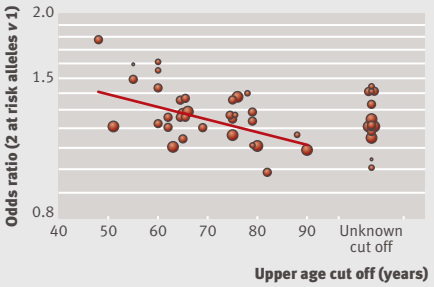
# SHORT CUTS

**ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS**

**Kristina Fister, associate editor, *BMJ* kfister@bmj.com**

**"This stern paper from the USA points out the Jacobean tragedy that awaits even the most bumbling pipe smoker: increased cotinine levels and decreased lung function"**
Richard Lehman's journal blog, doc2doc.bmj.com

**9p21 MARKERS AND RISK OF HEART DISEASE BY AGE OF ONSET**




Adapted from *JAMA* 2010;303:648-56

## Genetic testing for cardiovascular diseases falls short of clinical utility

As part of an extensive systematic review into 29 genes that might be the bearers of heredity for cardiovascular diseases, a meta-analysis reports an association between single nucleotide polymorphisms on chromosome 9p21 and heart disease. On the basis of data from 35 872 cases and 95 837 controls in the 22 included observational studies, researchers calculated that carriers of two at risk alleles were 1.25-fold more likely to develop heart disease (coronary heart disease, myocardial infarction, or coronary artery disease) than those who carried one risk allele. Similar results were found for carriers of one risk allele compared with those who carried none. The excess risk was age dependent: odds ratios increased with younger age at diagnosis.

The effect size was small, however. A 65 year old man with no traditional risk factors and no at risk alleles would have a 9.2% risk of heart disease over 10 years, whereas the risk increased to 11% and 13.2% for one and two at risk alleles, respectively. Corresponding numbers for a 40 year old woman would be 1.7%, 2%, and 2.4%.

Another study tested a literature based genetic risk score comprising 101 single nucleotide polymorphisms for prediction of myocardial infarction, stroke, arterial revascularisation, and death from cardiovascular disease. In a prospective cohort, 19 313 initially healthy women were followed over 12 years. The genetic risk score did not improve the prediction of cardiovascular events over the use of traditional risk factors. However, although the genetic risk score was not associated with incident events (hazard ratio 1.00, 95% CI 0.99 to 1.01), self reported family history remained a significant predictor in multivariate models.

***JAMA*** 2010;303:648-56,631-7

## Statins increase risk of diabetes

People who take statins have a 9% increased risk of type 2 diabetes compared with those on placebo or usual care. For one extra incident case of diabetes to occur, 255 (95% CI 150 to 852) people would need to take statins for four years. This was found in a collaborative meta-analysis of published and unpublished data from 13 randomised trials with a total of 91 140 participants. Only trials that lasted more than one year, had more than 1000 participants, and had identical follow-up in both groups were included.

No difference was found in the association with the risk of diabetes between hydrophilic and lipophilic statins. Residual confounding, such as improved survival with statins or an improved lifestyle with placebo, could account for the findings, but this is unlikely say the researchers. Similarly, low heterogeneity (11%) makes it implausible that an increased risk of diabetes is a chance finding.

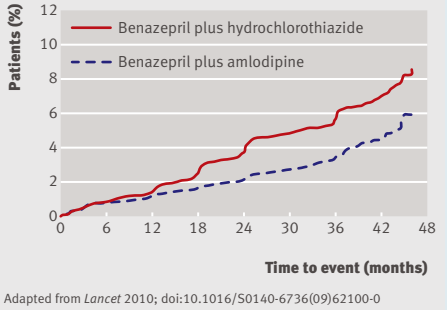
Given the cardiovascular benefits of statins, the authors advise that clinical management should not change for people with moderate or high cardiovascular risk. However, it may be best not to introduce statins in people at low risk, or in groups of patients for whom the benefits of statins have not been confirmed.

***Lancet*** 2010; doi:10.1016/S0140-6736(09)61965-6

## How best to protect kidneys in hypertension?

A randomised trial being undertaken in five countries has been stopped after 36 months because one combination of drugs—benazepril plus amlodipine—was better at reducing the relative risk of a composite cardiovascular outcome than the comparison combination—benazepril plus hydrochlorothiazide. Participants were 11 506 people with hypertension who were at high cardiovascular risk.

**EFFECT OF TREATMENT ON PROGRESSION OF KIDNEY DISEASE AND CARDIOVASCULAR DEATH**




Adapted from *Lancet* 2010; doi:10.1016/S0140-6736(09)62100-0

A prespecified secondary analysis of renal outcomes now indicates that benazepril plus amlodipine may also be better at slowing the progression of nephropathy in these patients. Progression of chronic kidney disease, defined as a doubling in the concentration of serum creatinine, or end stage renal disease, was seen in 113 (2%) of patients randomised to benazepril plus amlodipine, compared with 215 (3.7%) in the benazepril plus hydrochlorothiazide group (hazard ratio 0.52, 95% CI 0.41 to 0.65). A combined outcome of chronic kidney disease and all cause mortality also favoured benazepril plus amlodipine. The renoprotective effect was not seen for patients with diabetic nephropathy, however, who accounted for nearly 60% of patients with chronic kidney disease.

The editorialists (doi:10.1016/S0140-6736(10)60098-0) question the validity of the conclusions, which may have been compromised as a result of bias, reduced power, and a problem with the composite outcome.

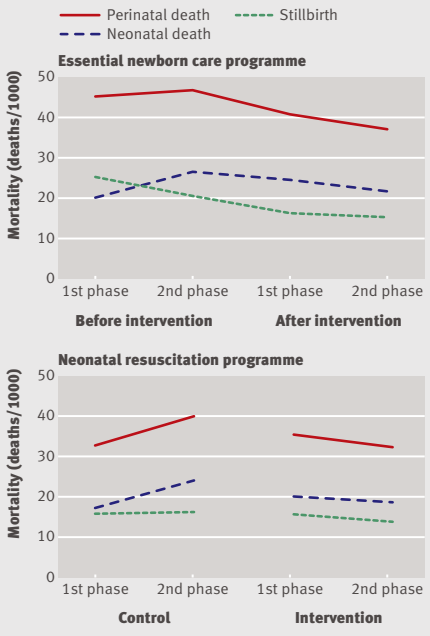
***Lancet*** 2010; doi:10.1016/S0140-6736(09)62100-0

## "Train the trainer" education linked to small improvements in outcomes for babies

A before and after study of 57 643 infants in five developing countries—Argentina, Democratic Republic of Congo, Guatemala, India, Pakistan, and Zambia—evaluated the World Health Organization course on essential newborn care. Before data were collected, all birth attendants underwent a three day course that included education on data collection, differentiation between stillbirth and early neonatal death, clinical assessments, and adult education techniques. Experienced trainers taught two master trainers, who taught one or more community coordinators, who then taught birth attendants (traditional birth attendants, nurses, midwives, and doctors).

A three day intervention course was then taught in a similar chain manner. This included routine neonatal care, initiation of breathing and resuscitation, thermoregulation, breast feeding, "kangaroo" (skin to skin) care, care of small babies, recognition of danger signs, and recognition and

**EFFECT OF TRAINING PROGRAMMES ON OUTCOMES**




Adapted from *N Engl J Med* 2010;362:614-23

initial management of complications. Finally, birth attendants taught mothers to implement the essential newborn care practices.

Only the rate of stillbirth improved after the intervention compared with baseline (relative risk 0.69, 95% CI 0.54 to 0.88). No change was seen for neonatal deaths in the seven days after birth, or in perinatal deaths. When the before and after periods were each divided into two—to test for time-trend effects—improvements were seen in seven day mortality but not in stillbirths or perinatal deaths (P=0.03, P=0.60, and P=0.32, respectively).

An additional three day course in neonatal resuscitation, which was taught after the essential newborn care course and was tested in a cluster randomised manner, did not improve any of the outcomes for babies.

***N Engl J Med*** 2010;362:614-23

## Patients with superficial vein thrombosis may need a more careful check

Two hundred and eleven vascular centres in France were invited to participate in an observational study of superficial vein thrombosis. Ninety six centres (45.5%) accepted and 844 consecutive patients were recruited. At presentation, nearly a quarter also had deep vein thrombosis (198; 23.5%) or symptomatic pulmonary embolism (33; 3.9%).

Researchers followed up for three months those patients who did not have deep vein thrombosis or pulmonary embolism at presentation. Of these, 10.2% (58/600) developed vascular complications: three (0.5%) developed pulmonary embolism, 15 (2.8%) developed deep vein thrombosis, 18 (3.3%) had asymptomatic downstream extension of superficial vein thrombosis, and 10 (1.9%) had recurrence of superficial vein thrombosis. Recruitment was slow, and the study ended before it could gather the 1200 patients needed to estimate the incidence of venous thromboembolic events with a precision of plus or minus 1%.

Independent risk factors for complications were male sex, absence of varicose veins, and a history of deep vein thrombosis or cancer. Nearly all patients had received elastic stockings after the baseline event (584/597; 97.7%), and nine in 10 had been taking anticoagulant drugs either therapeutically (374/597; 62.9%) or prophylactically (216/597; 36.7%).

***Ann Intern Med*** 2010;152:218-24

## No change needed in the standard dose of prophylactic platelet transfusion

A multicentre trial tested whether halving or doubling the standard dose—$2.2\times10^{11}$ platelets per square metre of body surface area—currently used for prophylactic transfusion of platelets improves outcomes related to haemostasis and transfusion. Participants were 1272 people with cancer admitted to hospital for haematopoietic stem cell transplantation or chemotherapy, in whom platelet counts of 10 000/mm$^3$ (the threshold for transfusion) or lower were expected for five or more days.

The primary outcome (bleeding of grade 2 or higher, using the World Health Organization criteria) did not differ between the groups, being 68% in the low dose group, 67% in the medium dose group, and 69% in the high dose group. Furthermore, the groups did not differ in the highest grade of bleeding seen, number of days to occurrence of the primary outcome, number of days for which the primary outcome was observed, or the need for red cell transfusions. The only death judged to be caused by bleeding occurred in the high dose group.

As expected, the low dose group received the least platelets and the high dose group received the most. However, people randomised to the low dose group had a median of five transfusions, whereas those in the medium dose and high dose groups received three.

***N Engl J Med*** 2010;362:600-13

## Doctor-doctor communication can improve patient outcomes

A meta-analysis has found that two way communication between primary care doctors and specialists via telephone, videoconferencing, planned face to face meetings, or written correspondence may improve patient outcomes in mental health and endocrinology. The meta-analysis included 23 trials and before and after studies, which mostly looked at the care of people with depression or diabetes. The reviewers also searched for studies of communication interventions in the care of people with cancer, but they found none. They faced various methodological problems, including non-specification of primary outcomes in many studies, high heterogeneity, and low internal and external validity.

For patients with depression, they found that doctor-doctor communication achieved improvements that corresponded to 4.6 points on the Centre for Epidemiologic Studies depression scale, or even 5.3 points when the non-randomised trials were pooled. This is a larger effect size than seen in some trials of antidepressant drugs, say the authors. In people with diabetes, they found an improvement equivalent to a 1.4% lowering in glycated haemoglobin, but only non-randomised studies were available.

Because communication was usually studied as part of a multifaceted intervention, it is unclear whether improved outcomes were the consequence of better communication or other features of collaboration, such as shared records and shared management of care. Although little information on costs was available, the researchers believe the findings support research and funding of communication strategies for improving patients' health.

***Ann Intern Med*** 2010;152:247-58

Cite this as: *BMJ* 2010;340:c1067