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[Intervention Review]

Screening for prostate cancer

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ABSTRACT

Background

Any form of screening aims to reduce disease-specific and overall mortality, and to improve a person's future quality of life. Screening for prostate cancer has generated considerable debate within the medical and broader community, as demonstrated by the varying recommendations made by medical organizations and governed by national policies. To better inform individual patient decision-making and health policy decisions, we need to consider the entire body of data from randomised controlled trials (RCTs) on prostate cancer screening summarised in a systematic review. In 2006, our Cochrane review identified insufficient evidence to either support or refute the use of routine mass, selective, or opportunistic screening for prostate cancer. An update of the review in 2010 included three additional trials. Meta-analysis of the five studies included in the 2010 review concluded that screening did not significantly reduce prostate cancer-specific mortality. In the past two years, several updates to studies included in the 2010 review have been published thereby providing the rationale for this update of the 2010 systematic review.

Objectives

To determine whether screening for prostate cancer reduces prostate cancer-specific mortality or all-cause mortality and to assess its impact on quality of life and adverse events.

Search methods

An updated search of electronic databases (PROSTATE register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CANCERLIT, and the NHS EED) was performed, in addition to handsearching of specific journals and bibliographies, in an effort to identify both published and unpublished trials.

Selection criteria

All RCTs of screening versus no screening for prostate cancer were eligible for inclusion in this review.

Data collection and analysis

The original search (2006) identified 99 potentially relevant articles that were selected for full-text review. From these citations, two RCTs were identified as meeting the inclusion criteria. The search for the 2010 version of the review identified a further 106 potentially relevant articles, from which three new RCTs were included in the review. A total of 31 articles were retrieved for full-text examination based on the updated search in 2012. Updated data on three studies were included in this review. Data from the trials were independently extracted by two authors.

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Main results

Five RCTs with a total of 341,342 participants were included in this review. All involved prostate-specific antigen (PSA) testing, with or without digital rectal examination (DRE), though the interval and threshold for further evaluation varied across trials. The age of participants ranged from 45 to 80 years and duration of follow-up from 7 to 20 years. Our meta-analysis of the five included studies indicated no statistically significant difference in prostate cancer-specific mortality between men randomised to the screening and control groups (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.86 to 1.17). The methodological quality of three of the studies was assessed as posing a high risk of bias. The European Randomized Study of Screening for Prostate Cancer (ERSPC) and the US Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial were assessed as posing a low risk of bias, but provided contradicting results. The ERSPC study reported a significant reduction in prostate cancer-specific mortality (RR 0.84, 95% CI 0.73 to 0.95), whilst the PLCO study concluded no significant benefit (RR 1.15, 95% CI 0.86 to 1.54). The ERSPC was the only study of the five included in this review that reported a significant reduction in prostate cancer-specific mortality, in a pre-specified subgroup of men aged 55 to 69 years of age. Sensitivity analysis for overall risk of bias indicated no significant difference in prostate cancer-specific mortality when referring to the meta analysis of only the ERSPC and PLCO trial data (RR 0.96, 95% CI 0.70 to 1.30). Subgroup analyses indicated that prostate cancer-specific mortality was not affected by the age at which participants were screened. Meta-analysis of four studies investigating all-cause mortality did not determine any significant differences between men randomised to screening or control (RR 1.00, 95% CI 0.96 to 1.03). A diagnosis of prostate cancer was significantly greater in men randomised to screening compared to those randomised to control (RR 1.30, 95% CI 1.02 to 1.65). Localised prostate cancer was more commonly diagnosed in men randomised to screening (RR 1.79, 95% CI 1.19 to 2.70), whilst the proportion of men diagnosed with advanced prostate cancer was significantly lower in the screening group compared to the men serving as controls (RR 0.80, 95% CI 0.73 to 0.87). Screening resulted in a range of harms that can be considered minor to major in severity and duration. Common minor harms from screening include bleeding, bruising and short-term anxiety. Common major harms include overdiagnosis and overtreatment, including infection, blood loss requiring transfusion, pneumonia, erectile dysfunction, and incontinence. Harms of screening included false-positive results for the PSA test and overdiagnosis (up to 50% in the ERSPC study). Adverse events associated with transrectal ultrasound (TRUS)-guided biopsies included infection, bleeding and pain. No deaths were attributed to any biopsy procedure. None of the studies provided detailed assessment of the effect of screening on quality of life or provided a comprehensive assessment of resource utilization associated with screening (although preliminary analyses were reported).

Authors' conclusions

Prostate cancer screening did not significantly decrease prostate cancer-specific mortality in a combined meta-analysis of five RCTs. Only one study (ERSPC) reported a 21% significant reduction of prostate cancer-specific mortality in a pre-specified subgroup of men aged 55 to 69 years. Pooled data currently demonstrates no significant reduction in prostate cancer-specific and overall mortality. Harms associated with PSA-based screening and subsequent diagnostic evaluations are frequent, and moderate in severity. Overdiagnosis and overtreatment are common and are associated with treatment-related harms. Men should be informed of this and the demonstrated adverse effects when they are deciding whether or not to undertake screening for prostate cancer. Any reduction in prostate cancer-specific mortality may take up to 10 years to accrue; therefore, men who have a life expectancy less than 10 to 15 years should be informed that screening for prostate cancer is unlikely to be beneficial. No studies examined the independent role of screening by DRE.

PLAIN LANGUAGE SUMMARY

Screening for prostate cancer

Prostate cancer is one of the most prevalent forms of cancer in men worldwide. Screening for prostate cancer implies that diagnostic tests be performed in the absence of any symptoms or indications of disease. These tests include the digital rectal examination (DRE), the prostate-specific antigen (PSA) blood test and transrectal ultrasound (TRUS) guided biopsy. Screening aims to identify cancers at an early and treatable stage, therefore increasing the chances of successful treatment while also improving a patient's future quality of life. This review identified five relevant studies, comprised of 341,342 participants in total. Two of the studies were assessed to be of low risk of bias, whilst the remaining three had more substantive methodological weaknesses. Meta-analysis of all five included studies demonstrated no statistically significant reduction in prostate cancer-specific mortality (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.86 to 1.17). Meta-analysis of the two low risk of bias studies indicated no significant reduction in prostate cancer-specific mortality (RR 0.96, 95% CI 0.70 to 1.30). Only one study included in this review (ERSPC) reported a significant 21% relative reduction (95% CI 31% to 8%) in prostate cancer-specific mortality in a pre-specified subgroup of men. These results were primarily driven by two countries within the ERSPC study that had very high prostate cancer mortality rates and unusually large reduction estimates. Among men aged 55 to 69 years in the ERSPC study, the study authors reported that 1055 men would need to be screened to prevent one additional death from prostate cancer during a median follow-up duration of 11 years. Harms included overdiagnosis and harms associated with overtreatment, including false-positive results for the PSA test, infection, bleeding, and pain associated with subsequent biopsy.