Aspirin and cancer

'Aspirin reduces cancer risk by 20%' said the headlines. However all the commentators were quick to point out that aspirin was associated with harms and that people considering taking aspirin should see their GP. But what does a 20% relative risk reduction mean to the patient sitting in front of us? What sort of a benefit is that in real terms? And what are the harms?

Here I have summarised the research and tried to unpick the numbers behind it so we have sensible data to offer to our patients (Lancet 2010 DOI:10.1016/S0140-6736(10)62110-1).

The trials

This research was a meta-analysis pooling data from 8 trials (25 000 patients). All the trials were RCTs designed to look at aspirin in the context of cardiovascular disease prevention (all but one were primary prevention trials).

Aspirin was used for a minimum of 4 years in the trials included in the meta-analysis, but some of the studies involved taking aspirin significantly longer than that.

The main analysis was done after 5 years follow up, however in 3 of the (UK based) trials follow up for 20 years was possible, and a second analysis was done after 20 years follow up for this smaller data set.

The results

Here we will quote the data from the paper (so sorry for offering a combination of hazard ratios and odds ratios – consider them roughly the same in this context) but then we will look at what that means in terms of useful numbers we can share with our patients.

- After 5 years follow up, cancer deaths were reduced by 21% (odds ratio 0.79, CI 0.68-0.92).
- After 20 years follow up, cancer deaths were reduced by 20% (hazard ratio 0.8, CI 0.72-0.88).
- The benefit was greater for gastrointestinal cancers than all other cancers.
- Aspirin had no impact on some cancers (eg. haematological malignancies).
- The benefit was not apparent until at least 5 years follow up, but took longer for some cancers. Benefits were seen at 5 years for oesophageal, pancreatic, brain and lung cancers but took longer than this for stomach, colorectal and prostate cancers.
- The benefit was the same for all doses of 75mg and above.
- The results were the same for men and women, smokers and non-smokers.
- The benefit increased with age.
- For the first 15 years, as well as a reduction in cancer deaths, there was also an 8% reduction in all cause mortality. This was entirely attributable to the reduction in cancers. At 20 years, there was still a reduction in cancer deaths but there was no reduction in all cause mortality. It is not clear why this is so.
What does this mean in practice?
Relative risk (a 20% reduction in cancer) is all very well, but what does this mean to the patient sitting in front of us? Sadly the Lancet paper didn’t quote numbers need to treat (NNTs). So, we have worked them out from the data in the paper.

- Having used aspirin for around 5 years, 20 years later, one cancer related death would be prevented for every 29 people who took aspirin (NNT 29, 20 years after taking aspirin for 5y).

But age matters...
Taking aspirin under the age of 55 did not offer a statistically significant reduction in cancers.

In those who took aspirin for 5 years aged around 55-64y, one cancer related death would be prevented for every 22 people taking aspirin (NNT 22, 20 years after taking aspirin for 5y).

In those who took aspirin for 5 years aged 65 and older, one cancer related death would be prevented for every 14 people taking aspirin (NNT 14, 20 years after taking aspirin for 5y).

But these aren’t the figures quoted in the BMJ editorial?
No. The meta-analysis was pooled data from RCTs designed to measure the effect of aspirin on cardiovascular prevention. Most of these trials lasted around 5 years. The BMJ editorial focuses on deaths from cancer during the period of these RCTs. The figures are not very impressive, with 20 fewer cancers during the course of the RCTs (the editors calculated this to be an NNT of 200 after almost 6y of taking aspirin) (BMJ 2010;340:c7326). However the crucial data, which I have given above, focuses on reduction in cancers 20 years on. This is much more impressive, and I believe, much more important.

Other benefits of aspirin
So that’s the cancer benefit. What about the cardiovascular benefits of aspirin?

Cardiovascular benefits
The cardiovascular benefits of aspirin are discussed in more detail in the cardiovascular chapter of the GP Update Handbook, but the figures are (Lancet 2009;373:1849):

- For secondary prevention (ie. in those who have had a heart attack or a stroke):
  For every 66 people treated over 1 year, 1 cardiovascular event will be prevented (NNT 66).
  For every 334 people treated over 1y, 1 cardiovascular death will be prevented (NNT 334).

- In primary prevention, aspirin does not reduce cardiovascular mortality, but does reduce cardiovascular events, however the benefit is small. One thousand six hundred and sixty six people need to take aspirin every day for a year to prevent one cardiovascular event (NNT 1 666).

Colorectal cancer mortality and aspirin (from Lancet 2010;376:1741)
- In those who take aspirin for 5 years, 20 years later, for every 57 who took aspirin, 1 extra colon cancer death would be prevented (NNT 57, 20 years after taking aspirin for 5y).

What about the harms of aspirin?
Again, the BMJ editorial gave the wrong impression. The authors quoted a relative risk increase of 50% in risk of serious gastrointestinal or extra-cranial bleeds in those on aspirin from the Anti-thrombotic Trialists Collaboration data. This sounds rather worrying. However
this is a relative risk increase, and actually translates into an NNH (number needed to harm) of 3 333 over 1 year, or 667 for those taking aspirin over 5 years (assuming the harms are cumulative). That is for every 667 patients taking aspirin over a 5 year period, 1 would have a significant GI or extra-cranial bleed who wouldn’t have done if they had not been on aspirin (Lancet 2009;373:1849). This is a much less scary number than saying the risk increase was 50%, and yet is exactly the same statistic.

How long do you need to take the aspirin for?
This study shows benefit after 5 years use. Longer use gave additional benefits.

How might aspirin reduce cancer risks?
This is thought to be due to inhibition of COX enzymes, reduced prostaglandin production and action through other inflammatory mediators.

So what are we saying to our patients?
At the end of this Update Update you will find the information leaflet we have written for our patients. You are welcome to use it.

And so, if you were over 55 would you take aspirin?
This is the question our patients really want to know the answer to, and we are often reluctant to give an answer.

As we have discussed already, the BMJ editorial on this meta-analysis was fairly negative, partly because they focussed on the wrong time frame.

The Lancet editorial was also fairly cautious about the results, because the exact magnitude of the benefit could be as low as a 13% reduction in cancers (Lancet 2011;377:31). They also pointed out that it is hard to generalise this to specific groups of people – does a woman who has never smoked get a benefit from aspirin? And if so what is the magnitude of this benefit? These are important points. And at GP Update we are very aware of how fast the evidence moves. By next year, in 5 or 10 years times, things may change.

However, having said all that, given the evidence available to us, (and accepting that this may change over time!), if I was over 55 and I had no contraindications I would probably take 75mg of aspirin daily, as the benefits are large (NNT 29, 20 years after taking aspirin for 5 years) and the harms are relatively small (NNH 667, during the 5 years of taking aspirin).

<table>
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<tr>
<th>Take home messages: Aspirin and cancer</th>
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<tbody>
<tr>
<td>• Aspirin reduces the risk of cancer, even 20 years after stopping.</td>
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<td>• Benefits are seen after taking aspirin for 5 years.</td>
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<td>• Doses of 75mg are effective. Higher doses do not give additional benefit.</td>
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<td>• The benefit is age related, with those under 55 appearing to have no benefit, and those over 65 having the greatest benefit.</td>
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<td>• Having used aspirin for around 5 years, 20 years later, one cancer related death would be prevented for every 29 people who took aspirin.</td>
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<td>• Aspirin is also beneficial in secondary prevention of cardiovascular disease but not in primary prevention of cardiovascular disease.</td>
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<tr>
<td>• Compared to the benefits, the harms are relatively small: one significant gastrointestinal(extra-cranial bleed for every 667 people taking aspirin for 5 years.</td>
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Aspirin and cancer: what does it all mean?

You probably heard the news stories following the publication of some research in the medical journal The Lancet. What does it all mean? Here is a summary of the research relating to the benefits and harms of aspirin.

Aspirin use has been shown to reduce the risk of dying from many cancers.

You need to take aspirin for at least 5 years, at a dose of 75mg. There doesn’t appear to be any benefit if you are under 55 years old, so this applies only to those aged over 55.

How much benefit will you get?
For every 29 people who take aspirin for a period of 5 years, 20 years later, one of them would not die from cancer because they took the aspirin. The other 28 would have taken aspirin every day for 5 years but had no benefit from it.

We also know that if you have had a stroke or a heart attack, aspirin reduces your risk of having a further heart attack or stroke, so for some years aspirin has been recommended to those who have had a heart attack, stroke or mini-stroke/TIA (regardless of age).

We used to recommend aspirin in some people who were high risk of heart attacks/strokes but who had not had one. However the benefit to these people (reducing the risk of heart attacks/strokes) is very small so as to make it not worth it.

What are the harms of taking aspirin?
Over a 5 year period of taking aspirin, one in 667 people would have a serious stomach or other bleed, that they would not have had if they had not been taking aspirin. The other 666 people would take aspirin but have no serious bleeding.

There are also certain people who should not take aspirin at all (for example those who are allergic to it).

How does aspirin reduce the risk of cancer?
Aspirin reduces inflammation within the body, and this may be how it reduces cancers, but no one is exactly sure how this occurs.

So should you take aspirin?
• Firstly, this applies only to those over 55. Those under 55 have not been shown to benefit.
• Secondly, we strongly recommend that if you are thinking of taking aspirin, please discuss this with your doctor/nurse, so they can take into account your own medical history.

This leaflet was written by the GP Update team, a small group of GPs who turn research evidence into material that is useful for GPs, practice nurses and their patients.

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London - Friday October 14
London - Saturday October 15
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