cases of pancreatic cancer during 18 years of follow-up among 88,378 women. These 161 cases translate to about 182 cases in 100,000 women.

United States epidemiologic data indicate that the annual incidence rate of pancreatic cancer in the adult female population, though it changes according to different age decades, could be estimated in a conservative way as approximately 4 cases per 100,000 women (2). The cumulative incidence rate over a period of 18 years would therefore be 72 cases. If we calculate the number needed to harm (NNH), an indicator of the harm of health care interventions expressing the number of patients that need to be treated to have one that develops an additional negative outcome, i.e., harm) for the association of aspirin use and risk of pancreatic cancer, a hypothetical NNH of approximately 910 emerges from the data of Schernhammer et al. Such an NNH is hypothetical because the incidence of pancreatic cancer in the Nurses’ Health Study is compared with the incidence of this neoplasm in the general population, not with that in a control group that did not take aspirin. An NNH greater than 250–300 is usually considered not clinically significant; in general, the higher the NNH, the safer the intervention under consideration. On the basis of our calculation, aspirin use appears to be relatively safe, regarding its association with the risk of pancreatic cancer, contrary to the assertions of Schernhammer et al. (1).

Overall, no statistically significant difference in risk of pancreatic cancer between aspirin users and nonusers was shown in the article by Schernhammer et al. (1), and the relative risks reported are only modestly increased (3). Among women reporting aspirin use on at least two of three consecutive biennial questionnaires, the risk increased with increased use and achieved a statistically significant value only when at least 14 tablets per week (and no fewer) were used. These data are of course confined to women.

In conclusion, an NNH of 900–1000, spread over a time period of almost two decades, is high, even for cancer, and is susceptible to further increases resulting from higher estimations of the annual incidence rate of pancreatic cancer in the adult female population. In contrast, there remains a consolidated number needed to treat (NNT, an indicator of the benefits of health care interventions expressing the number of patients who need to be treated with the experimental intervention to create one additional improved outcome in comparison with the control intervention) ranging from 20 to 90 for the use of aspirin in the secondary prevention of cardiovascular diseases (4,5).

In interpreting and balancing such numbers (a neoplastic NNH of 900–1000 versus a cardiovascular NNT of 20–90), we therefore ask authors so that others can always provide the complete data to assess established benefits and putative risks.

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REFERENCES


NOTES

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RESPONSE

We thank Dr. Gensini et al. for their interesting contribution. They suggest that we, as well as other authors of observational studies, should always
provide number needed to treat (NNT) and number needed to harm (NNH) to assess risk–benefit profiles for public health recommendations. Our analyses, based on data from the Nurses’ Health Study cohort, revealed an elevated pancreatic cancer risk among women who reported extended periods of regular aspirin use (1).

Aspirin is widely used, both in therapeutic and preventive health care settings. In addition to its well-established beneficial effects on cardiovascular risk, there is good evidence for a protective effect of aspirin on colon carcinogenesis (2). There are also risks associated with the use of aspirin, such as higher risks for gastrointestinal bleeding and cerebral hemorrhage. Thus, a full risk–benefit analysis of regular aspirin use actually goes well beyond the concept of NNH and NNT for pancreatic cancer only.

Ultimately, the purpose of our analysis was to examine the relation between aspirin use and the risk of pancreatic cancer. We believe that such an analysis not only offers important insights into cancer prevention but also provides vital clues to pancreatic cancer biology. Although our results in a large prospective cohort study have merit, other large studies are needed to confirm our findings before we can accurately conduct a risk–benefit analysis of aspirin use that incorporates pancreatic cancer risk.

With respect to the particular analysis proposed in the letter by Gensini et al., there are a number of important factual problems. Specifically, the authors provide an inaccurate estimate of pancreatic cancer for women in the United States. Surveillance, Epidemiology, and End Results (SEER)1 Program data indicate an annual incidence rate of 9.8 per 100 000 women (3), not four per 100 000. Furthermore, the calculations provided by the authors would vary greatly depending on age. Consistent with data on pancreatic cancer in the SEER database, the incidence rate of pancreatic cancer in our cohort is very low in younger women but much higher among older women. Thus, the NNH varies greatly with the age distribution of the population being studied. Gensini et al. also incorrectly identify the comparison group for our analysis. Rather than the general population, the referent group in our cohort was women of approximately the same age as those in the study group who avoided regular aspirin use.

Notwithstanding, if we accept the calculations of Gensini et al. and the notion that the association between aspirin use and pancreatic cancer is truly causal, we submit that an NNH of 900 is not trivial. The Environmental Protection Agency regulates exposures at levels with far smaller adverse effects, often as low as one in 20 000. Any excess death due to pancreatic cancer would be a cause for concern and should be weighed in making decisions.

REFERENCES


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1Editor’s note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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