Use of nonsteroidal anti-inflammatory drugs and prostate cancer risk: a meta-analysis

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CRD summary
This review of observational studies concluded that epidemiological evidence for a protective effect of aspirin and other nonsteroidal anti-inflammatory drugs against prostate cancer was suggestive but not conclusive. The review was generally well-conducted apart from the absence of a formal validity assessment. The cautious conclusion is probably reliable.

Authors' objectives
To assess the evidence for an association between use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) and the risk of prostate cancer.

Searching
MEDLINE, EMBASE, BIOSIS Previews, CINAHL, CancerLit, Web of Science, Science Citation Index, Scopus, the Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (CENTRAL) databases and Google Scholar were searched up to June 2008.

Search terms were reported. References of identified studies were checked.

Study selection
Observational studies that measured exposure to any particular NSAID or to a mixture of NSAIDs and assessed the incidence of prostate cancer were eligible for inclusion.

Most of the included studies assessed aspirin exposure. Studies were conducted in USA, Canada, New Zealand, Denmark, France and Italy. Mean age of participants in included studies ranged from 63 to 75 years. All studies except two assessed incidence of prostate cancer as the primary outcome; two studies assessed prostate cancer mortality.

Three reviewers independently assessed the studies for inclusion.

Assessment of study quality
The authors stated that they did not perform a formal assessment of validity, but they extracted data on aspects of study design relevant to such an assessment. These included methods used to account for bias, accuracy of exposure measurements and outcome determination. It appeared that this was undertaken independently by three reviewers.

Data extraction
Data were extracted to enable calculation of odds ratios with 95% confidence intervals (CI). Study authors were contacted for missing data on odds ratios.

Three reviewers independently extracted the data using a prespecified form; discrepancies were resolved through consensus.

Methods of synthesis
Pooled odds ratios with 95% CI were calculated using the DerSimonian and Laird random-effects model. Analyses were stratified by drug type and by whether the outcome assessed was advanced or total prostate cancer. Subgroup analyses were performed based on study design, period of recruitment, geographic region and accounting for biases. Meta-regression was used to assess the impact of these factors on change in the pooled odds ratios. Statistical heterogeneity was assessed using Cochran's Q. Publication bias was assessed using funnel plot analyses and Begg's and Egger's tests.
Results of the review
Twenty-four studies (24,230 cases) were included in the review: 14 cohort studies and 10 case-control studies.

There was no statistically significant relationship between all NSAIDs and total prostate cancer (10 studies); there was significant heterogeneity in this analysis (p<0.001). There was a statistically significant benefit to NSAID exposure for advanced prostate cancer (OR 0.75, 95% CI 0.60 to 0.93; three studies) with no significant heterogeneity.

All studies except one reported a relative risk that was less than 1.0 for the relationship between aspirin use and incidence of total prostate cancer; seven studies reported statistically significant results. Pooled odds ratios for aspirin exposure and total prostate cancer was 0.83 (95% CI 0.77 to 0.89; 17 studies) with evidence of statistical heterogeneity (p= 0.050); the odds ratio for advanced prostate cancer was 0.81 (95% CI: 0.72 to 0.92; 10 studies) with no evidence of heterogeneity.

There was no statistically significant relationship between non-aspirin NSAIDs and either total (11 studies) or advanced prostate cancer (six studies).

No evidence of publication bias was found.

Authors’ conclusions
Epidemiological evidence for a protective effect of aspirin and other NSAIDs against prostate cancer was suggestive but not conclusive.

CRD commentary
The review question was clear and inclusion criteria were defined for intervention and outcome. The authors searched multiple databases and other sources, which reduced risks of publication bias and omission of relevant studies. The authors reported that they used methods designed to reduce reviewer bias and error at all stages of the review process, but did not conduct a formal validity assessment of the included studies. The synthesis was appropriate. Heterogeneity between studies was explored.

The authors’ cautious conclusions reflect the results of the review and are probably reliable.

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

Research: The authors stated a need for well-designed observational studies with adequate exposure measurements, accurate case definition, attention to latency effects and careful adjustment for screening and other biases.

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