: effectiveness and harms of screening.**



BMJ = *British Medical Journal*; ERSPC = European Randomized Study of Screening for Prostate Cancer; PLCO = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

* Not a randomized, controlled trial; systematic review; or meta-analysis; or was a nonrandomized analysis of a randomized, controlled trial.

Appendix Figure 2. **Summary of literature search and selection: effectiveness and harms of treatment.**



KQ = key question; RCT = randomized, controlled trial.
* Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
† Identified from reference lists, suggested by experts, or other methods.
‡ Excluding studies of androgen deprivation therapy, cryotherapy, and high-intensity focused ultrasonography (see the full technical report [10]).

Appendix Table 1. Randomized, Controlled Trials of Prostate-Specific Antigen–Based Screening

Study, Year (Reference)	Study Population	Study Sample	Intervention	Median/ Maximum Length of Follow-up, y	Results	Limitations	Quality Rating	Comments
ERSPC, 2009 (7)	Men in 7 European countries enrolled 1991–2003	182 160 men aged 50–74 y; 162 387 men in prespecified "core" subgroup age 55–69 y 82 816 assigned to screening; 82% had ≥1 PSA test during trial 99 184 assigned to control group; based on single site, screening in controls ~20%	Variable by center; see Appendix Table 2 for details Most centers performed PSA every 4 y; some also used DRE or TRUS PSA cut points were 2.5–10.0 μg/L; 3.0 μg/L most often used; some ancillary testing with lower PSA values Positive screening result led to biopsy; treatments according to local policies and guidelines	9/14.5	No difference in prostate cancer–specific mortality in all enrolled men: RR, 0.85 (95% CI, 0.73–1.00) Reduced prostate cancer–specific mortality in "core" subgroup: ARR, 0.071%; RR, 0.80 (CI, 0.65–0.98); NNS = 1410; NNT = 48	Inconsistencies in screening intervals and PSA thresholds among study centers Methods of allocation concealment not described Differences in exclusion of men by age between centers Exclusion of data from 2 study centers (Portugal and France, which would bring the number of participating countries to 9) Inadequate reporting of attrition	Fair	
Substudy of ERSPC (Göteborg), 2010 (21)	Men born between 1930 and 1944 identified from the population register of Göteborg, Sweden, in December 1994	19 904 men aged 50–64 y 9952 invited to screening; 76% had at least 1 PSA 9952 controls not invited to screening; contamination rate estimated at 3%	PSA every 2 y for 7 rounds PSA cut point 2.5–3.0 μg/L, depending on year Positive screening result led to DRE, TRUS, and biopsy Treatment was at the discretion of the participant's personal physician	14/14	Reduced prostate cancer–specific mortality: ARR, 0.40% (CI, 0.17%–0.64%); RR, 0.56 (CI, 0.39–0.82); NNS = 293 (CI, 177–799); NNT = 12	60% of participants (men born between 1930 and 1939) previously included in overall ERSPC results No baseline sociodemographic comparison of the 2 groups Inadequate reporting of attrition Contamination rate in controls not formally assessed; unclear how 3% estimate obtained	Fair	This publication represents single-center results reported separately from the overarching ERSPC trial
Sandblom et al, 2004 (19), 2011 (20)	Male residents of Nörrkoping, Sweden, who were identified in the Swedish National Population Register in 1987	9026 men aged 50–69 y 1494 men (every sixth man) invited for screening; 70%–78% received screening, depending on year 7532 controls received usual care; unknown how many received screening	DRE only in 1987 and 1990 DRE and PSA in 1993 and 1996 PSA cut point >4.0 μg/L Positive result on screening test led to biopsy; confirmed prostate cancer treated according to regional standardized management program	6.3/20	No difference in prostate cancer–specific mortality (RR, 1.16 [CI, 0.78–1.73]) or overall survival (log-rank test P = 0.14) between invited and noninvited groups	Inadequate randomization and allocation concealment procedure (predictable group assignment) No comparison of baseline sociodemographic characteristics of the 2 groups Contamination rate in control group not assessed Inadequate reporting of attrition	Poor	Trial included in the 2008 evidence review and previously considered by the USPSTF
PLCO, 2009 (6)	Men enrolled at 10 study centers in the United States 1993–2001	76 693 men aged 55–74 y 38 343 men assigned to screening; overall adherence to screening was 85% for PSA and 86% for DRE 38 350 men assigned to usual care; 52% had ≥1 PSA test during trial	Annual PSA for 6 y Annual DRE for 4 y PSA cut point >4.0 μg/L Positive PSA or DRE result referred to patient's primary care physician for management	11.5/14.8	No difference in prostate cancer–specific mortality at 7 or 10 y: rate ratios, 1.13 [CI, 0.75–1.70] and 1.11 [CI, 0.83–1.50], respectively No difference in overall mortality (excluding from prostate, lung, or colorectal cancer) at 7 or 10 y: rate ratios, 0.98 [CI, 0.92–1.03] and 0.97 [CI, 0.93–1.01], respectively	High rate of contamination in control group (up to 52% by 6 y) Approximately 44% of men in each group had undergone ≥1 PSA test before trial entry	Fair	

Continued on following page

Appendix Table 1—**Continued**

Study, Year (Reference)	Study Population	Study Sample	Intervention	Median/ Maximum Length of Follow-up, y	Results	Limitations	Quality Rating	Comments
Labrie et al, 2004 (17)	Men registered on the Quebec City area electoral rolls in 1988	46 486 men aged 45–80 y 31 133 men invited for screening; 23.6% received screening 15 353 controls not invited; 7.3% received screening	DRE and PSA at first visit PSA alone at subsequent screenings PSA cut point >3.0 μg/L; if PSA previously >3.0 μg/L, a PSA increase of 20% over previous year's value or over predicted PSA Positive screening test result led to TRUS-guided biopsy	7.9/11	No difference in prostate cancer–specific mortality when data are analyzed via intention-to-screen: RR, 1.01 (CI, 0.82–1.40)	No information to assess adequacy of randomization or allocation concealment Unclear whether outcome assessment was blinded No baseline sociodemographic comparison of the 2 groups Inadequate reporting of attrition Authors did not primarily use intention-to-screen analysis	Poor	Trial included in the 2008 evidence review and previously considered by the USPSTF
Kjellman et al, 2009 (16)	Men living in the catchment area of Stockholm South Hospital in Sweden in 1988	26 602/27 204 men aged 55–70 y 2400 men invited for screening, 74% received screening 24 202/24 804 controls from source population received usual care; contamination not reported	Single screening with DRE, TRUS, and PSA Abnormal DRE or TRUS led to biopsy PSA cut point >7.0 ng/mL led to repeat TRUS PSA cut point >10.0 μg/L led to biopsy Treatment was "the standard care at the clinic at that time"	12.9/15.7	No difference in prostate cancer–specific mortality: IRR, 1.10 (CI, 0.83–1.46) No difference in death from other causes: IRR, 0.98 (CI, 0.92–1.05)	Methods of randomization and allocation concealment unclear Unclear whether outcome assessment was blinded No baseline sociodemographic comparison of the 2 groups Contamination rates in control group not assessed Inadequate reporting of attrition Limited applicability to current U.S. practice (high PSA threshold)	Poor	Report has internal discrepancies about the total number in the original cohort because the file containing the registration numbers of the original cohort could not be retrieved

ARR = absolute risk reduction; DRE = digital rectal examination; ERSPC = European Randomized Study of Screening for Prostate Cancer; IRR = incidence rate ratio; NNS = number needed to screen; NNT = number needed to treat; PLCO = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; PSA = prostate-specific antigen; RR = relative risk; TRUS = transrectal ultrasonography; USPSTF = U.S. Preventive Services Task Force.

Appendix Table 2. Studies of Treatments for Localized Prostate Cancer

Study, Year (Reference)	Interventions	Definition of Watchful Waiting	Mean Duration of Follow-up	Mean Age, y	Stage at Diagnosis	Variables Adjusted for in Analysis	Outcomes	Quality Score
RCTs								
Bill-Axelson et al, 2011 (23) Other publications: Johansson et al, 2009 (41); Bill-Axelson et al, 2008 (22); Holmberg et al, 2006 (27); Bill-Axelson et al, 2005 (24); Steineck et al, 2002 (42); Holmberg et al, 2002 (28)	Watchful waiting (n = 348) Radical prostatectomy (n = 347)	No immediate treatment	13 y (range, 3 wk–20.2 y); 15-y estimates reported	65	T1b: 12% (83/695) T1c: 12% (81/695) T2: 76% (529/695) Unknown: T2 <1% (2/695) Mean PSA level: 12.9 μg/L	NA (RCT)	Prostate cancer–specific mortality All-cause mortality	Good
Fransson et al, 2001 (39) Other publications: Fransson et al, 2009 (40)	Watchful waiting (n = 27) Radiation therapy (n = 27)	Regular monitoring and deferred treatment until time of progression	10 y	78	T1: 25% (14/57) T2: 75% (43/57)	NA (RCT)	Disease-specific quality of life Generic quality of life	Fair
Iversen et al, 1995 (29) Other publications: Byar and Corle, 1981 (25); Graversen et al, 1990 (26)	Watchful waiting (n = 68) Radical prostatectomy (n = 74)	Oral placebo, no other treatment	23 y (range, 19–27 y)	64	WHO stage I: 54% (76/142) WHO stage II: 46% (66/142)	NA (RCT)	All-cause mortality	Poor
Cohort studies								
Albertsen et al, 2007 (30)	No initial therapy (n = 114) Surgery (n = 802) Radiation (n = 702)	Observation only (not defined)	Varied according to treatment group: median, 13.1–13.6 y	68	Gleason score 2–4: 4% Gleason score 5: 6% Gleason score 6: 47% Gleason score 7: 26% Gleason score 8–10: 17%	Gleason score, PSA, clinical stage, age at diagnosis, and Charlson comorbidity score	Prostate cancer–specific mortality	Fair
Bacon et al, 2001 (43)	Watchful waiting (n = 31) Prostatectomy (n = 421) EBRT (n = 221) Brachytherapy (n = 69) Hormone (n = 33) Other* (n = 67)	Not defined	5 y	71	T1: 3% (23/842) T2: 86% (726/842) Other: 11% (93/842)	Age, marital status, waist circumference, metabolic equivalent hours of physical activity/wk, smoking status, alcohol intake, comorbid conditions, Gleason score	Disease-specific quality of life Generic quality of life	Fair
Choo et al, 2010 (44)	Watchful waiting (n = 9) Radiation therapy (n = 52; EBRT, n = 22; brachytherapy, n = 30)	Not defined	2 y	64	Tx: 4% (3/75) T1: 55% (41/75) T2: 37% (28/75) T3: 4% (3/75)	No adjustment for variables; adjustment made for repeat measures	Disease-specific quality of life	Fair
Galbraith et al, 2001 (46)	Watchful waiting (n = 30) Surgery (n = 59) Conventional radiation (n = 25) Proton-beam radiation (n = 24) Mixed-beam radiation (n = 47)	Not defined	2 y	68	Stage NR (mean PSA values ranged from 9.8 to 17.6 μg/L at baseline depending on treatment group)	No adjustment for variables	Disease-specific quality of life Generic quality of life	Fair
Hoffman et al, 2003 (47)	No treatment (n = 230) ADT (n = 179) Radiation (n = 583) Radical prostatectomy (n = 1373)	No active treatment	2 y	66	Stage NR (all were T1 or T2)	Demographic, socioeconomic, and clinical variables (not further defined)	Disease-specific quality of life	Fair

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Appendix Table 2—Continued

Study, Year (Reference)	Interventions	Definition of Watchful Waiting	Mean Duration of Follow-up	Mean Age, y	Stage at Diagnosis	Variables Adjusted for in Analysis	Outcomes	Quality Score
Ladjevardi et al, 2010 (31)	Conservative management† (watchful waiting [*n* = 935] and palliative treatment, including ADT [*n* = 3210]) Radical prostatectomy (*n* = 12 950) Radiation therapy (*n* = 6308; EBRT, *n* = 4443; and brachytherapy, *n* = 1865)	Not defined	Median, 4 y (range, 0–12 y)	65	T0: <1% T1: 49% T2: 35% T3: 15% Tx: <1%	Age, Gleason score, PSA	All-cause mortality	Fair
Litwin et al, 1995 (48) Other publication: Litwin et al, 1995 (49)	Observation (*n* = 60) Prostatectomy (*n* = 98) Radiation (*n* = 56)	Not defined	6 y	73	Tumor stage NR (all were clinically localized)	Age; comorbid conditions (diabetes cardiovascular disease, respiratory disease, gastrointestinal disease, renal disease, depression, alcohol or drug problems, smoking)	Disease-specific quality of life Generic quality of life	Fair
Litwin et al, 2002 (50)	Watchful waiting (*n* = 66) Radical prostatectomy (*n* = 282) Radiation (*n* = 104)	Not defined	2 y	66	T1: 30% (136/452) T2: 66% (298/452) T3/4 or N+ or M+: 4% (18/452)	Comorbid conditions, PSA, Gleason score, age	Generic quality of life	Fair
Lu-Yao et al, 2008 (32)	Conservative management (*n* = 11 404) Primary ADT (*n* = 7867)	No use of surgery, radiation, or ADT	Median, 7 y	78	T1: 58% T2: 42%	Instrumental variable analysis (covariates in analysis included age, race, comorbidity status, cancer stage, cancer grade, income status, urban resident, marital status, and year of diagnosis)	Prostate cancer–specific mortality All-cause mortality	Fair
Lubeck et al, 1999 (51)	Observation (*n* = 87) Prostatectomy (*n* = 351) Radiation therapy (*n* = 75)‡	No surgery, radiation, or medical therapy in the first year after diagnosis	2 y	66	T1: 25% (174/692) T2: 62% (427/692) T3/T4: 5% (33/179) Other: 8% (52/692)	Time (mixed model used to evaluate rate of quality-of-life change); age	Disease-specific quality of life Generic quality of life	Fair
Merglen et al, 2007 (33)	Watchful waiting (*n* = 378) Prostatectomy (*n* = 158) Any EBRT (*n* = 205; EBRT alone, *n* = 152; EBRT + ADT, *n* = 53) ADT (*n* = 72) Other treatment (*n* = 31; not described)	Active follow-up with treatment for disease progression	7 y	71	Stage 1: 29% Stage 2: 40% Stage 3: 31% PSA <10 μg/L: 22% PSA 11–29 μg/L: 28% PSA >30 μg/L: 23% PSA unknown: 27%	Age, period of diagnosis, method of detection, lymph node status, clinical tumor stage, differentiation, and PSA level	Prostate cancer–specific mortality All-cause mortality	Fair
Potosky et al, 2002 (52)	Observation (*n* = 416) ADT (*n* = 245)	No therapy	1 y	Mean age, NR 40–59 y: 4% (27/661) 60–69 y: 22% (145/661) 70–79 y: 53% (350/661) ≥80 y: 21% (139/661)	T1: 33% (221/661) T2: 51% (338/661) Unknown: 15% (101/661)	Sociodemographic and clinical characteristics, presence of sexual partner, impotence, comorbid conditions, prostate cancer symptoms	Disease-specific quality of life Generic quality of life	Good
Schapira et al, 2001 (53)	Expectant management (*n* = 29) Radical prostatectomy (*n* = 42) Radiation therapy (*n* = 51)	Not defined	1 y	Median age, 69	T1: 50% (61/122) T2: 50% (61/122)	Comorbid conditions, stage, age, years of education, race, marital status, employment status	Disease-specific quality of life Generic quality of life	Fair

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Appendix Table 2—**Continued**

Study, Year (Reference)	Interventions	Definition of Watchful Waiting	Mean Duration of Follow-up	Mean Age, y	Stage at Diagnosis	Variables Adjusted for in Analysis	Outcomes	Quality Score
Schymura et al, 2010 (34)	Watchful waiting (n = 614) Radical prostatectomy (n = 1310) Radiation therapy (EBRT or brachytherapy; n = 1037) ADT (n = 339)	No therapy within 6 mo of diagnosis	5 y	Mean age, NR <60 y: 18% 60–64 y: 17% 65–69 y: 22% 70–74 y: 21% 75–79 y: 14% ≥80 y: 8%	PSA <10 μg/L: 57% PSA 10–20 μg/L: 26% PSA >20 μg/L: 11% PSA unknown: 13%	Age at diagnosis, race/ethnicity, marital status, state, PSA value, Gleason score, comorbidity score, time since diagnosis	Disease-specific quality of life Generic quality of life	Fair
Siegel et al, 2001 (54)	Watchful waiting (n = 64) Radical prostatectomy (n = 419) EBRT (n = 319)	Follow-up every 3–4 mo for 1 y, every 6 mo subsequently	4 y	66	Grade A: 7% (58/802) Grade B: 89% (713/802) Unknown: 4% (31/802)	No adjustment for variables	Disease-specific quality of life	Fair
Smith et al, 2000 (55)	Observation (n = 120) Radical prostatectomy (n = 1247) Radiation therapy (n = 189) Hormonal therapy (n = 67) Cryotherapy (n = 28)	Not defined	4 y	67	T1/T2: 98% (2194/2234) T3: <1% (9/2234) T4: 1% (29/2234)	Age, current comorbid conditions, education, time since diagnosis	Disease-specific quality of life Generic quality of life	Fair
Smith et al, 2009 (56)	Active surveillance (n = 200) Radical prostatectomy (n = 981) EBRT (n = 123) ADT (n = 61) Combined EBRT/ADT (n = 166) Low-dose brachytherapy (n = 58) High-dose brachytherapy (n = 47)	Active surveillance (not further defined)	3 y	61	T1: 54% (889/1636) T2: 46% (747/1636)	Age, insurance status, comorbidity score, stage, Gleason score, PSA	Disease-specific quality of life Generic quality of life	Good
Stattin et al, 2010 (35)	Surveillance (n = 2021) Radical prostatectomy (n = 3399) Radiation (n = 1429)	Combined active surveillance and watchful waiting (no further definition)	Median, 8.2 y	63	T1: 59% T2: 41% Mean PSA: 8.2 μg/L	Prostate cancer risk category, Charlson comorbidity index, socioeconomic status	Prostate cancer–specific mortality All-cause mortality	Fair
Talcott et al, 2003 (57) Other publication: Clark and Talcott, 2001 (45)	Observation (n = 19) Radical prostatectomy (n = 129) EBRT (n = 182) Brachytherapy (n = 80)	Not defined	2 y	65	Exact proportion of patients with T1 and T2 unclear because of reporting method; most (>70%) were T1	Age, D'Amico risk category, marital status, education, other variables (not defined)	Disease-specific quality of life	Fair
Tewari et al, 2007 (36)	Conservative management (n = 197) Radiation therapy (n = 137) Radical prostatectomy (n = 119)	Not defined	5 y	63	Stage 3: 100%	Propensity analysis (propensity score based on age at diagnosis, race, socioeconomic status, Charlson comorbidity index, and year of diagnosis)	Prostate cancer–specific mortality All-cause mortality	Fair
Thong et al, 2010 (58)	Active surveillance (n = 71) EBRT (n = 71)	Stage and tumor grade ≤2 at time of diagnosis, no active treatment	5–10 y	76	T1: 80% (114/142) T2: 20% (28/142)	Demographic and clinical characteristics	Disease-specific quality of life Generic quality of life	Good

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Appendix Table 2—**Continued**

Study, Year (Reference)	Interventions	Definition of Watchful Waiting	Mean Duration of Follow-up	Mean Age, y	Stage at Diagnosis	Variables Adjusted for in Analysis	Outcomes	Quality Score
Wong et al, 2006 (37)	Observation (n = 12 608) Active treatment (n = 32 022; includes radical prostatectomy [n = 13 292] and EBRT or brachytherapy [n = 18 249], alone or in combination)	No Medicare data for prostatectomy, radiation, or hormonal therapy	12 y	72	Stage ≤T2a : 55% Stage T2b–T2c: 45%	Propensity-adjusted (propensity score based on age at diagnosis, SEER site, year of diagnosis, tumor size, tumor grade, marital status, residence in urban setting, race, income, educational achievement, and comorbid conditions)	All-cause mortality	Fair
Zhou et al, 2009 (38)	No treatment (n = 1716) Monotherapy Radical prostatectomy (n = 889) EBRT (n = 783) Brachytherapy (n = 595) ADT (n = 2049) Combination therapy Radical prostatectomy + EBRT, ADT, or both (n = 181) EBRT + ADT (n = 1286) Brachytherapy + EBRT or ADT (n = 756)	No definitive therapy within 6 mo of diagnosis	7 y	NR; for total cohort (including 1924 patients with distant or unknown stage): 65–69 y: 21% 70–74 y: 32% ≥75 y: 46%	66% Gleason score <7	Age, race, tumor stage, Gleason score, pretreatment comorbidity	Prostate cancer–specific mortality	Fair

ADT = androgen deprivation therapy; EBRT = external-beam radiation therapy; NA = not applicable; NR = not reported; PSA = prostate-specific antigen; RCT = randomized, controlled trial; SEER = Surveillance, Epidemiology, and End Results; WHO = World Health Organization.

* Definition unclear; results not abstracted.

† Conservatively managed patients included those who received ADT.

‡ Results from the hormone therapy group were not abstracted; 32% (57/179) were at stage T3 or higher at baseline.

Appendix Table 3. Prostate Cancer–Specific and All-Cause Mortality

Study, Year (Reference) and Duration of Follow-up	Prostate Cancer–Specific Mortality	All-Cause Mortality
RCTs	**Prostatectomy vs. watchful waiting**	**Prostatectomy vs. watchful waiting**
Bill-Axelson et al, 2011 (23)	15% (CI, 11%–19%) vs. 21% (CI, 17%–26%); HR, 0.62 (CI, 0.44–0.87)	46% (CI, 41%–52%) vs. 53% (CI, 47%–59%); HR, 0.75 (CI, 0.61–0.92)
Other publications: Bill-Axelson et al, 2008 (22); Holmberg et al, 2006 (27); Bill-Axelson et al, 2005 (24); Steineck et al, 2002 (42); Holmberg et al, 2002 (28)	Subgroups: Risk 6.5% (CI, 3.5%–14%) vs. 11% (CI, 6.8%–18%); HR, 0.53 (CI, 0.24–1.1) Subgroups: Age Age <65 y: 16% (CI, 11%–24%) vs. 26% (CI, 20%–34%); HR, 0.49 (CI, 0.31–0.79) Age ≥65 y: 13% (CI, 8.9%–19%) vs. 16% (CI, 11%–23%); HR, 0.83 (CI, 0.50–1.3)	Subgroups: Risk Low risk: 31% (CI, 24%–41%) vs. 45% (37% vs. 54%); HR, 0.62 (CI, 0.42–0.92) Subgroups: Age Age <65 y: 34% (CI, 27%–43%) vs. 47% (CI, 40%–56%); HR, 0.52 (CI, 0.37–0.73) Age ≥65 y: 57% (CI, 50%–65%) vs. 57% (CI, 50%–66%); HR, 0.98 (CI, 0.75–1.3)
Follow-up duration: 13 y	Subgroups: Risk + age Age <65 y and low risk: 7.1% (CI, 2.7%–19%) vs. 12% (CI, 6.0%–23%); HR, 0.41 (CI, 0.14–1.2) Age <65 y and low risk: 6.6% (CI, 2.5%–17%) vs. 10% (CI, 5.1%–21%); HR, 0.76 (CI, 0.35–2.3)	Subgroups: Risk + age Age <65 y and low risk: 17% (CI, 9.5%–30%) vs. 36% (CI, 26%–50%); HR, 0.36 (CI, 0.18–0.7) Age ≥65 y and low risk: 47% (CI, 35%–62%) vs. 53% (CI, 41%–68%); HR, 0.92 (CI, 0.57–1.5)
Iversen et al, 1995 (29) Other publications: Byar and Corle, 1981 (25); Graversen et al, 1990 (26) Follow-up duration: 23 y	NR	Median duration of survival: 8 y vs. 11 y; $P > 0.05$
Cohort studies	**Prostatectomy vs. watchful waiting**	**Prostatectomy vs. watchful waiting**
Albertsen et al, 2007 (30) Follow-up duration: 13 y	14% vs. 4%; RR, 3.4 (CI, 1.9–5.9)	NR
Ladjevardi et al, 2010 (31) Follow-up duration: 4 y	NR	HR, 0.41 (CI, 0.36–0.48) Subgroups: Risk Gleason score 7: HR, 0.78 (CI, 0.63–0.97) Gleason score 8–10: HR, 0.65 (CI, 0.47–0.90)
Merglen et al, 2007 (33) Follow-up duration: 7 y	5-y mortality: 8/158 (5%) vs. 43/378 (11%); HR, 0.56 (CI, 0.24–1.3) 10-y mortality: 15/158 (9%) vs. 70/378 (11%); HR, 0.59 (CI, 0.26–0.91) Subgroups: Risk 10-y mortality, Gleason score <7: 9/112 (8%) vs. 31/225 (14%); HR, 0.5 (CI, 0.22–1.1) 10-y mortality, Gleason score ≥7: 4/31 (13%) vs. 28/76 (37%); HR, 0.23 (CI, 0.06–0.91) Subgroups: Age 10-y mortality, age <70 y: 5/118 (4%) vs. 13/104 (13%); HR, 0.12 (CI, 0.04–0.42) 10-y mortality, age ≥70 y: 10/40 (25%) vs. 57/274 (21%); HR, 1.25 (CI, 0.59–2.5)	5-y mortality: 21/158 (13%) vs. 147/378 (39%); HR, 0.71 (CI, 0.4–1.4) 10-y mortality: 34/158 (22%) vs. 223/378 (60%); HR, 0.67 (CI, 0.4–1.1)
Schymura et al, 2010 (34) Follow-up duration: 5 y	NR	6% vs. 25%; HR, 0.44 (CI, 0.33–0.59)
Stattin et al, 2010 (35) Follow-up duration: 8 y	2.4% (CI, 1.8%–3.3%) vs. 3.6% (CI, 2.7%–4.8%); HR, 0.49 (CI, 0.34–0.71) Subgroups: Risk Low-risk: 0.4% (CI, 0.13%–0.97%) vs. 2.4% (CI, 1.2%–4.1%); HR, 0.29 (CI, 0.09–0.87) Intermediate-risk: 3.4% (CI, 2.5%–4.7%) vs. 5.2% (CI, 3.7%–6.9%); HR, 0.53 (CI, 0.35–0.80)	11% (CI, 10%–13%) vs. 23% (CI, 21%–26%); HR, 0.49 (CI, 0.41–0.57)
Tewari et al, 2007 (36) Follow-up duration: 4–6 y*	18/119 (15%) vs. 85/197 (43%); HR, 0.31 (CI, 0.17–1.2)	27/119 (23%) vs. 139/197 (71%); HR, 0.32 (CI, 0.20–0.51)
Wong et al, 2006 (37) Follow-up duration: 12 y	NR	HR, 0.50 (CI, 0.47–0.53)
Zhou et al, 2009 (38) Follow-up duration: 7 y	HR, 0.25 (CI, 0.13–0.48)	NR
Cohort studies	**Radiation therapy vs. watchful waiting**	**Radiation therapy vs. watchful waiting**
Albertsen et al, 2007 (30) Follow-up duration: 13 y	9% vs. 14%; rate ratio, 1.5 (CI, 0.9–2.6)	NR
Ladjevardi et al, 2010 (31) Follow-up duration: 4 y	NR	HR, 0.62 (CI, 0.54–0.71) Subgroups: Risk Gleason score 7: HR, 0.81 (CI, 0.66–0.99) Gleason score 8–10: HR, 0.71 (CI, 0.55–0.92)
Stattin et al, 2010 (35) Follow-up duration: 8 y	3.3% (CI, 2.5%–5.7%) vs. 3.6% (CI, 2.7%–4.8%); HR, 0.70 (CI, 0.45–1.1) Subgroups: Risk Low risk: 1.8% vs. 2.4% (CI, 1.2%–4.1%); HR, 0.94 (CI, 0.31–2.85) Intermediate risk: 3.8% (CI, 2.6%–5.4%) vs. 5.2% (CI, 3.7%–6.9%); HR, 0.66 (CI, 0.42–1.1)	18% (CI, 16%–21%) vs. 23% (CI, 21%–26%); HR, 0.68 (CI, 0.057–0.82)
Tewari et al, 2007 (36) Follow-up duration: 4–6 y*	23/137 (17%) vs. 85/197 (43%); HR, 0.63 (CI, 0.38–1.1)	58/137 (42%) vs. 139/197 (71%); HR, 0.70 (CI, 0.50–0.99)
Wong et al, 2006 (37) Follow-up duration: 12 y	NR	HR, 0.81 (CI, 0.78–0.85)
Zhou et al, 2009 (38) Follow-up duration: 7 y	EBRT: HR, 0.66 (CI, 0.41–1.0) Brachytherapy: HR, 0.45 (CI, 0.23–0.87) EBRT + ADT: HR, 0.97 (CI, 0.70–1.33) Brachytherapy + EBRT or ADT: HR, 0.46 (CI, 0.27–0.8)	EBRT: HR, 0.63 (CI, 0.53–0.75) Brachytherapy: HR, 0.4 (CI, 0.32–0.52) EBRT + ADT: HR, 0.57 (CI, 0.49–0.66) Brachytherapy + EBRT or ADT: HR, 0.32 (CI, 0.26–0.41)
Cohort studies	**ADT vs. watchful waiting**	**ADT vs. watchful waiting**
Lu-Yao et al, 2008 (32) Follow-up duration: 7 y	867/32 744 (rate, 2.6/100) events per person-year vs. 693/55 424 (rate, 1.3/100) events per person-year; HR, 1.8 (CI, 1.6–1.9) Subgroups: Risk Moderately differentiated tumors: HR, 1.8 (CI, 1.6–2.1) Poorly differentiated tumors: HR, 1.1 (CI, 1.0–1.3)	4729/39 767 (rate, 11.9/100) events per person-year vs. 6316/66 567 (rate, 9.5/100) events per person-year; HR, 1.2 (CI, 1.1–1.2) Subgroups: Risk Moderately differentiated tumors: HR, 1.2 (CI, 1.1–1.2) Poorly differentiated tumors: HR, 1.0 (CI, 1.0–1.1)
Zhou et al, 2009 (38) Follow-up duration: 7 y	HR, 1.3 (CI, 1.0–1.7)	HR, 0.91 (CI, 0.83–1.0)

ADT = androgen deprivation therapy; EBRT = external-beam radiation therapy; HR = hazard ratio; NR = not reported; RCT = randomized, controlled trial; RR = relative risk.
* Duration varied by treatment group.

Appendix Table 4. Erectile Dysfunction and Urinary Incontinence

Study, Year (Reference)	Urinary Incontinence	Erectile Dysfunction
RCTs	**Prostatectomy vs. watchful waiting**	**Prostatectomy vs. watchful waiting**
Johansson et al, 2009 (41); Steineck et al, 2002 (42)	Urinary incontinence	Erectile dysfunction
Follow-up duration: 2–8 y	49% (79/162) vs. 21% (33/155); RR, 2.3 (CI, 1.6–3.2)	81% (128/159) vs. 45% (71/158); RR, 1.8 (CI, 1.5–2.2)
Cohort studies	**Prostatectomy vs. watchful waiting**	**Prostatectomy vs. watchful waiting**
Hoffman et al, 2003 (47)	Urinary leakage, daily or more often	No erections
Follow-up duration: 2 y	35% (484/1373) vs. 8% (19/230); RR, 4.3 (CI, 2.8–6.6)	55% (757/1373) vs. 26% (60/230); RR, 2.1 (CI, 1.7–2.6)
Litwin et al, 1995b (49)	No urinary control or frequent dribbling	Poor or very poor sexual function
Follow-up duration: 6 y	19% (19/98) vs. 10% (6/60); RR, 1.9 (CI, 0.82–4.6)	78% (76/98) vs. 52% (31/60); RR, 1.5 (CI, 1.2–2.0)
Schapira et al, 2001 (53)	Urinary incontinence	Impotence
Follow-up duration: 1 y	44% (16/36) vs. 4% (1/25); RR, 11 (CI, 1.6–78)	89% (33/37) vs. 68% (17/25); RR, 1.3 (CI, 0.98–1.8)
Siegel et al, 2001 (54)	NR	Erection insufficient for intercourse
Follow-up duration: 4 y		90% (353/392) vs. 63% (40/64); RR, 1.4 (CI, 1.2–1.8)
Smith et al, 2009 (56)	Urinary incontinence	Impotence
Follow-up duration: 3 y	12% (111/981) vs. 3% (6/200); RR, 3.7 (CI, 2.4–5.7)	71% (695/981) vs. 47% (94/200); RR, 1.5 (CI, 1.3–1.8)
RCTs	**Radiation therapy vs. watchful waiting**	**Radiation therapy vs. watchful waiting**
Fransson et al, 2009 (40)	Urinary incontinence, proportion of patients using pads	NR
Follow-up duration: 3 y	17% (10/59) vs. 2% (1/49); RR, 8.3 (CI, 1.1–63)	
Cohort studies	**Radiation therapy vs. watchful waiting**	**Radiation therapy vs. watchful waiting**
Hoffman et al, 2003 (47)	Urinary leakage, daily or more often	No erections at all
Follow-up duration: 2 y	12% (71/583) vs. 8% (19/230); RR, 1.5 (CI, 0.91–2.39)	39% (228/583) vs. 26% (60/230); RR, 1.5 (CI, 1.2–1.9)
Litwin et al, 1995b (49)	No urinary control or frequent dribbling	Poor or very poor sexual function
Follow-up duration: 6 y	7% (4/56) vs. 10% (6/60); RR, 0.71 (CI, 0.21–2.4)	66% (39/59) vs. 52% (31/60); RR, 1.28 (CI, 0.94–1.7)
Schapira et al, 2001 (53)	Urinary incontinence	Impotence
Follow-up duration: 1 y	8% (3/38) vs. 4% (1/25); RR, 2.0 (CI, 0.22–18)	75% (30/40) vs. 68% (17/25); RR, 1.1 (CI, 0.80–1.5)
Siegel et al, 2001 (54)	NR	Erection insufficient for intercourse
Follow-up duration: 4 y		85% (269/315) vs. 63% (40/64); RR, 1.4 (CI, 1.1–1.7)
Smith et al, 2009 (56)	Urinary incontinence	Impotence
Follow-up duration: 3 y	2% (3/123) vs. 3% (6/200); RR, 0.81 (CI, 0.21–3.2)	59% (72/123) vs. 47% (94/200); RR, 1.2 (CI, 1.0–1.5)
Thong et al, 2010 (58)	NR	Problem getting an erection nearly all the time
Follow-up duration: 5–10 y		68% (43/63) vs. 47% (28/60); RR, 1.5 (CI, 1.1–2.0)
Cohort studies	**ADT vs. watchful waiting**	**ADT vs. watchful waiting**
Hoffman et al, 2003 (47)	Urinary leakage daily or more often	No erections at all
Follow-up duration: 2 y	11% (20/179) vs. 8% (19/230); RR, 1.4 (CI, 0.74–2.5)	75% (135/179) vs. 26% (60/230); RR, 2.9 (CI, 2.3–3.6)
Potosky et al, 2002 (52)	NR	Impotence
Follow-up duration: 1 y		77% (68/88) vs. 27% (60/223); RR, 2.9 (CI, 2.2–3.7)
Smith et al, 2009 (56)	Urinary incontinence	Impotence
Follow-up duration: 3 y	3% (2/61) vs. 3% (6/200); RR, 1.1 (CI, 0.23–5.3)	74% (45/61) vs. 47% (94/200); RR, 1.6 (CI, 1.3–1.9)

ADT = androgen deprivation therapy; NR = not reported; RCT = randomized, controlled trial; RR = relative risk.

Appendix Table 5. **Summary Scores for Disease-Specific and Generic Health-Related Quality of Life**

Scale	Radical Prostatectomy vs. Watchful Waiting		Radiation Therapy vs. Watchful Waiting		ADT vs. Watchful Waiting	
	Studies, *n* (References)	Median Difference in Mean Scores (Range)	Studies, *n* (References)	Median Difference in Mean Scores (Range)	Studies, *n* (References)	Median Difference in Mean Scores (Range)
UCLA-PCI scores						
Urinary function	6 (43, 48, 51, 53, 55, 56)	−18 (−30 to −9)	7 (43, 48, 51, 53, 55, 56, 58)	−4 (−5 to 1)	3 (43, 55, 56)	−4 (−9 to 1)
Urinary bother	6 (43, 48, 51, 53, 55, 56)	−8 (−17 to −1)	7 (43, 48, 51, 53, 55, 56, 58)	−3 (−19 to 3)	3 (43, 55, 56)	−11 (−17 to −5)
Sexual function	6 (43, 48, 51, 53, 55, 56)	−19 (−34 to −2)	6 (43, 48, 51, 53, 55, 56)	−11 (−20 to −4)	3 (43, 55, 56)	−31 (−36 to −29)
Sexual bother	6 (43, 48, 51, 53, 55, 56)	−27 (−35 to 22)	6 (43, 48, 51, 53, 55, 56)	−5 (−18 to 17)	3 (43, 55, 56)	−15 (−20 to 1)
Bowel function	5 (43, 48, 51, 53, 56)	−1 (−5 to 2)	6 (43, 48, 51, 53, 56, 58)	−6 (−10 to −2)	2 (43, 56)	Not calculated (−10 and −5)
Bowel bother	5 (43, 48, 51, 53, 56)	0 (−5 to 5)	6 (43, 48, 51, 53, 56, 58)	−8 (−15 to −3)	2 (43, 56)	Not calculated (−6 and −1)
SF-36 scores						
Physical component summary score	2 (43, 56)	Not calculated (2 and 3)	3 (43, 56, 58)	0 (−3 to 0)	2 (43, 56)	Not calculated (−8 and −3)
Mental component summary score	2 (43, 56)	Not calculated (0 and 1)	3 (43, 56, 58)	0 (−2 to 1)	2 (43, 56)	Not calculated (−3 and 0)
Physical function	6 (43, 46, 48, 51, 53, 55)	8 (2 to 16)	7 (43, 46, 48, 51, 53, 55, 58)	−5 (−10 to 4)	2 (43, 56)	Not calculated (−7 and 3)
Physical role function	6 (43, 46, 48, 51, 53, 55)	2 (−10 to 9)	7 (43, 46, 48, 51, 53, 55, 58)	−9 (−22 to 1)	3 (43, 52, 56)	−11 (−23 to −11)
Bodily pain	6 (43, 46, 48, 51, 53, 55)	3 (−5 to 10)	7 (43, 46, 48, 51, 53, 55, 58)	−5 (−11 to 0)	3 (43, 52, 56)	−6 (−8 to −1)
General health	6 (43, 46, 48, 51, 53, 55)	4 (2 to 21)	7 (43, 46, 48, 51, 53, 55, 58)	1 (−9 to 3)	2 (43, 56)	Not calculated (−5 and −2)
Vitality	7 (43, 46, 48, 50, 51, 53, 55)	3 (−2 to 14)	8 (43, 46, 48, 50, 51, 53, 55, 58)	−4 (−5 to 1)	3 (43, 52, 56)	−7 (−7 to −7)
Social function	6 (43, 48, 50, 51, 53, 55)	3 (−2 to 11)	7 (43, 46, 48, 51, 53, 55, 58)	−2 (−9 to 1)	2 (43, 56)	Not calculated (−10 and −4)
Emotional role function	7 (43, 46, 48, 50, 51, 53, 55)	8 (−5 to 13)	8 (43, 46, 48, 50, 51, 53, 55, 58)	−4 (−9 to 19)	3 (43, 52, 56)	−15 (−16 to −3)
Mental health	7 (43, 46, 48, 50, 51, 53, 55)	−1 (−4 to 10)	8 (43, 46, 48, 50, 51, 53, 55, 58)	−2 (−6 to 2)	3 (43, 52, 56)	−4 (−6 to 0)

ADT = androgen deprivation therapy; SF-36 = Short Form-36 Health Survey; UCLA-PCI = University of California, Los Angeles, Prostate Cancer Index.