That aspirin can help to prevent cancer has caught the public’s attention. How does this benefit compare with the rather modest benefit in lowering cardiovascular events previously reported in those at low cardiovascular risk? In a previous study of such patients, the prevention was only three events in 1000 people studied over 6-4 years. The cost was 2.5 major bleeds per 1000 per 5 years in women and three in men, so the overall benefit was truly modest. By contrast, the cancer prevention rates in the study by Rothwell and colleagues included 15 gastrointestinal cancer deaths per 1000 people over 5 years. These benefits vastly outweigh the risk of major bleeds.

In view of these new facts, we should no longer be reserved about recommending aspirin even for those at low cardiovascular risk. However, we are still lacking firm data on when aspirin should be started in those at low risk, and at which dose. The doses of aspirin protecting from cancer in Peter Rothwell and colleagues’ study were in the range of 75–300 mg daily. My guess is to start at a low dose—say 75 mg—in the early 50s.

I declare that I have no conflicts of interest.

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Author’s reply
We agree with N J Wald and colleagues that our results and their analyses do suggest that aspirin should be included in polyprill regimens, although the balance of risk and benefit is less certain in older individuals owing to the increase in risk of bleeding with age.

We thank Janusz Jankowski and colleagues for their comments. However, our estimate of the effect of aspirin on death due to oesophageal cancer was based on 68 events and not 23 as Jankowski and colleagues state. The 20-year risk of death due to adenocarcinoma of the oesophagus, the predominant histological subtype in Barretts’ oesophagus, was substantially reduced by allocation to aspirin in the trials (hazard ratio 0.36, 95% CI 0.21–0.63, p=0.0001).

It is difficult to conceive of how this estimate might have been biased by inclusion of some trials that included patients with established vascular disease, as Jankowski and colleagues suggest. Moreover, the effect was significant in both of the large randomised trials of daily aspirin versus control in primary prevention that we studied—ie, the Thrombosis Prevention Trial (0.42, 0.22–0.78, p=0.004) and the British Doctors Aspirin Trial (0.45, 0.19–0.99, p=0.04). The figure shows a pooled analysis of the effect in these two trials.

Additionally, our estimates of the effect of aspirin on risk of death due to gastrointestinal cancers as a whole were based on more than 500 deaths and not on 182 as stated by Jankowski and colleagues, with a highly statistically robust reduction in 20-year mortality (0.65, 0.53–0.78, p<0.0001).

Luca Mascitelli and Mark Goldstein raise the issue of the possible effect of aspirin treatment on iron loss as a mechanism for the reduction in cancer deaths. We deliberately did not review the many suggested mechanisms by which aspirin might reduce the risk of death due to cancer, but it is possible that reduced iron stores might contribute. There are currently insufficient data on the associations between iron stores and cancer risk to determine whether their pattern closely mirrors that of the effects of aspirin on deaths due to the specific cancers that we noted.

Mark Nelson raises the issue of the risk of bleeding on aspirin. We deliberately made no specific recommendations about the widespread use of aspirin in healthy individuals, but we did discuss the issue of bleeding in some detail. Our analyses showed that taking aspirin daily for 5–10 years would reduce all-cause mortality (including any fatal bleeds) during that time by about 10% in relative terms. Subsequently, there would be further delayed reductions in risk of cancer death even if aspirin was stopped.

In healthy middle-aged individuals, the risk of major bleeding on aspirin is relatively low (about 0.2 per 1000 patients per year—only a small proportion of which are fatal), and is already offset in many groups by the small reduction in risk of ischaemic vascular events. The reduction in risk of cancer is therefore additional to this existing balance in which the bleeding risk is already taken into account. However, the risk of bleeding on aspirin increases steeply with age and so we did not comment on use of aspirin in healthy individuals older than 75 years. The results of the ASPREE trial will be of great importance in this respect.

Figure: Pooled analysis of the effect of randomised allocation to aspirin versus control for a duration of about 5–8 years on the 20-year risk of death due to adenocarcinoma of the oesophagus, during, and after two trials in patients without previous vascular events