Aspirin and nonsteroidal anti-inflammatory drug use and risk of pancreatic cancer: a meta-analysis
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CRD summary
The authors concluded that current evidence does not support a link between aspirin and non-steroidal anti-inflammatory drug use and risk of pancreatic cancer. The limited search, absence of a formal validity assessment and limited details about the included studies make it difficult to assess the reliability of the authors’ conclusions.

Authors’ objectives
To investigate the relationship between use of non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, and risk of pancreatic cancer.

Searching
MEDLINE was searched from 1966 to October 2006 for articles in any language; the search terms were reported. The reference lists of retrieved articles were handsearched.

Study selection
Study designs of evaluations included in the review
Case-control or prospective study designs were eligible for inclusion if they reported relative risk (RR) estimates with 95% confidence intervals (CIs) or showed sufficient data to enable their calculation.

Specific interventions included in the review
Studies evaluating exposure to aspirin or other NSAIDs were eligible for inclusion. The majority of studies were of aspirin alone; some studies assessed non-aspirin NSAIDs and others assessed NSAIDs in general. Exposure to NSAIDs varied from no exposure to use more than seven times a week for more than 20 years.

Participants included in the review
Inclusion criteria for the participants were not specified. Some studies appeared to include only women. The majority of studies were carried out in the USA.

Outcomes assessed in the review
Studies measuring pancreatic cancer incidence or mortality were eligible for inclusion. The majority of studies reported pancreatic cancer incidence.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how many reviewers performed the data extraction. RRs and corresponding 95% CIs for the association between NSAID use and risk of pancreatic cancer were extracted. Factors controlled for during the analysis were also extracted. Odds ratios from case-control studies were considered to approximate to RRs as the incidence of pancreatic cancer is rare.

Methods of synthesis
How were the studies combined?
Summary RR estimates with 95% CIs were calculated using the DerSimonian and Laird random-effects model. Where results were reported separately for aspirin and NSAIDS, only data for aspirin was included in the meta-analysis to
avoid double-counting of cases. Publication bias was assessed using Egger’s regression asymmetry test.

How were differences between studies investigated?
Differences between the studies were investigated using the chi-squared and I-squared statistics. Separate analyses were carried out for different study designs, aspirin use alone, non-aspirin use alone, frequent aspirin use and long-term aspirin use.

Results of the review
Eleven studies (n=1,390,304) were included: one randomised controlled trial (n=39,876), 7 cohort studies (n=1,341,280), 2 hospital-based case-control studies (n=7,100) and one population-based case-control (n=2,048).

Use of aspirin or NSAIDs was not associated with an increased risk of pancreatic cancer when all studies were combined (RR 1.01, 95% CI: 0.91, 1.11). There was weak evidence of heterogeneity (I-squared 38.8%; p=0.09) and no evidence of publication bias (p=0.78). The results remained the same when different study designs were analysed separately.

Frequent aspirin use, defined as six or more tablets/times per week, was not associated with an increased risk of pancreatic cancer (RR 0.86, 95% CI: 0.61, 1.23; based on 4 studies). There was weak evidence of heterogeneity (I-squared 57.4%; p=0.07). Long-term use of aspirin, defined as more than 20 years, was not associated with an increased risk of pancreatic cancer (RR 1.21, 95% CI: 0.74, 1.96; based on 2 studies). There was weak evidence of heterogeneity (I-squared 69.4%; p=0.07).

When the studies of aspirin alone, non-aspirin NSAIDs and all NSAIDs were evaluated separately, there was no association between exposure to medication and risk of pancreatic cancer.

Authors' conclusions
Current epidemiological evidence does not suggest that aspirin or NSAID use lowers the risk of pancreatic cancer.

CRD commentary
Inclusion criteria for the outcomes, interventions and study design were reported clearly, although those for study design were broad and resulted in a range of included study designs. Attempts were made to minimise language bias in the search, but no attempts were made to locate unpublished studies. Publication bias was assessed and no evidence was found of bias. However, the search was restricted to one database and important data might therefore have been missed. There was insufficient information on the study selection and data extraction processes to rule out the possibility of bias and error in the review process. A validity assessment does not appear to have been carried out and there was insufficient detail on the individual studies to determine study quality. Indeed, very few details about the included studies were reported, especially in relation to populations studied, thus the generalisability of the results is unclear. The majority of the studies were conducted in the USA, which may also affect the generalisability of the results. The decision to combine the results in a meta-analysis was appropriate, although the review might have benefited from a more in-depth investigation of heterogeneity between the studies. The limited search, absence of a formal validity assessment, and limited details reported on the included studies make it difficult to assess the reliability of the authors’ conclusions.

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

Research: The authors stated that further research is required to determine whether long-term aspirin use increases the risk of pancreatic cancer.

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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.