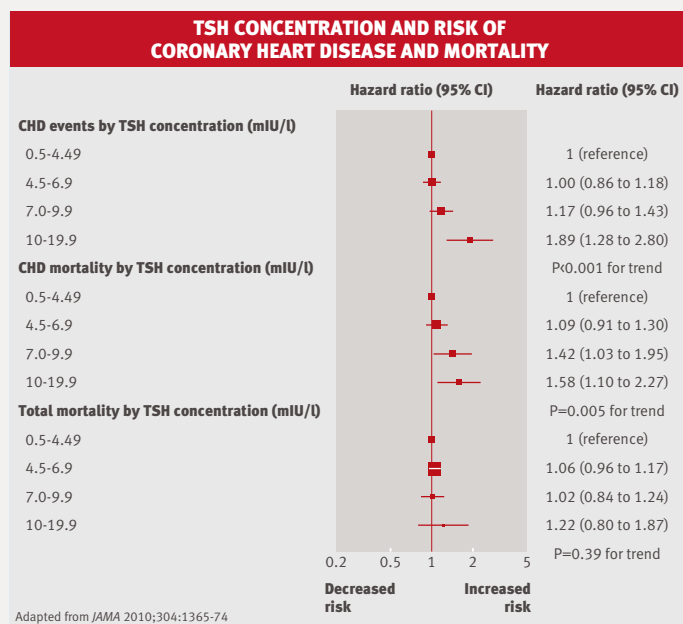


SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

Alison Tonks, associate editor, *BMJ* atonks@bmj.com

Subclinical hypothyroidism linked to coronary heart disease, again



Further evidence of a link between subclinical hypothyroidism and coronary heart disease has emerged from a meta-analysis of 55 287 adults in 11 prospective cohorts from the US, Europe, Japan, Brazil, and Australia. Risk of coronary heart disease (CHD) (including death) rose with serum concentrations of thyroid stimulating hormone (TSH), and became significant once concentrations reached 10 mIU/l (hazard ratio for coronary heart disease events 1.89, 95% CI 1.28 to 2.80, relative to euthyroid people). The authors defined subclinical hypothyroidism as a TSH concentration between 4.5 and 19.9 mIU/l in people with normal serum concentrations of thyroxine. They did not find an association between subclinical hypothyroidism and total mortality.

This large study had the power to fine tune previous estimates and explore subgroups. The authors were also able to adjust for the confounding effects of age, sex, previous cardiovascular disease, and cardiovascular risk factors such as smoking. The results remained essentially the same.

The next step is to find out who, if anyone, would benefit from thyroid replacement, say the authors. Trials should be done, perhaps starting with adults at the top end of the TSH spectrum. Slightly raised concentrations weren't associated with coronary heart disease in this analysis.

JAMA 2010;304:1365-74

The end of one chapter and the start of another for young women at risk of HIV

Another vaginal gel has failed to protect young women from HIV in sub-Saharan Africa. Two different formulations of the microbicide PRO2000 made no difference to the incidence of HIV infection in young women in a placebo controlled trial, despite apparently excellent adherence (4.5/100 women years, 95% CI 3.8 to 5.4; 4.3, 3.6 to 5.2 for placebo; 4.7, 3.8 to 5.8 for a stronger formulation that was discontinued early). The women in the trial were given free condoms and safe sex counselling as well as the gel, which they applied one hour before sex. Similar incidence rates in the gel and placebo groups spell the end of the road for this particular gel, says a linked comment (doi:10.1016/S0140-6736(10)61309-8). PRO2000 joins a long list of other microbicides that have failed to realise in humans the promise they showed in monkeys and in the laboratory.

Just one gel has bucked this dismal trend, says the comment. A 1% formulation of tenofovir cut women's risk of HIV by almost 40% in a trial published earlier this year, a true breakthrough after decades of disappointing results. Young women

have been hit hardest by the HIV epidemic in sub-Saharan Africa. They urgently need a prophylactic that, unlike condoms, doesn't depend on negotiations with a partner. Topical antivirals may prove useful, but in the meantime researchers and funding agencies should also consider the empowering effect of cash, says the comment. Young women with resources have less transactional sex and can spend longer in school. Both have been linked to a lower risk of HIV.

Lancet 2010; doi:10.1016/S0140-6736(10)61086-0

One vodka binge induces subtle myocardial injury

Two researchers from Berlin in Germany recently persuaded 23 healthy young adults to simulate a vodka binge so they could assess the damage done to myocardium by excessive acute alcohol consumption. The volunteers drank enough vodka over a few hours to generate an average blood alcohol that peaked at 1.3 g/l. All had a hangover when they had cardiac magnetic resonance imaging one day later.

Compared with baseline scans, the new scans showed measurable myocardial oedema (T2 signal intensity) and hyperaemia (global

relative enhancement), which were also evident in a comparison with scans from eight non-drinking controls. The vodka had no discernible effect on left ventricular function, although three of the volunteers developed small pericardial effusions. Six of the 12 volunteers tested had raised serum concentrations of high sensitivity cardiac troponin I, suggesting subtle cardiac injury. All changes on magnetic resonance imaging had resolved one week later.

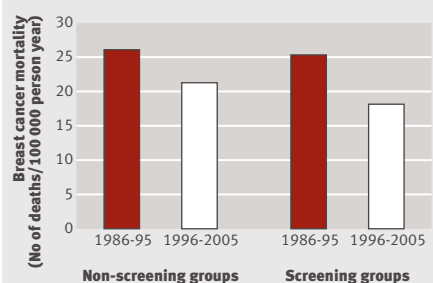
These preliminary findings suggest that binge drinking can induce reversible changes in the myocardium and serological markers that are consistent with an inflammatory reaction, say the researchers. Because they found no evidence of irreversible tissue injury, the researchers say a single binge is unlikely to trigger an acute cardiac event, at least in healthy volunteers. The story may be different if the bingeing continues.

JAMA 2010;304:1328-30

Breast cancer screening saves lives, but not many

Screening mammography was responsible for about a third of the drop in breast cancer mortality that took place in Norway between 1986

BREAST CANCER DEATHS IN WOMEN SCREENED AT AGE 50-69



Adapted from *N Engl J Med* 2010;363:1203-10

and 2005, say researchers. Even the most optimistic estimates from their nationwide study suggest that mammography for women aged 50-69 reduced deaths from breast cancer by just 10% (or by 2.4 deaths/100 000 person years). This was less than expected, and much less than the impact on deaths reported in early trials.

The study, which compared death rates over time in both screened and unscreened populations, was designed to isolate the effects of screening from other factors that have also improved survival, such as heightened awareness and better treatment. The results are believable, says one commentator, and they probably reflect the current benefits of screening middle aged women in a modern health system (p 1276).

For women in the US, these figures mean that mammography prevents one death from breast cancer for every 2500 women screened, he writes. It's also responsible for up to 1000 false alarms among the remaining 2499, half of whom will have an unnecessary biopsy. With these estimates, the decision to opt in or opt out is, he says, "a close call" for women. The world has moved on and mass screening for breast cancer may not be the effective strategy it once was.

N Engl J Med 2010;363:1203-10

Who needs compression stockings after a stroke?

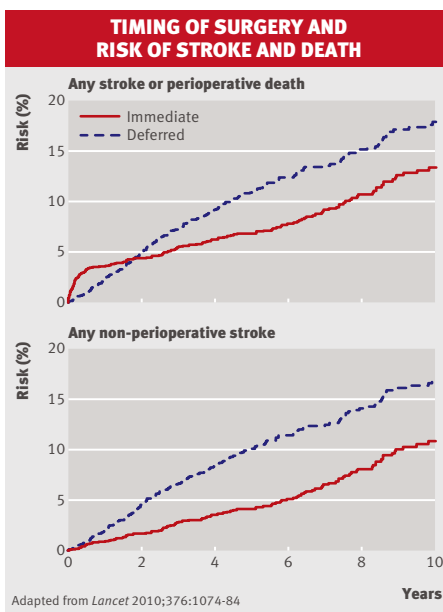
In 2009, the first in a family of three large trials reported (unexpectedly) that thigh length compression stockings don't prevent venous thromboembolism in people immobilised by a stroke. The second trial, which compared thigh length and below knee stockings, immediately stopped recruiting. But the collaboration had plenty of outcomes data by then, and a direct comparison now suggests that thigh length stockings are associated with significantly fewer proximal deep vein thromboses (6.3% (98/1552) v 8.8% (138/1562); adjusted odds ratio 0.69, 95% CI 0.53 to 0.91). But if thigh length stockings don't work, how can they work better than knee length stockings?

One possibility is that knee length stockings actually increase the risk of deep vein thrombosis in people with stroke. Another is that thigh length stockings work, but not well enough to make a statistically discernible difference, even in a large trial. For now, doctors should probably assume that thigh length stockings provide modest protection at best, and that knee length stockings provide less, says an editorial (www.annals.org/content/early/2010/09/20/0003-4819-153-9-201011020-00285.full?aimhp). Thigh length stockings caused more skin breakdown in this trial (3.9% (61/1552) v 2.9% (45/1562)), which looked at 3114 men and women with acute stroke.

Low dose heparins, cautiously prescribed, remain the best option for people without contraindications, says the editorial. Thigh length stockings are a reasonable alternative for the rest, including those with haemorrhagic stroke. All participants in this trial were treated according to local protocols, which might include antithrombotic, antiplatelet, or anticoagulant drugs.

Ann Intern Med 2010; www.annals.org/content/early/2010/09/20/0003-4819-153-9-201011020-00280.full?aimhp

Early surgery looks best for asymptomatic carotid stenosis



Adapted from *Lancet* 2010;376:1074-84

Long term follow-up from a trial that began in 1993 has confirmed that carotid endarterectomy is the best option for adults with an asymptomatic carotid stenosis. Compared with a "wait and see" strategy, early surgery cut the risk of a later stroke by around half over 10 years (ratio of non-perioperative stroke rates in patients allocated immediate surgery versus those allocated deferral was 0.54, 95% CI 0.43 to 0.68; $P < 0.0001$). The ben-

efits of early surgery were clear by five years, even when researchers accounted for perioperative risk of stroke or death (3%, 2.4% to 3.9%).

Researchers recruited 3120 patients between 1993 and 2003. Half had immediate surgery. The rest were deferred, although a quarter had a carotid endarterectomy some time during follow-up (26%; 407/1560). All had recommended medical treatments as required, including antihypertensive and antithrombotic drugs, and more recently, statins.

In subgroup analyses, the long term benefits of early surgery were clearest for patients under 75 years. The interplay of perioperative risk and longer term benefit may be different for older patients with a shorter life expectancy, say the authors. Results may also be different in centres with higher rates of surgical morbidity and mortality, and international audits should be set up to track surgical risks out there in the real world, they write.

Lancet 2010;376:1074-84

Endobronchial valves are not recommended for severe emphysema

People with emphysema have hyperinflated lungs, and evidence indicates that reducing lung volume can improve symptoms and prolong life expectancy. Surgery is one option, but it is risky. Endobronchial valves are a less invasive alternative. They can be placed using a bronchoscope and reduce hyperinflation (in theory) by letting air out of the worst affected segments without letting any more in. But do they work in practice? A randomised trial recently reported mixed results. Compared with medical management alone, placement of one to nine valves per patient was associated with small but significant improvements in lung function, walking distance (an extra 19 m in six minutes, 95% CI 1.3 m to 36.8 m), and quality of life. The valves were also associated with an excess of serious complications (10.3% v 4.6%), including pneumonia distal to the valves, exacerbations of chronic obstructive pulmonary disease (7.9% v 1.1%; $P = 0.03$) and haemoptysis (6.1% v 0.0%, $P = 0.01$). Thirty one of 220 patients had their endobronchial valves removed less than a year after placement. Three others spontaneously coughed up at least one valve during two further years of follow-up.

These results aren't good enough for routine use, says an editorial, and doctors should concentrate on optimising medical management first (p 1280). Drug treatments were left to the discretion of the attending doctors in this trial. It is not clear how many patients were managed in full accordance with international guidelines.

N Engl J Med 2010;363:1233-44

Cite this as: *BMJ* 2010;341:c5275