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Low-dose Aspirin and Pancreatic Cancer Risk—Response to Brasky and Wactawski-Wende

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Keywords

Aspirin; Case-control Studies; Pancreatic Cancer

I thank Drs. Brasky and Wactawski-Wende for their positive and constructive observations about our observed reduced risk of pancreatic cancer with aspirin use (1). The risk relationship is interesting, especially since a number of plausible mechanisms for aspirin involvement in risk have been suggested, but none verified in the human context, including the apparent lack of appreciable anti-inflammatory properties of low-dose aspirin, as they mention (2). However, two recent studies are worth noting. The first examined imaging-based morphologic changes in intraductal papillary mucinous neoplasms (IPMNs), precursor lesions for pancreatic cancer, with respect to the use of low-dose aspirin (3). This study suggested that the growth of such cysts may be slowed by the use of low-dose aspirin. The second study showed that low-dose aspirin inhibits platelet c-MYC regulation and PANC-1 cancer-cell proliferation (4). If these findings are confirmed, they would provide possible mechanisms for the reduced risk of pancreatic cancer that has been increasingly seen in studies of aspirin use (1).

Drs. Brasky and Wactawski-Wende note that in Figures 1 and 2 of our paper (1), the years shown with the individual studies do not correspond to the publication years of the papers. This observation is correct; the years are the approximate midpoints of the periods of case collection in each of the studies. This fact is noted in the column headings of the figures and in the figure legends, but given the usual convention of citing studies by first author and publication year, the years in the figure can be easily misinterpreted.

Since our original manuscript was accepted for publication, an additional study examining aspirin use and risk of pancreatic cancer in Queensland, Australia, has been published (5). Inclusion of the Queensland data in our meta-analysis of ever regular use of any type of aspirin changed the summary odds ratio negligibly, but slightly lessened the decreasing trend with study mid-year (Figure 1): declining odds ratio of 1.9% per year (95% CI 0.9% to

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2.8%, $P=0.00012$). For a recent study conducted with mid-point in 2011, the predicted odds ratio = 0.69 (95% CI 0.62 to 0.78, $P=10^{-8.9}$).

Data for ever regular use of low-dose aspirin is also available for the Queensland study, as well as for the Women's Health Initiative, which was missed in our original analysis (1). A trend in odds ratio with study mid-year for ever regular use of low-dose aspirin is still seen (Figure 2), with decline in odds ratio of 2.6% per year (95% CI 0.8% to 4.5%, $P=0.0059$). The predicted odds ratio for a recent study conducted with exposure mid-point in 2011 would be 0.68 (95% CI 0.55 to 0.82, $P=10^{-4.0}$). The complete list of studies examined for these analyses is given in Supplementary Table 1. I thank Drs. Brasky and Wactawski-Wende for pointing out the omission.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

CI	confidence interval
IPMN	intraductal papillary mucinous neoplasm

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Figure 1.

Adjusted odds ratio of pancreatic cancer according to ever regular use of aspirin. Squares are plotted descending in order of increasing mid-years of study subject aspirin-use ascertainment. Black squares denote case-control studies; gray squares cohort studies; white squares randomized controlled trials or their extensions; diamonds denote summary estimates. Horizontal lines in each square represent the 95% CI, and the area of each square is proportional to its weight in the analyses. The diagonal dotted line is the regression line of the log odds ratio according to study mid-year, calculated by inverse variance-weighted

linear regression of the log odds ratios. The Current Regression Estimate is the regression odds ratio predicted at the mid-point of the most recent study (2011).

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Figure 2.

Adjusted odds ratio of pancreatic cancer according to ever regular use of low-dose aspirin. Squares are plotted descending in order of increasing mid-years of study subject aspirin-use ascertainment. Black squares denote case-control studies; gray squares cohort studies; white squares randomized controlled trials or their extensions; diamonds denote summary estimates. Horizontal lines in each square represent the 95% CI, and the area of each square is proportional to its weight in the analyses. The diagonal dotted line is the regression line of the log odds ratio according to study mid-year, calculated by inverse variance-weighted linear regression of the log odds ratios. The Current Regression Estimate is the regression odds ratio predicted at the mid-point of what would be a recent study as in Figure 1 (2011).