Drug eluting stents seem safe in the medium to long term

Continuing uncertainty about the long term safety of drug eluting stents led Swedish researchers to take a close look at what happened to Swedish adults who received any kind of stent between 2003 and 2006. The drug eluting option seemed safe in analyses with up to five years of follow-up. The researchers found no extra deaths (relative risk 0.94, 95% CI 0.85 to 1.05) and no extra heart attacks (0.97, 0.88 to 1.06) in patients who had drug eluting stents compared with those who had bare metal stents. Drug eluting stents were associated with a lower risk of restenosis (0.43, 0.36 to 0.52) that was most marked in patients with the worst lesions.

The main analysis was confined to the 28953 adults who had just one stent during index percutaneous coronary intervention. The findings were similar when the analysis was extended to all adults who received one or more stents (n=47 967). All analyses were carefully adjusted for clinical and demographic differences between adults receiving drug eluting stents and those receiving bare metal stents.

This study extends an earlier report examining the same national register that hinted at greater long term mortality with drug eluting stents than with bare metal stents. The new study—which includes more data and a longer follow-up—seems reassuring, say the researchers.

In a separate randomised trial published in the same issue of the New England Journal of Medicine (pp 1946-59), drug eluting stents also seemed safe for 3006 people with acute myocardial infarction. Those individuals given a paclitaxel eluting stent had no more adverse cardiovascular events over one year than did controls given a bare metal stent (8.1% v 8.0%; hazard ratio 1.02, 95% CI 0.76 to 1.36). The combined safety end point included death, reinfarction, stroke, and stent thrombosis. People given a paclitaxel eluting stent needed significantly fewer revascularisation procedures in the first year than those given a bare metal stent. N Engl J Med 2009;360:1933-45

Anticoagulation guided by ultrasound reduces recurrent deep vein thrombosis

People with a deep vein thrombosis (DVT) need anticoagulation, but specialists are still arguing about how long to treat them and, more specifically, how to tell when treatment can be stopped safely. Ultrasound scanning of the affected vein to look for residual thrombosis is the latest strategy to be tested in a randomised trial. People treated flexibly on the basis of scan results had fewer recurrences of DVT than did people treated for a fixed period (32/270 (11.9%) v 46/268 (17.2%); hazard ratio 0.64, 95% CI 0.39 to 0.99).

Participants in the fixed treatment group took warfarin for three or six months after a provoked or unprovoked DVT in the proximal leg veins. People treated flexibly were scanned regularly and continued warfarin only if the scan showed residual thrombosis. In this group, those with a provoked DVT were treated for up to 12 months and those with an unprovoked DVT for up to 24 months.

So, should we be scanning everyone for residual thrombosis? Probably not, says an accompanying editorial (pp 644-6). This trial wasn’t big enough to establish safety, and the flexibly treated group had more major bleeds than the fixed treatment group, although the difference wasn’t statistically significant (4/270 (1.5%) v 2/268 (0.7%)). Also, we still don’t know how serial scanning fits in with more traditional risk profiling using clinical, demographic, and genetic factors. Ann Intern Med. 2009;150:577-85

Microalbuminuria doubles the risk of venous thromboembolism

Microalbuminuria is a known risk factor for heart attacks and strokes. Urinary excretion of albumin was also an independent risk factor for venous thromboembolism (VTE) in a large cohort of adults from the Netherlands.

Overall, 129 of the 8574 participants had a deep vein thrombosis or pulmonary embolus during nearly nine years of follow-up. Risk went up in line with urinary albumin excretion, and a clear and significant association emerged after multiple adjustments for other factors associated with VTE. Incidence of VTE was higher even for individuals with urinary albumin excretion within the established normal range. Patients excreting more than 30 mg of albumin a day at baseline were twice as likely to have a VTE as those excreting less (adjusted hazard ratio 2.00, 95% CI 1.34 to 2.98). The link between
Microalbuminuria and VTE was strongest for unprovoked events.

Microalbuminuria is probably a marker for diffuse endothelial dysfunction, which alters blood concentrations of procoagulant proteins, say the researchers. The disorder is common and might be treatable with agents that inhibit the renin-angiotensin system. Trials to find out if such agents protect against VTE would be worth while. *JAMA* 2009;301:1790-7

**Governments need two drugs, not one, to combat pandemic influenza**

Most countries are currently stockpiling a single antiviral, oseltamivir, to use against potentially pandemic influenza viruses including swine flu. Governments will also need a smaller supply of an alternative antiviral to help prevent the spread of drug resistance, say researchers.

In their mathematical model, using a “spare” drug at the start of a pandemic curbed the spread of resistance to the primary drug (oseltamivir), reduced the overall attack rate of the virus, and reduced the proportion of the population infected by resistant strains. Two strategies seemed to work equally well—using the spare drug and the primary drug in combination until the spare drug ran out; and using up the spare drug first before distributing the primary drug. A small stockpile of zanamivir or even amantadine might be enough to prevent resistance to oseltamivir emerging early and spreading further, the researchers conclude. Early use of a spare antiviral agent seemed to work both for the source population and for other populations infected later by travellers, so long as the source population used the spare agent first.

No mathematical model is completely watertight, but the researchers say their findings justify further work to find out which drug would be the best spare and which of the two strategies (combined or sequential) would have the greatest impact on the morbidity and mortality associated with drug resistant pandemic influenza. *PLoS Medicine* 2009; doi:10.1371/journal.pmed.1000085

**Lukewarm reception for prognostic markers for prostate cancer**

Distinguishing lethal from non-lethal disease is one of the most pressing priorities in prostate cancer research, and attention has focused recently on molecular markers present in biopsy or prostatectomy specimens. The latest study looked for potential markers in biopsy specimens from 1172 US veterans diagnosed with prostate cancer between 1991 and 1995. Three markers were associated with an increased risk of death over 11-16 years of follow-up: *p53* (adjusted hazard ratio for positive v negative staining 1.48, 95% CI 1.06 to 2.08); bcl-2 (1.61, 1.01 to 2.57); and microvessel density (adjusted hazard ratio for highest v lowest quartile 3.20, 1.77 to 5.78).

The biology of these markers explains why they might be linked to mortality in prostate cancer. The presence of *p53* or bcl-2 indicates a loss of tumour suppression or inhibition of apoptosis, respectively, and a high density of microvessels suggests uncontrolled angiogenesis.

These findings are a small step forward, but there’s still a long way to go, says a linked editorial (pp 647-9). The associations with mortality in this study are relatively weak, and all three markers are easy to miss or at least misinterpret in specimens from needle biopsies. Both shortcomings limit the usefulness of these markers in modern practice. In the US, most prostate cancers are now detected through screening for prostate specific antigen and are early, localised, and have an excellent prognosis. The tests evaluated in this study are complex and unlikely to help doctors decide which patients to treat aggressively and which to reassure. Even in this historical cohort, only one fifth of the deaths were caused by prostate cancer (181/842). *Ann Intern Med* 2009;150:595-603

**Housing the homeless cuts hospital admissions and visits to emergency departments**

Homelessness is an increasing problem in the US, where a relatively new approach called Housing First is attracting attention. Housing First offers stable housing without the usual requirements that clients first seek help for addictions and stop drinking. Observational evidence from Seattle, WA, indicates that housing with no strings attached can help keep the most vulnerable homeless people out of hospitals and jails. More recently, an intervention based on Housing First seemed to work for chronically homeless people in Chicago, IL, reducing days spent in hospital and visits to emergency departments compared with usual care.

Participants had at least one chronic medical condition—such as hypertension, diabetes, or lung disease—and were recruited on discharge from two Chicago hospitals. The intervention included a case manager who organised respite care then stable housing, coordinated medical and social care, and met with clients twice a week. Relative to controls, hospital admissions and days spent in hospital fell by nearly a third over 18 months (29%, 95% CI 10% to 44% and 29%, 8% to 45%, respectively) and visits to emergency departments fell by a quarter (24%, 3% to 40%).

Unexpectedly, the intervention made no difference to quality of life or physical functioning.

An editorial adds that the support might not save money either (pp 1822-4). Housing interventions typically cost $12 000-$16 000 (£7970-£10 625; €9000-€12 000) per person per year. Crude estimates suggest healthcare savings of around $9800 per person per year for this particular client group. *JAMA* 2009;301:1771-8

Cite this as: BMJ 2009;338:b1895