

# Does low-dose aspirin decrease a woman's risk of ovarian cancer?

While low-dose aspirin (ASA) is recommended as chemoprophylaxis for some cancers, **there are insufficient data to support its use to reduce ovarian cancer** incidence. Although recent prospective study of more than 200,000 women indicates a decreased risk of ovarian cancer with the use of low-dose ASA, the reported statistical significance recedes when controlling for clinically important confounders. The study findings are therefore not generalizable or clinically applicable. This lack of association is congruent with previously published prospective research.

## **FAST TRACK**

*The finding that current low-dose aspirin use was associated with decreased risk of ovarian cancer did not maintain significance after controlling for hypertension, autoimmune disease, etc.*

### **EXPERT COMMENTARY**

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*Barnard M, Poole EM, Curhan GC, et al. Association of analgesic use with risk of ovarian cancer in the Nurses' Health Studies. JAMA Oncol. October 4, 2018. doi: 10.1001/jamaoncol.2018.4149.*

**E**pidemiologic studies conducted in ovarian cancer suggest an association between chronic inflammation and incidence of disease.<sup>1</sup> Nonsteroidal

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anti-inflammatory drugs (NSAIDs) work to decrease inflammation through the inhibition of cyclo-oxygenase (COX). Therefore, anti-inflammatory agents such as NSAIDs have been proposed to play a role in the pathophysiology of ovarian cancer.

Previous studies of this association show conflicting data. The majority of these studies are retrospective, and those that are prospective do not include detailed data regarding dosing and frequency of ASA use.<sup>2-6</sup>

### **Details of the study**

This study by Barnard and colleagues is a prospective cohort study evaluating a total of 205,498 women from 1980–2015 from 2 separate cohorts (the Nurses' Health Study and the Nurses' Health Study II). The primary outcome was "to evaluate whether regular aspirin or nonaspirin NSAID use and patterns of use are associated with lower ovarian cancer risk." Analgesic use and data regarding covariates were obtained via self-reported questionnaires. Ovarian cancer diagnosis was confirmed via medical records.

Results demonstrated that current low-dose aspirin use was associated with a decreased risk of ovarian cancer (hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.61–0.96). This significance was not maintained upon further controlling for inflammatory factors (hypertension, autoimmune disease, inflammatory diet scores, smoking, etc) (HR, 0.94; 95% CI, 0.69–1.26). Other significant findings included an increased risk of developing ovarian cancer with standard-dose ASA use of  $\geq 5$  years or standard-dose use at 6 to 9 tablets per week (HR, 1.77; 95% CI, 1.13–2.77 and HR, 2.00; 95% CI, 1.27–3.15, respectively). An increased risk of developing ovarian cancer also was found for  $>10$ -year use or use of  $>10$  tablets per week of nonaspirin NSAIDs (HR, 2.00; 95% CI, 1.27–3.15 and HR, 1.35; 95% CI, 1.02–1.79, respectively).

The authors concluded that there was a slight inverse association for low-dose aspirin and ovarian cancer risk and that standard aspirin or NSAID use actually may be associated with an increased risk of ovarian cancer.

### Study strengths and weaknesses

This study has many strengths. It was a large prospective cohort investigation with adequate power to detect clinically significant differences. The authors collected detailed exposure data, which was novel. They also considered a latency period prior to the diagnosis of ovarian cancer during which a patient may increase their analgesic use in order to treat pain caused by the impending cancer.

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Based on these current data, there is insufficient evidence to suggest the use of low-dose aspirin for chemoprophylaxis of ovarian cancer. In order to suggest the use of a drug for prophylaxis the benefits must outweigh the risks, and in the case of NSAIDs, this has yet to be confirmed.

However, the conclusions of the authors seem to be overstated in the setting of the data. Specifically, the deduction regarding a decreased risk of ovarian cancer with low-dose aspirin use given the loss of the statistical significance when controlling for pertinent cofounders. Further, the study authors did not evaluate adverse effects associated with low-dose aspirin use, which would be clinically applicable when determining whether the results from this study should become formal recommendations. Lastly, other important clinical factors, such as the presence of genetic mutations or endometriosis, were not considered, and these considerations would greatly affect results.

In the setting of previous large prospective studies that suggest no association between ASA use and ovarian cancer risk,<sup>4-6</sup> data from this study are not compelling enough to recommend regular low-dose aspirin use to all women. ●

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