Reviewer’s report

Title: Regular Aspirin Use and Lung Cancer Risk

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Reviewer: Prof Randall E Harris

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

Compulsory Revisions:

1. Corrections are needed in the abstract. Odds ratios of 0.63 and 0.45 indicate 37% and 55% reductions in lung cancer risk, respectively. Pooled results for non-small cell lung cancer should be included and will no doubt indicate a significant reduction in the risk for NSCLC, as well as small cell lung cancer.

2. In the methods section, n=868 cases (note the typographical error). While the frequency of conditions among the hospital controls are given, controls might also have been stratified into “cancer controls” versus “non-cancer controls”. This is important since many studies suggest low user rates of NSAIDs for cases with other cancers. Comparison of lung cancer cases with cancer controls would therefore be expected to bias results toward the null.

3. A possible flaw in the experimental design is the inclusion of only aspirin data. Was information on the use of other NSAIDs and analgesics collected? If so, what was done with the data? If not, it should be recognized that subjects using other NSAIDs (e.g., ibuprofen and prescription compounds) would tend to contaminate the reference category and bias results toward the null.

4. In the results, further comparisons of cases with "cancer controls" and "non-cancer controls" should be included and/or the data should be checked to rule out bias from the type of controls used. Also, data on NSCLC should be pooled to add statistical power. Odds ratios for NSCLC should reflect significant decreases in the risk with aspirin use.
5. In the discussion, it should be acknowledged that use of “cancer controls” would tend to bias results toward the null, since many epidemiologic studies show that NSAIDs are protective for a variety of neoplasms (e.g., breast, prostate, colon, malignant melanoma, etc.). Also, there is a strong possibility of "contamination bias" since users of non-aspirin NSAIDs would be included in the reference group (see Chapter 20, COX-2 in Cancer Prevention and Therapy, Humana, Inc., 2002).

6. In Table 1, the explanation of key results for the Rosenberg et al. report needs to be clarified. In Table 3, results should be extended to examine contrasts of cases with "cancer controls" and "non-cancer controls". In Table 5, pooled results should be given for NSCLC.

**Competing interests:**

None declared.