All you need to read in the other general medical journals
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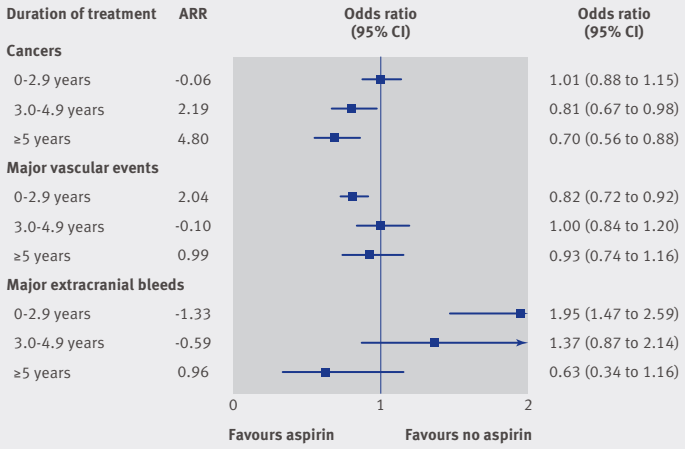
"When in Japan, do not attempt to drop down dead . . . teams of emergency medical service personnel stand ready to rush out and perform resuscitation for out-of-hospital cardiac arrest"
Richard Lehman's blog at www.bmj.com/blogs
Richard Lehman has just been voted the "Number one medical blogger" by readers of *Pulse*

Summary risks and benefits from six primary prevention trials



ARR=Absolute risk reduction/1000 patients/year
Adapted from *Lancet* 2012; doi:10.1016/S0140-6736(11)61720-0

Further evidence that aspirin helps prevent cancer

Further evidence of the anticancer effects of aspirin have emerged from a series of new meta-analyses reporting that an aspirin a day reduces deaths from cancer (odds ratio 0.85, 95% CI 0.76 to 0.96) and the incidence of cancer (0.76, 0.66 to 0.88), and can even help prevent the spread of existing adenocarcinomas (hazard ratio for subsequent metastasis 0.45, 0.28 to 0.72).

The evidence looked strongest for colorectal cancer but extended to a range of other types, including other gastrointestinal cancers and breast cancer. The new analyses strengthened previously weak evidence for an anticancer effect in women.

The authors began with 51 randomised trials of daily aspirin at any dose for the primary or secondary prevention of vascular disease. A reduction in cancer deaths emerged after five years of treatment; a reduction in incidence emerged after three.

Aspirin was associated with more serious bleeds than were the control treatments, but only during the first three years. Bleeding risk seemed to fall away after that, and so did the vascular benefits, leaving just aspirin's beneficial effects on cancer risk. In one analysis, major extracranial bleeds looked less lethal among adults taking aspirin than among controls (case fatality 8/203 *v* 15/132, odds ratio 0.32, 0.12 to 0.83).

Should we all be taking an aspirin a day to protect ourselves from cancer? It's still too early for that, says a linked commentary (doi:10.1016/S0140-6736(11)61654-1). These analyses, though impressive, were confined to trials of daily aspirin and had to exclude two of the biggest—the Women's Health Study and the Physicians Health Study—because they tested an aspirin every other day instead. Neither of these trials reported a lower risk of cancer or cancer death among participants taking aspirin.
Lancet 2012; doi:10.1016/S0140-6736(11)61720-0, doi:10.1016/S0140-6736(12)60209-8

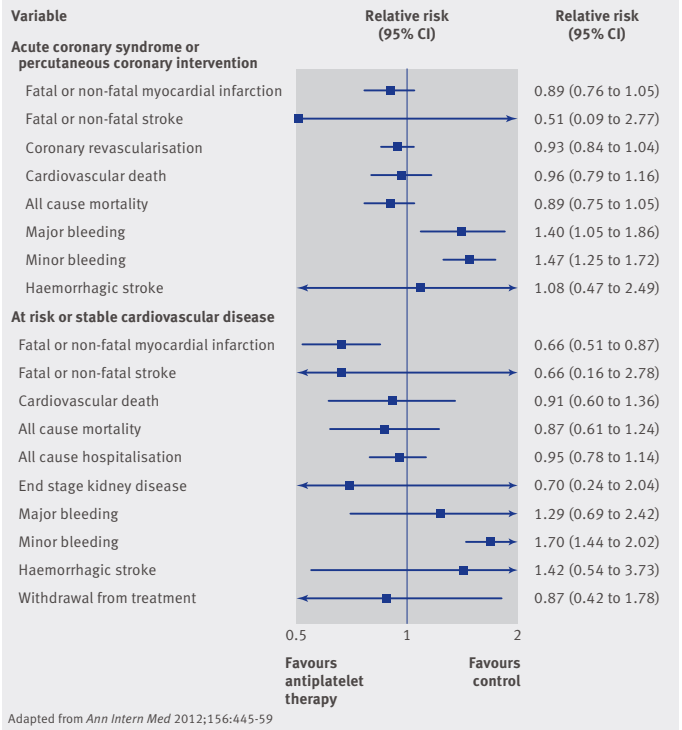
Antiplatelet drugs for adults with chronic kidney disease?

Adults with chronic kidney disease are unlikely to get the expected cardiovascular benefits from antiplatelet drugs such as aspirin and clopidogrel, say researchers. A systematic search for clinical trials found few that were good enough to guide prescribing in adults with chronic kidney disease, and pooled results showed a clear risk of bleeding, particularly for those needing a percutaneous coronary intervention. Clopidogrel or glycoprotein IIb/IIIa inhibitors did not save lives or prevent heart attacks, strokes, or further revascularisations in these patients, although the evidence was weak and relied exclusively on unplanned subgroup analyses (nine trials).

Another 31 trials contributed data on longer term treatment for adults with stable cardiovascular disease (and a few with none). Agents such as aspirin or dipyridamole reduced the risk of heart attack but not of stroke, death, or end stage kidney disease. Minor bleeding was significantly more common among those given antiplatelet agents.

The totality of evidence was so weak that the researchers urge a ban on prescribing antiplatelet drugs to people with chronic kidney disease outside dedicated clinical trials. The effects of antiplatelet drugs at different stages of kidney disease are unknown. The researchers found no trial data at all on adults with renal transplants.
Ann Intern Med 2012;156:445-59

Summary treatment effects



Adapted from *Ann Intern Med* 2012;156:445-59

Adding predictive power to the Framingham risk score, or not

Dozens of new cardiovascular risk factors and biomarkers have emerged since the Framingham risk score was established as the standard way to predict the likelihood of new disease in healthy people. In a study of 12 newer predictors just two improved the performance of the traditional score enough to be clinically useful. Measuring coronary artery calcium added the most, improving discrimination (correctly reclassifying people as high or low risk) by 19.3% (95% CI 12.5% to 26.2%) and adding 0.05 (0.02 to 0.06) to the C statistic—a measure of the area under the receiver operating characteristics curve. Serum concentrations of *N*-terminal prohormone of brain natriuretic peptide (NT-proBNP) came a close second.

The other 10 markers—including concentrations of fibrinogen, C reactive protein, and homocysteine; a white cell count; and measures of renal function, peripheral artery disease, and carotid disease (intima media thickness)—boosted the Framingham score's predictive power by less than 10%.

The authors tested the newer markers in a long running cohort of middle aged men and women from Rotterdam in the Netherlands—a good place to start, says a linked editorial (pp 468-9). The two most promising markers should now be evaluated in other cohorts and eventually in new randomised trials. Only then will we know if the extra predictive power translates to a healthier future for people managed with the newer markers. There will be inevitable trade-offs: measuring coronary artery calcium is expensive and exposes healthy asymptomatic people to radiation.

Ann Intern Med 2012;156:438-44

Everolimus eluting stent associated with lowest risk of stent thrombosis

Stent wars have been raging for some years now, most recently around the vexed question of stent thrombosis, a rare but potentially catastrophic complication that often presents with heart attack or death. Early drug eluting stents were implicated and drove the development of a second generation of stents with different materials, architecture, and drugs. One of them, an everolimus eluting stent made of a polymer coated alloy of cobalt and chromium has emerged the clear winner from a state of the art meta-analysis comparing the thrombosis risk associated with first and second generation drug eluting stents and bare metal stents.

It was the only drug eluting stent associated with significantly fewer thromboses than bare metal stents over two years of follow-up (odds ratio 0·35 (95% CI 0·17 to 0·69). It also looked safer than other drug eluting stents—including two versions of a zotarolimus eluting stent and earlier generation stents eluting sirolimus and paclitaxel—and safer than other stents in direct and indirect comparisons and in short term (one month) and longer term (one month to a year) analyses.

Network meta-analyses such as this one aren't perfect, but they do help us compare treatments indirectly when there are few head to head trials. The findings are reassuring but not definitive, says a linked comment (doi:10.1016/S0140-6736(12)60440-1). Will this stent look as good beyond two years when late thromboses still occur, and is it the cobalt-chromium alloy, the fluoropolymer coating, the thin struts, or the everolimus that makes it less thrombogenic than other stents (if it really is)? Only head to head trials will provide the answers. And only then if they recruit around 10 000 patients, say the authors. The Cardiovascular Research Foundation funded their meta-analysis without help from the sponsors of individual studies.

Lancet 2012; doi:10.1016/S0140-6736(12)60324-9

Tenecteplase for selected patients with ischaemic stroke

The tissue plasminogen activator alteplase is the current standard thrombolytic for eligible patients with acute ischaemic stroke. Tenecteplase may work better, say researchers from Australia. In a preliminary trial, tenecteplase restored perfusion around the infarct and improved stroke symptoms significantly more than did alteplase within 24 hours of treatment (79.3% *v* 55.4% reperfusion, P=0.004; and an 8 point *v* 3 point improvement on a stroke severity score running from 0 to 42, P<0.001). Adults given tenecteplase were also significantly less disabled than were controls after three months.

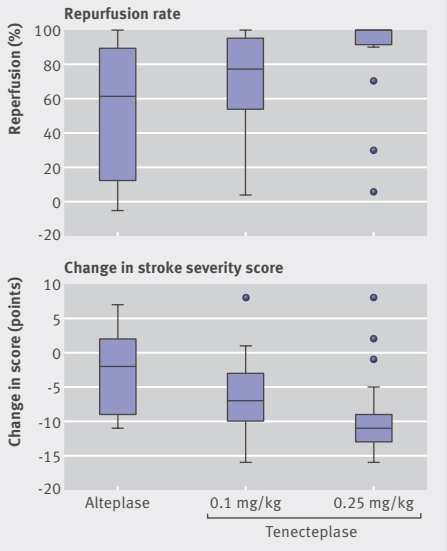
The trial tested two doses of tenecteplase, and the higher dose worked best, apparently without increasing bleeding risk. Two of the 50 patients given either dose of tenecteplase (4%) and 4 of the 25 given alteplase (16%) developed large parenchymal haematomas.

The authors selected their patients carefully, using computed tomography to identify those most likely to benefit from thrombolysis. They screened 604 eligible for thrombolysis and recruited just 75. All participants had a discernible intracerebral occlusion and salvageable perfusion lesion around their infarct. They were treated three hours on average after symptoms started.

Tenecteplase looked superior and should be tested in broader populations of adults with ischaemic stroke, say the authors.

N Engl J Med 2012;366:1099-107

Box and whisker plots of outcomes at 24 hours



Adapted from *N Engl J Med* 2012;366:1099-107

Intracoronary abciximab saves a little myocardium after anterior MI

Intracoronary thrombus can embolise during a percutaneous coronary intervention (PCI), and researchers are currently exploring whether patients do better if visible thrombus is manually removed first or treated with intracoronary abciximab. The abciximab seemed to work better in a recent trial of selected adults with new anterior infarcts. One month after a PCI, the 229 given intracoronary abciximab had slightly but significantly smaller infarct size (as percentage of total left ventricular mass) than the 223 given placebo infusions (median 15.1% *v* 17.9%, P=0.03). Aspiration of thrombus with an intracoronary catheter made no difference to infarct size at 30 days, and neither strategy improved short term clinical outcomes.

Abciximab inhibits platelet aggregation, so bleeding is the biggest safety concern. Participants given the drug did bleed more than controls on most measures, but none of the differences was significant, and severe bleeding was rare in all groups.

These adults were hand picked. They were treated within three hours of first symptoms, and had the kind of pathology most likely to respond to intracoronary treatments—anterior infarcts, poor flow in a major coronary artery that was reasonably straight, and no diffuse atheroma or calcification. They had all the recommended drug treatments during and after the procedure, including bivalirudin for per procedural anticoagulation. A modest reduction in infarct size may be the best we can achieve with intracoronary abciximab, say the authors. It's unlikely to be more effective in real world populations.

JAMA 2012; doi:10.1001/jama.2012.421

Cite this as: *BMJ* 2012;344:e2269