bmjupdates+

Low dose aspirin for cardiovascular prevention increases risk of bleeding, but absolute risks remain small

Research question What are the bleeding risks associated with antiplatelet agents for cardiovascular prophylaxis?

Answer The absolute risks associated with low dose aspirin are small

Why did the authors do the study? As the population ages, more and more people will need antiplatelet treatment for primary and secondary prevention of cardiovascular disease. These authors wanted to know the absolute increases in bleeding risk associated with low dose aspirin and clopidogrel, the two most commonly used agents, so doctors have clinically relevant information to guide their prescribing.

What did they do? They systematically searched PubMed and the Cochrane Central Register of Controlled Trials for published randomised trials of low dose aspirin (75-325 mg/day) or clopidogrel for primary or secondary prevention of cardiovascular disease. Trials in any language comparing either drug with placebo, with each other, or with a combination of the two were included. All trials lasted at least two months and included at least 100 patients in the active treatment arm. The authors graded the trials for quality. They pooled data from individual trials to give estimates of the relative and absolute risks of any major bleeding, major gastrointestinal bleeding, and intracranial bleeding. Bleeds that resulted in transfusion, hospitalisation, or death were major.

What did they find? They found 25 randomised trials reporting data suitable for meta-analysis; 22 of them compared low dose aspirin with placebo. The trials were generally sound: all but two had a Jadad score of ≥ 3 out of a possible 5.

Compared with placebo, low dose aspirin increased the risk of any major bleeding by 71% (relative risk 1.71 (95% CI 1.41 to 2.08)). But the absolute risk remained small, an increase in incidence of 0.13% (0.08% to 0.2%) per year on top of the 0.18% annual incidence among patients taking placebo. That's a number needed to harm of 769. The absolute risk increases for major gastrointestinal bleeding (0.12% (0.07% to 0.19%)) and intracranial bleeding (0.03% (0.01% to 0.08%)) were also small and add up to one extra gastrointestinal bleed for every 833 patients treated for a year or one extra intracranial bleed for every 3333 patients treated for a year.

Low dose aspirin was associated with a higher risk of major gastrointestinal bleeding than clopidogrel in the one head to head trial (relative risk 1.45 (1.00 to 2.10), absolute risk increase 0.12% (0.00% to 0.28%) per year). Combined treatment was associated with significantly more bleeding, major bleeding, and major gastrointestinal bleeding than either agent alone.

What does it mean? Although low dose aspirin increases the risk of major bleeding by about 70% in this patient group, the risks look a lot smaller when viewed in absolute terms. Treating about 800 patients with low dose aspirin for a year would result in one extra serious bleeding event.

It's harder to assess the absolute risks for clopidogrel because there are no placebo controlled trials. The only head to head trial against aspirin suggests that clopidogrel is safer, but not much. Treating 883 patients with aspirin instead of clopidogrel would result in one extra serious gastrointestinal bleed a year.

McQuaid et al. Systematic review and meta-analysis of adverse events of low-dose aspirin and clopidogrel in randomized controlled trials. *Am J Med* 2006;119:624-38

This summarises a paper that has been selected by bmjupdates. To register for bmjupdates (free email alerts about high quality new papers in your favourite subjects) go to **http://bmjupdates.com/**

Editor's choice

Character building

Career Focus this week collects together a series of "character building" experiences (http://careerfocus.bmjjournals.com). These include being suspended from practice for a cocaine habit, being exposed as a plagiarist, and being a colleague of serial murderer Harold Shipman and subsequently being criticised by a public inquiry.

The point is that all these doctors survived these experiences and probably came away from them stronger. The anonymous former cocaine addict found that the strictness of the General Medical Council's processes worked in his favour and became a powerful motivator to his becoming abstinent. The former plagiarist, writing under a pen name, has clearly learnt her lesson—possibly because the personal consequences of being found out were severe. And Raj Patel, who practised opposite Harold Shipman's practice and sometimes countersigned his cremation forms, explains how, stung by criticism over the way his practice continued to handle cremation forms, he and his colleagues started to behave differently. What started with routine discussion with relatives and examination of the medical records when countersigning cremation forms developed into other forms of "cultural openness."

These are all extreme episodes, but this week's journal contains other reminders that life as a doctor can be difficult, both personally and professionally. According to a research paper by Erica Frank and colleagues, bullying and harassment are rife among US medical students, 42% having experienced bullying and 84% belittlement during their time in medical school (p 682). The reported rates are lower among UK students, explains Diana Wood in her editorial, possibly because of cultural differences, but the negative effects can be severe (p 664). In his personal view (p 709) Arnob Chakraborti muses over the appropriateness of disclosing personal details to patients as a means of showing empathy in a therapeutic relationship: "it is so easy to get it wrong." A series of letters show how well intentioned measures may have perverse effects. Graham Mackenzie and colleagues criticise the eligibility criteria for over the counter statins in UK pharmacies for misclassifying people at both ends of the risk range (p 704). D Schlosshan and colleagues struggle with the use of an absolute left ventricular ejection fraction as an eligibility criterion for the use of trastuzumab in early breast cancer: there are three ways of measuring it (producing different results) and no consensus on what is normal (p 704). And there's more on plagiarism, including Andrew Weeks' suggestion that Google can help identify the cheats (p 706).

Finally, it seems that someone in government reads the *BMJ*. In April Fiona Godlee wrote in her editor's choice: "Gordon Brown's first act as chancellor was to give the Bank of England independence to set interest rates. His first act as prime minister should be to give independence to the NHS." This week Mr Brown (though not yet prime minister) has proposed to do just that (p 669).

Jane Smith *deputy editor (jsmith@bmj.com)*