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Response to comment from Brasky et al.

We thank Brasky et al. for their review (Brasky et al., 2016) of our meta-analysis on the association between NSAID use and risk of endometrial cancer (Verdoodt et al., 2016). We welcome the additional information on two of their studies, and the discussion points they have raised, which are valuable contributions to the topics discussed in our meta-analysis. Below we respond to the issues raised by Brasky et al.

Regarding the choice of point estimate for the VITAL cohort study (Brasky et al., 2013), we have included a conservative estimate in our analysis of regular aspirin use, leading to a pooled relative risk of 0.92 (95% CI = 0.84–1.00) for all cohort studies combined. Brasky et al. suggest using a different estimate, which would yield a pooled relative risk of 0.91 (95% CI = 0.83–0.99) (Brasky et al., 2016). Notwithstanding the principal choice of estimate, we do not believe that the small difference between the two pooled estimates for cohort studies justifies changing or adapting the conclusions in our meta-analysis, which were based on risk estimates for both cohort and case-control studies, and on a number of sensitivity and stratified analyses. Moreover, we do not support the argument of Brasky et al. regarding the importance of statistical significance as this alone can not be used for proving a specific hypothesis or measuring the importance of the result (Wasserstein and Lazar, 2016).

Decisions on the in- or exclusion of studies were based on pre-defined, objective criteria, as recommended by the Cochrane collaboration for systematic reviews of interventions (Higgins and Green, 2011). We avoided exclusion of studies based on subjective judgement of study quality, but instead have provided a narrative discussion on the influence of the heterogeneous character and potential biases of included studies.

Finally, with regard to low-dose versus high-dose aspirin, we would like to emphasise that the optimum dose and duration of aspirin use for cancer prevention is still debated, and several studies have indicated that low-dose aspirin (~75–150 mg) is as efficient as higher-dose aspirin in preventing colorectal cancer (Cuzick et al., 2015). Naturally, caution should be exercised in the interpretation of the results for colorectal cancer in relation to other cancer sites, however, there is increasing evidence that the underlying mechanisms for the anti-neoplastic effects of aspirin are complex and not only related to cyclooxygenase inhibition and anti-inflammatory effects (Thun et al., 2012).

Conflict of interest

The authors confirm that there are no conflicts of interest.

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