Population screening for prostate cancer: an overview of available studies and meta-analysis

CRD summary
The authors concluded that prostate cancer screening was associated with a significant increase in diagnosis of prostate cancer, diagnosis within a more localised stage and of less aggressive tumours. The authors' conclusions reflect the evidence presented, but potential biases, unclear quality of the included trials and unexplained heterogeneity between them suggests that the reliability of these conclusions is uncertain.

Authors' objectives
To evaluate the effect of population-based screening on the incidence of prostate cancer, prostate cancer tumour grade and stage, prostate cancer mortality and overall mortality.

Searching
PubMed and Web of Science were searched to April 2011 (search terms were reported); the PubMed search included an English language restriction. An additional search for systematic reviews and meta-analyses was conducted to identify further studies of potential relevance.

Study selection
Eligible studies for inclusion were randomised controlled and comparative trials that used personalised data to investigate screening versus no screening on one or more of the following: prostate cancer incidence; stage or grade of prostate cancer tumour at diagnosis; prostate cancer mortality; or overall mortality. Screening was defined as prostate-specific antigen and/or digital rectal examination of asymptomatic men.

Age of participants ranged from 45 to 80 years. All studies employed prostate-specific antigen as the primary screening tool; some also used digital rectal examination or transrectal ultrasound for testing. Screening intervals ranged from one single screening visit to seven years; compliance for screening ranged from 24% to 94.2 %. Follow-up duration ranged from four to 20 years. Contamination within control groups ranged from 6% to 52% (where reported).

The authors did not state how many reviewers were involved in the selection of studies.

Assessment of study quality
The authors stated that the quality of the included studies was not assessed because it had already been reported by two previous systematic reviews investigating screening for prostate cancer. Methodological weaknesses of the included trials were discussed in the paper.

Data extraction
Numbers of events for dichotomous outcomes were extracted to calculate risk ratios, estimated with 95% confidence intervals.

Data were extracted by two reviewers; any discrepancies were resolved through discussion with a third reviewer.

Methods of synthesis
Nine meta-analyses were conducted for the outcomes extracted. For each meta-analysis, risk ratios (RRs) and 95% confidence intervals (CIs) were pooled using a fixed-effect model in the absence of significant statistical heterogeneity, otherwise a random-effects model was used. Statistical heterogeneity was assessed using $X^2$ and $I^2$. All meta-analyses were based on intention-to-screen analyses.

For overall and prostate cancer mortality, an adjusted analysis was planned that excluded studies with a follow-up duration of less than 8 years, studies that reported participation in the screening groups as being less than 75%, or studies where prostate-specific antigen contamination in the non-screening group exceeded 33.3%.

Results of the review
Eight studies (571,594 participants) were included in the review, which contained 210,772 screening participants and 360,822 control participants. Seven of these studies were randomised controlled trials (426,337 participants). Total sample sizes ranged from 9,026 to 162,243; number of participants per screening arm ranged from 1,494 to 72,890; number of participants per control (non-screening) arm ranged from 7,532 to 133,287.

Compared to control groups, screened groups had a statistically significantly higher risk of being diagnosed with prostate cancer (RR 1.55, 95% CI 1.17 to 2.06, I²=99%, seven trials), and a significantly higher risk of prostate cancer tumours being diagnosed as localised (RR 1.81, 95% CI 1.15 to 2.86, I²=99%, four trials). The risk of having a diagnosis of metastatic prostate cancer was lower in screened groups versus control groups but was not statistically significant (RR 0.63, 95% CI 0.38 to 1.05, I²=88%, six trials).

Compared to control groups, screened groups had a statistically significantly higher risk of being diagnosed with a low-grade prostate cancer tumour (RR 2.32, 95% CI 1.39 to 3.88, I²=99%, six trials). The risk of being diagnosed with a high-grade prostate cancer tumour was lower in screened groups versus controls; this difference was not statistically significant (RR 0.91, 95% CI 0.73 to 1.14, I²=76%, six trials).

The risk of prostate cancer mortality was lower in screened groups versus control groups but was not statistically significant (RR 0.88, 95% CI 0.72 to 1.06, I²=65%, seven trials). Following exclusion of trials meeting specific criteria recorded at the data extraction stage, the risk of prostate cancer mortality was statistically significantly lower in screening groups compared with control groups (RR 0.76, 95% CI 0.58 to 0.98, I²=66%, four trials).

Differences in all-cause mortality were not statistically significant.

Authors' conclusions
Prostate cancer screening was associated with a significant increase in diagnosis of prostate cancer, and diagnosis within a more localised stage and of less aggressive tumours. The optimum screening strategy remained unclear.

CRD commentary
The review question was clear and inclusion criteria seemed sufficient for replication. Relevant electronic databases and additional literature were searched. Efforts were made to minimise reviewer error and bias during the data extraction stage, but the number of reviewers involved in study selection was not reported. Quality assessment was not reported as having been conducted, but the authors did report low participation and compliance, contamination within control groups and inadequacy of some trials’ follow-up periods.

Study characteristics were reported and indicated that one trial’s screened group was also a sub-set within the sample of one of the other trials included. This meant that some of the patients might have been counted twice in the meta-analyses, which could have biased the results. The methods of synthesis may not have been appropriate for the data presented, due to the lack of standardised quality assessment and limited efforts made for investigating sources of heterogeneity. The criteria for adjusted analyses were defined by the authors themselves and appeared to have been unplanned at the start, which increased the risk of bias for selection of statistical analyses.

The authors’ conclusions reflect the evidence presented, but potential biases, unclear quality of the included trials and unexplained heterogeneity between them suggests that the reliability of these conclusions is uncertain.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.