

SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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Trials fail to resolve PSA controversy

Twenty years after the first tests for prostate specific antigen (PSA), we still have no clear answer to the question, does screening men for prostate cancer do more good than harm? Two long awaited trials have reached different conclusions—one essentially positive, one essentially negative. Neither trial reports an unambiguous or definitive result for mortality, says an editorial (p 1351). Both could reasonably be criticised for reporting too early and leaving doctors and the “worried well” to deal with the confusion.

The European trial studied 162 243 men and compared screening with PSA measurement every four years with no screening. There were 20% fewer deaths from prostate cancer in the screened group after nine years (rate ratio 0.8, 95% CI 0.65 to 0.98), or seven fewer deaths for every 10 000 men screened.

The 76 693 men in the US trial had usual care or were screened with PSA tests and rectal examinations every year. Screening made no significant difference to deaths from prostate cancer over seven years (1.13, 0.75 to 1.70).

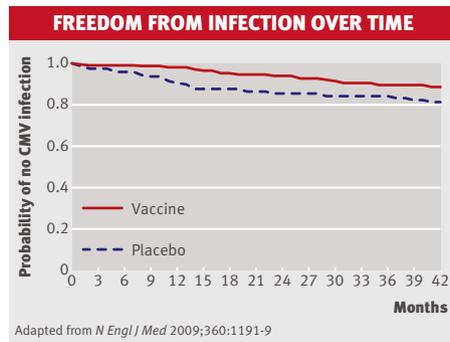
Overdiagnosis was a problem for screened men in both trials. Screening led to extra investigations and invasive treatments, including radical prostatectomies. In the European trial, an extra 48 men were treated for prostate cancer for every life saved.

Data on quality of life and cost effectiveness are on the way and should help clarify the benefits and harms of screening, says the editorial. For now, the harms look more obvious than the benefits.

N Engl J Med 2009;260:1310-9; 1320-8

New vaccine against CMV cuts women's risk of infection by half

The herpes virus, cytomegalovirus (CMV), passes from mother to child during pregnancy and can cause serious congenital defects. Seronegative women need a vaccine, and one candidate—developed from a viral protein and a new adjuvant MF59—was recently tested in a phase II trial. Vaccinated women had significantly fewer CMV infections than women given placebo injections (8% (18/225)



Adapted from *N Engl J Med* 2009;360:1191-9

vs 14% (31/216)). The new vaccine was about 50% effective over 42 months (95% CI 7% to 73%), and the result was conclusive enough to stop the trial early. All CMV infections were asymptomatic. The 464 participants were of childbearing age (recruited from postnatal wards) and were seronegative for CMV when they joined the trial. They had three doses of vaccine or placebo—one at baseline, one after one month, and one at six months.

The trial wasn't nearly big enough to look for an effect on congenital CMV infections in infants, although the authors did test all babies born during the trial. They found CMV infection in one of 81 babies born to vaccinated women and three of 97 babies born to women given a placebo. One of the babies had serious congenital abnormalities including microcephaly. An editorial (p 1250) comments that future trials will need to recruit between 3400 and 10 000 seronegative women to test the new vaccine's effect on infections in newborns. It will be even harder to evaluate whether it prevents congenital abnormalities.

N Engl J Med 2009;360:1191-9

Religious coping mechanisms are linked to aggressive treatments for terminal cancer

People who relied on faith to cope with terminal cancer had more aggressive treatment in the last week of life than others in a prospective study from the US. The authors measured religious coping with a few brief but validated questions to 345 people with advanced cancer, then followed them up until death an average of 122 days later. Patients with above average scores for positive religious coping—such as trusting in God to help and care for them—had a higher odds of mechanical ventilation

(adjusted odds ratio 2.81, 95% CI 1.03 to 7.69) and life prolonging treatments (2.90, 1.14 to 7.35) in the final week compared with patients with below average scores.

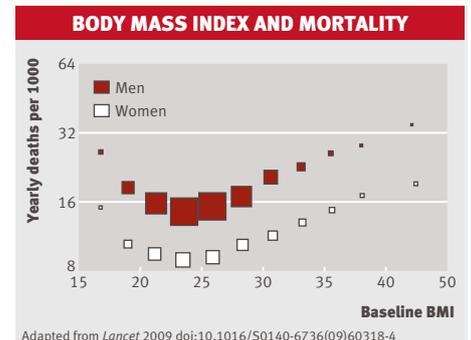
They were also less likely to plan care in advance by making living wills, establishing resuscitation preferences, or appointing a healthcare proxy. None of these factors accounted for their aggressive end of life care, however, which remained significantly more likely even after multiple adjustments. Participants were mostly Christian.

Aggressive intervention isn't necessarily the best option for patients dying of cancer, say the authors, and faith may be denying some people the chance of a good death. Doctors and those providing pastoral care should be sensitive to this possibility until we find out more about how religious belief drives end of life decisions.

JAMA 2009;301:1140-7

A body mass index above 25 can shorten your life

The latest study to look at the link between body mass index (BMI) and health reports that men and women of all ages should maintain a body mass index of 22.5-25 for the best chance of a long and healthy life. Mortality climbed by 30% for every increment of 5 above this optimum range (hazard ratio 1.29, 95% CI 1.27 to 1.32). Excess deaths from vascular disease dominated the overall picture, but incremental increases in body mass index were also associated with deaths from diabetes (2.16, 1.89 to 2.46), kidney disease (1.59, 1.27 to 1.99), liver disease (1.82, 1.59 to 2.09), respiratory disease (1.20, 1.07 to 1.34), and cancer (1.10, 1.06 to 1.15). A body mass index below the optimum range



Adapted from *Lancet* 2009 doi:10.1016/S0140-6736(09)60318-4

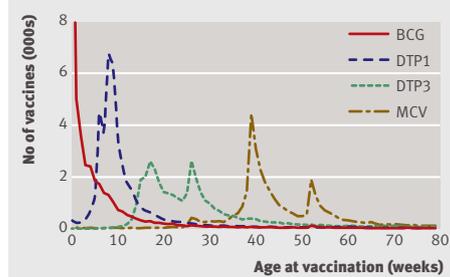
was associated with excess deaths from smoking related disease.

These figures come from 57 observational studies in nearly 900 000 people. The most likely explanation for the strong link between increasing body mass index and death is that one directly causes the other, say the authors. Increased body fat raises blood pressure and disrupts serum lipid balance and glucose metabolism. All are mediators of an early death from heart attack or stroke. The authors estimate that moderate obesity reduces survival by two to four years. Morbid obesity (body mass index over 40) reduces survival by eight to 10 years, about the same as a lifetime of heavy smoking.

Lancet 2009 doi:10.1016/S0140-6736(09)60318-4

Many developing countries struggle to deliver childhood immunisations on time

TIMING OF IMMUNISATIONS



Prevalence surveys help international authorities such as the World Health Organization monitor the proportion of children who receive scheduled immunisations. The snapshot figures give a poor idea of the timeliness of immunisation, however, so researchers analysed data from 45 low income and middle income countries to look for potentially important delays. Most of the countries were in Africa or the Americas.

They found wide variations in the timing of immunisations, both within and between countries. In most countries at least a quarter of children were immunised against diphtheria, pertussis, and tetanus (DTP); measles (MCV); and tuberculosis (BCG) at about the right time. In the 12 countries with longest delays, however, a quarter of children received their immunisations 10-19 weeks late. Delays were longest in rural areas.

At least some of the late immunisations may have been caused by national "catch-up" programmes designed to increase final coverage, say the researchers. But Chad, Cambodia, Mali, Mauritania, and Niger had long delays and poor overall coverage.

The data are necessarily rough and ready, because accurate timing was available for only 68% of immunisations, but the results could have important implications if delays mean less effective protection or a higher risk of side effects.

Lancet 2009 doi:10.1016/S0140-6736(09)60317-2

A BNP test makes little difference to severely breathless patients

Measurement of B-type natriuretic peptide (BNP) is a good test for heart failure, which makes it potentially useful for doctors faced with a severely breathless patient. At least one early trial suggested the test could improve management enough to reduce hospital stays and save money. But a more recent trial from Australia found the opposite. BNP tests on breathless patients in two emergency departments made no difference to clinical management, admissions (85.6% *v* 86.6%), or length of stay (median 4.4 *v* 5.0), even though they discriminated between those with and without heart failure. Similar proportions of tested and untested patients were given bronchodilators (39.8% *v* 36.6%), diuretics (36% *v* 35.6%), antibiotics (32.7% *v* 36.6%), steroids (26.1% *v* 21.2%), morphine (5.6% *v* 5.6%), and other treatments in the emergency department. Doctors had BNP test results within 60 minutes for patients in the tested group. Controls were not tested for BNP.

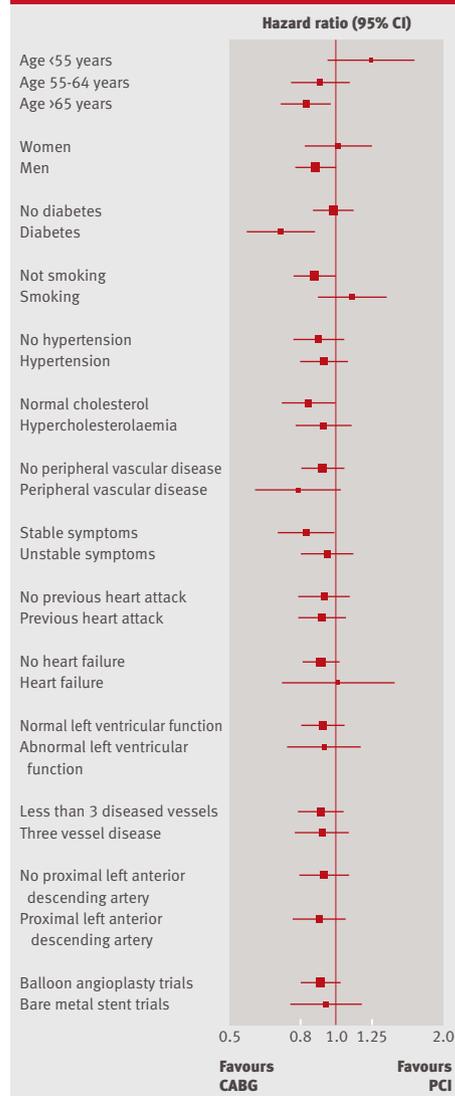
Routine testing may not be justified in this clinical setting, say the authors. Their participants were all severely breathless and in need of urgent medical care. A BNP test made little difference to management or outcome. Nearly 7% of patients in both groups died within 30 days of admission. Around 45% (274/612) had heart failure.

Ann Intern Med 2009;150:365-71

CABG looks best for patients with multivessel heart disease and diabetes

The best choice of revascularisation technique isn't always clear for patients with multivessel coronary artery disease. The choice is particularly difficult for those with moderate disease and normal left ventricular function who could reasonably have either a coronary artery bypass graft (CABG) or the less invasive percutaneous coronary intervention (PCI). Mortality rates over six years looked about the same for both procedures in a new meta-analysis of 10 trials, but a careful look at subgroups suggests that CABG is better for patients with diabetes (hazard ratio for death 0.7, 95% CI 0.56

MORTALITY AFTER TREATMENT WITH CABG AND PCI



to 0.87) and for those aged 65 or more (0.82, 0.70 to 0.97). Patients who had CABG needed fewer repeat procedures and had less angina at one year than those who had PCI.

These trials were done before drug eluting stents came along, but they are broadly consistent with other emerging evidence, says one observer (doi:10.1016/S0140-6736(09)60574-2). It is now fairly clear that CABG is the better procedure for people with multivessel disease who need revascularisation. Those with severe disease or diabetes should be offered CABG first. Those with one or two affected vessels, good left ventricular function, and no diabetes may not need revascularisation at all, however. Many of the patients in this meta-analysis would now be managed with best medical therapy instead.

Lancet 2009 doi:10.1016/S0140-6736(09)60552-3

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