

## Does aspirin protect against cancer? More high-quality research is needed

There is a growing body of evidence and opinion that aspirin can play a role in the prevention of some cancers, particularly colorectal cancer.<sup>1</sup> This mechanism is thought to be related to the anti-platelet effects of aspirin due to the inhibition of the cyclo-oxygenase (COX) -1 and -2 pathways.<sup>1</sup>

A recent 2014 review that investigated the protective effect of aspirin for the primary prevention of cancer and cardiovascular events has been widely reported in the media. The review found that long-term aspirin prophylaxis in people aged 50 – 65 years had a net health overall benefit due to reductions in the rates of cancer.<sup>2</sup> However, the reliability of these results was questionable due to major inconsistencies in the research methodology.

**At this stage, there is not enough evidence to recommend any change in practice.**

### What did the review report?

The authors of the review calculated that people aged 50 – 65 years who took aspirin for the primary prevention of cancer and cardiovascular events for at least five years would have lower rates of some cancers and some cardiovascular events (Table 1). The optimum dose for preventing cancer was unclear – indirect comparisons showed little difference between low (75 – 100 mg/day) and standard dose (300 – 325 mg/day) aspirin.<sup>2</sup>

The authors balanced the benefits of aspirin treatment against the increased risk of adverse events. It was calculated that depending on age and sex, major bleeding events would increase by between 0.16% and 0.81% over a 15 year period.<sup>2</sup> The net absolute reduction in mortality due to taking aspirin was almost entirely due to a reduction in deaths from cancer and varied depending on the sex and age of the patient; due to differences in baseline incidence rates of various cancers.<sup>2</sup> The authors estimated that the benefits of treatment with aspirin for 20 years would range from a 0.47% decrease in deaths (from all causes) for women starting treatment aged 50 years,

to a 2.18% reduction in deaths for men starting treatment at age 65 years.<sup>2</sup> This equated to a number needed to treat (NNT) to save one life of 46 to 213.<sup>2</sup>

It was reported that the effects of aspirin on the risk of cancer were not apparent until after at least three years of treatment, but that some of these benefits were sustained for several years after cessation of treatment in long-term users.<sup>2</sup>

### What were the problems with the research?

There were a number of issues regarding the compilation and interpretation of the evidence and whether the methods used were systematic. Some of the inconsistencies with the review included:

- It was not clear whether it was a systematic review, and therefore whether the included evidence was rigorously assessed for quality and risk of bias
- A meta-analysis was not performed. The authors performed their own estimates of risk
- The cardiovascular risk data was obtained from one meta-analysis<sup>3</sup>
- The methods stated that the evidence for cancer risk were obtained from the most recent systematic reviews (published between 2009 – 12) and some individual studies on specific cancers. However, not all recent systematic reviews were included in the review and there was no information provided as to how the included studies were selected
- Most of the evidence that was included in the review was obtained from observational studies with few randomised trials included
- An unpublished analysis was used to estimate the rates of bleeding and peptic ulcer
- Several assumptions were made regarding the effects of aspirin on the rates of cancer and cardiovascular events
- Several of the authors are consultants to, or have affiliations with, pharmaceutical companies who are conducting research into anti-platelet medicines

The authors arrived at a more positive conclusion regarding the beneficial effects of aspirin for cancer prevention than a thorough and well-reported systematic review published in 2013.<sup>4</sup> This 2013 review was not discussed in the current review.

The authors of the 2013 systematic review concluded that the uncertainty around their cancer estimates remained high.<sup>4</sup> The long-term all-cause mortality data did not provide compelling evidence for the use of aspirin for protection against cancer and cardiovascular mortality.<sup>4</sup> It was reported that the absolute benefits and harms of aspirin for the primary prevention of cancer and cardiovascular disease were low, with only 34 – 36 colorectal cancer deaths and 60 – 84 major cardiovascular events averted per 10 000 people over ten years.<sup>4</sup>

### Conclusions and implications for clinical practice

Although the 2014 review reported promising results for aspirin as prophylaxis for certain types of cancer it is unclear how reliable the results are. More high-quality research is needed, including long-term randomised trials, before any definite conclusions can be drawn regarding the benefits and harms of aspirin for the primary prevention of cancer. It is important that clinicians weigh up the benefits and adverse events associated with aspirin before prescribing it, especially in older patients, as gastrointestinal bleeding and peptic ulcer are common in this group.

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### References

1. Thun MJ, Jacobs EJ, Patrono C. The role of aspirin in cancer prevention. *Nat Rev Clin Oncol* 2012;9:259–67.
2. Cuzick J, Thorat MA, Bosetti C, et al. Estimates of benefits and harms of prophylactic use of aspirin in the general population. *Ann Oncol* 2014; [Epub ahead of print].
3. Antithrombotic Trialists' (ATT) Collaboration, Baigent C, Blackwell L, et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009;373:1849–60.
4. Sutcliffe P, Connock M, Gurung T, et al. Aspirin for prophylactic use in the primary prevention of cardiovascular disease and cancer: a systematic review and overview of reviews. *Health Technol Assess Winch Engl* 2013;17:1–253.

## CORRESPONDENCE

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We have received many letters in regards to our recent and ongoing series on the use of oxycodone in New Zealand. We have dedicated the correspondence section in this edition to these letters. To respond to any of these letters and express your views, you can add to the discussion online at: [www.bpac.org.nz/BPJ/2014/September/correspondence.aspx](http://www.bpac.org.nz/BPJ/2014/September/correspondence.aspx)

### What are the real reasons behind the use of oxycodone?

Dear Editor,

Re: Oxycodone – How did we get here and how do we fix it?

I read with interest the prescribing rates for oxycodone in your latest update sent to all GPs. I would like to make a few points.

The first is that the article is unlikely to be convincing to those doctors who prescribe oxycodone, and is more likely to be a pleasant message to those who do not. If this is true the article is pointless as nothing will change!

Thinking on that a little deeper the question is “why do we (GPs and hospital doctors) prescribe oxycodone?”

I think the answer is the widely held belief that this is a medication with some reduction in side effects. I think perhaps that needs to be directly and thoroughly addressed, quoting serious research, if there is to be a sea change in prescribing habits. Having said that there are countless times that GPs have claimed certain drugs are better or worse despite so called evidence and in the end we have often been found to be correct. So the research has to be very, very good, i.e. double blind crossover, etc.