Prevalence of osteoporosis in prostate cancer survivors: a meta-analysis
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CRD summary
This review concluded that the prevalence of osteoporosis in patients with prostate cancer who were undergoing androgen deprivation therapy was high, and that variation appeared to be due to treatment duration, disease stage, ethnicity, and skeletal site of diagnosis. These conclusions largely reflect the evidence presented. Methodological limitations mean that the overall reliability of the review is uncertain.

Authors' objectives
To evaluate the prevalence of osteoporosis in men with prostate cancer who were undergoing androgen deprivation therapy.

Searching
EMBASE, PubMed, and Scopus were searched to December 2012, for studies published in English. Search terms were reported.

Study selection
Eligible studies were prospective longitudinal and cross-sectional studies of men with prostate cancer undergoing androgen deprivation therapy. The primary outcomes of interest were the prevalences of osteoporosis, osteopenia and normal bone mass, as defined by the World Health Organization. Case reports, conference abstracts, and letters to editors were excluded, as were studies that did not differentiate between osteoporosis and osteopenia, and those that did not categorise men by androgen deprivation therapy status.

The included studies were published between 1999 and 2012, and were carried out in Japan, China, Australia, the USA, or Europe (including one study from the UK). The median age of patients was 72.9 years (range 64.5 to 80.0). Most patients were Caucasian; other ethnic origins were Asian, Hispanic, African American, or Mediterranean. Disease stage or grade was not well reported in the studies. The median duration of androgen deprivation therapy was 28.5 months (range 16.0 to 53.2). All of the studies used dual-energy X-ray absorptiometry to determine bone mineral density. All studies administered orchiectomy or gonadotropin-releasing hormone agonists, or both (sometimes alongside non-steroidal anti-androgens).

The authors did not state how many reviewers were involved in study selection.

Assessment of study quality
Study quality was assessed using a published checklist (referenced in the review). Four criteria related to external validity and six related to internal validity. Scores of 4 or less indicated a high risk of bias, scores of 5 to 7 indicated a moderate risk of bias, and scores of 8 to 10 indicated a low risk of bias.

The authors did not state how many reviewers were involved in the quality assessment process.

Data extraction
Data on the prevalence of normal bone mass, osteoporosis and osteopenia were extracted to calculate prevalence effect estimates and 95% confidence intervals. The studies were categorised into subgroups according to low (less than 15%), moderate (15-45%), or high (more than 45%) prevalence of osteoporosis. The authors did not state how many reviewers were involved in the data extraction process.

Methods of synthesis
Effect estimates and 95% confidence intervals for individual studies were pooled using a model that gave more weight to higher quality studies. Meta-analyses were performed separately for subgroups of osteoporosis prevalence. All meta-analyses were performed on the double arcsine square root transformed proportion, with results back transformed to the natural scale.
Statistical heterogeneity was assessed using $T^2$, Cochran's Q and $I^2$. Sensitivity analyses were performed for study characteristics, such as participant ethnicity and age, median duration or type of treatment, and regions of interest examined. The sources of heterogeneity were explored by examining the reasons for differing effect sizes in the meta-analyses.

**Results of the review**

Thirteen studies were included in the review (1,394 patients; range 18 to 343). Nine were cross-sectional, two were retrospective, one was prospective longitudinal, and one was a prospective trial. Two studies had quality scores of 4 (high risk of bias), 10 had scores of 6 or 7 (moderate risk of bias), and one had a score of 8 (low risk of bias).

The pooled prevalence of osteoporosis ranged from 9% (95% CI 6.0 to 12.0; six studies) to 53% (95% CI 48.0 to 57.0; four studies). Statistical heterogeneity was observed in studies with a low prevalence of osteoporosis (six studies; $I^2=72\%$) and in studies with a moderate prevalence (three studies; $I^2=58\%$).

Studies of non-Asian patients reported a higher prevalence of osteoporosis (34.7%, 95% CI 23.3 to 44.9; 10 studies) than those of Asian patients (15.8%, 95% CI 4.3 to 30.9; three studies). The pooled prevalence of osteoporosis was lower in studies with a median treatment duration of less than 24 months (19.8%, 95% CI 6.7 to 34.6; four studies), than those with a median duration of 24 to 30 months (20.2%, 95% CI 6.7 to 36.3; four studies) and of more than 30 months (42.7%, 95% CI 27.9 to 56.8; five studies).

Studies of patients aged 70 years or more reported a lower prevalence of osteoporosis (27.0%, 95% CI 17.6 to 36.1; nine studies) than those of younger patients (43.6%, 95% CI 23.3 to 61.2; four studies). The pooled prevalence was higher in studies measuring at the third distal radius (alone or with hip or lumbar spine; 34.3%, 95% CI 27.0 to 42.0; four studies) than at the hip or lumbar spine (31.4%, 95% CI 18.7 to 42.6; nine studies).

Further results (including those for normal bone mass and osteopenia) were reported.

**Authors’ conclusions**

The prevalence of osteoporosis in prostate cancer patients undergoing androgen deprivation therapy was high (9% to 53%), and variation in prevalence seemed to be due to duration of treatment, disease stage, ethnicity and skeletal site used to diagnose osteoporosis.

**CRD commentary**

The review question was clear and supported by reproducible inclusion criteria. Suitable databases were searched, but the restriction to studies in English and the exclusion of conference abstracts mean that relevant studies may have been missed. It was unclear whether the review processes were performed by two people, so reviewer error and bias may have been present.

The quality assessment tool appears to have been suitable and the authors acknowledged several methodological limitations in the studies, including potential selection bias and randomisation issues, non-response bias, and in the reporting of the sampling frame. The stages or grades of disease were not always reported by the studies, and there was no sensitivity analysis to explore the impact of this on the overall findings. A range of sensitivity analyses were performed to explore the influence of several other study characteristics.

The authors’ conclusions reflect the evidence presented on all aspects apart from the impact of disease stage or grade. Other potential limitations in the review and in the included studies mean that the overall reliability of the review is uncertain.

**Implications of the review for practice and research**

**Practice:** The authors stated that there was a real need for bone health conversation between health professionals and prostate cancer patients. Prior to androgen deprivation therapy, preventive strategies, such as calcium and vitamin D supplementation, were needed to avoid osteoporosis problems.

**Research:** The authors stated that research was required to investigate the impact of co-morbidity, and dietary, exercise and lifestyle factors on osteoporosis in prostate cancer patients.
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