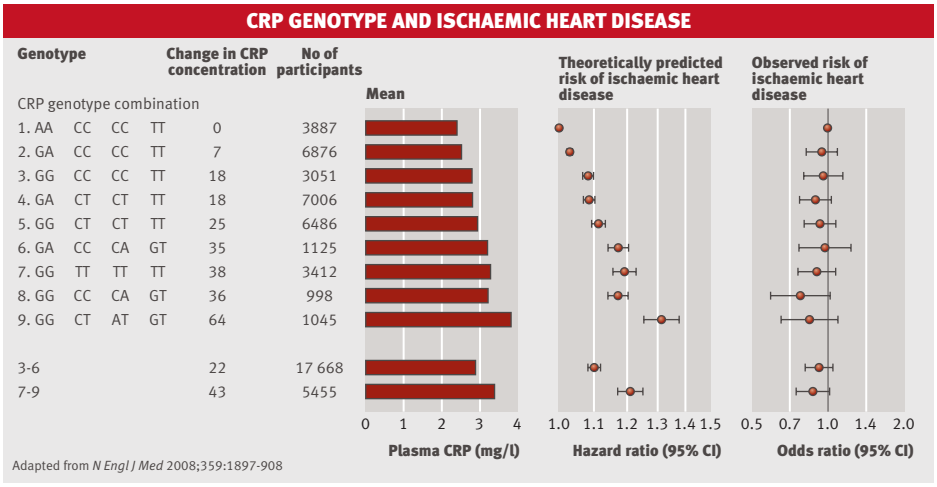
SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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

CRP is unlikely to cause vascular disease



Adapted from *N Engl J Med* 2008;359:1897-908

C reactive protein (CRP) may be a well known biomarker for atherosclerotic disease but the association is unlikely to be causal, according to a new genomic study. The authors began with the idea that if CRP causes vascular disease, then genetic polymorphisms responsible for lifelong high concentrations of CRP should also predict vascular disease. They then tested this theory in four cohorts of Danish adults.

The studies confirmed that high concentrations of CRP were associated with a 60% increase in the risk of heart disease and a 30% increase in the risk of cerebrovascular disease (hazard ratios 1.6, 95% CI 1.2 to 2.1 and 1.3, 0.8 to 2.0). They also confirmed that four genetic variants were associated with raised serum concentrations of CRP. In the final test, however, the genetic polymorphisms failed to predict either heart disease or cerebrovascular disease. The authors found no link between genotype and clinical disease in any of the four studies.

The findings strongly suggest that CRP doesn't cause vascular disease directly, says an editorial (p 1953), so treating high concentrations probably won't work. The well known link between CRP and vascular disease could be the result of confounding—perhaps inflammation causes both raised CRP concentrations and vascular disease. It is also possible that vascular disease simply causes raised concentrations of CRP.

N Engl J Med 2008;359:1897-908

Be selective with aggressive phototherapy in very premature babies

Phototherapy reduces the high serum concentrations of bilirubin associated with prematurity. But does it save lives or prevent disability? A team of researchers from the US recently compared more or less aggressive phototherapy in a carefully planned randomised trial. The more intensive regimen reduced the risk of neurodevelopmental impairment in premature infants but had no overall effect on mortality (24% (230/946) *v* 23% (218/944); relative risk 1.05, 95% CI 0.90 to 1.22). In fact, there was a worrying trend towards excess deaths in the smallest babies given aggressive phototherapy (39% (163/417) *v* 34% (142/412);1.13, 0.96 to 1.34). Exploratory analyses suggested an 89% chance that extra risk is real, and the researchers warn doctors to take it seriously.

All the infants in this trial weighed no more than 1000 g at birth. Overall, infants treated to lower target concentrations of bilirubin had a lower risk of severe hearing loss, athetosis, and mental impairment at the age of 18-22 months than controls treated to higher targets. These benefits are clinically relevant, say the researchers, particularly for babies weighing more than 750 g. The excess deaths were confined to the subgroup of babies weighing less than this. One possible explanation is that aggressive phototherapy causes oxidative injury to cell membranes in the smallest babies with the thinnest skin.

N Engl J Med 2008;359:1885-96

Ontario's natural experiment in influenza vaccination pays off

In 2000, the authorities in Ontario, Canada, launched the world's first universal vaccination programme against influenza, offering free vaccination to anyone over 6 months of age. The other Canadian provinces opted to continue targeted vaccination. This large natural experiment seems to have paid off. An ecological study shows that while deaths from flu fell everywhere in Canada after 2000, they fell furthest in Ontario (74% *v* 57% in other provinces combined, P=0.002). Health service use, including hospital admissions and doctors' visits for flu also fell significantly further in Ontario, particularly in people under 65, who had the most to gain from a universal programme.

The study essentially compared data on flu related outcomes before (1997-2000) and after (2000-4) the change in policy. The authors were limited to data available in regional and national records, but they did their best to strengthen the results with confirmatory sensitivity analyses.

The authors and a linked comment (doi:10.1371/journal.pmed.0050216) agree that this analysis of Ontario's unique programme provides at least circumstantial evidence that universal vaccination helps prevent death and disease caused by flu, even when uptake rates are relatively low. Between 2000 and 2004 mean vaccination rates for people over 12 reached 38% in Ontario compared with just 24% in the other provinces (P<0.001).

PLoS Med 2008 5:e211 doi:10.1371/journal.pmed.0050211

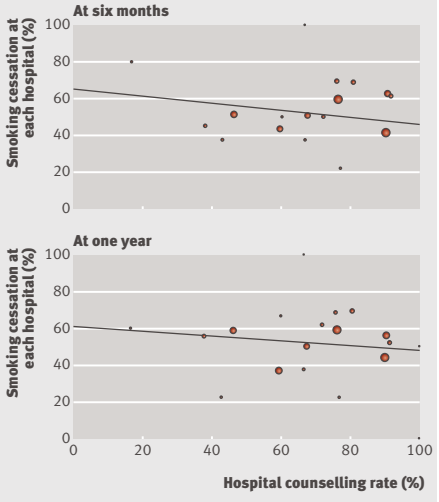
Poor data hamper safe and effective treatment of type 2 diabetes

A bewildering number of oral treatments are available for type 2 diabetes thanks to an explosion in drug development over the past decade or so. All licensed antidiabetic drugs control hyperglycaemia, and we already know that tighter glycaemic control protects against microvascular complications, such as retinopathy. It is much less clear how doctors should optimise treatment to prevent cardiovascular disease, the other serious threat to the lives and livelihoods of people with type 2 diabetes.

A systematic search for drug trials reporting cardiovascular events or deaths found 40. Most trials lasted only a few months. Reporting standards were generally poor, and the trials were mostly too small to be conclusive. Soldiering on, researchers combined the results in a meta-analysis. All they could say with any confidence was that metformin probably reduces the risk of cardiovascular death compared with placebo or other agents (pooled odds ratio 0.74; 95% CI 0.62 to 0.89). Rosiglitazone may have the opposite effect (odds ratio for cardiovascular morbidity 1.68, 95% CI 0.92 to 3.06). Other results were inconclusive.
Arch Intern Med 2008;168:2070-80

Quality indicator for US hospitals should be revised

HOSPITAL PERFORMANCE AND QUIT RATES



Adapted from *Arch Intern Med* 2008;168:2111-7

US hospital staff are meant to advise people with heart attack to stop smoking. A record of cessation counselling after heart attack is a key indicator of hospital performance and quality of care in the US. Hospitals that don't do it right risk losing status and income.

This approach is only fair if the indicator—documented counselling—actually stops people smoking. But when researchers followed up more than 800 smokers treated for heart attack at 19 hospitals, they found no link between documented counselling and higher quit rates. Patients with a record of counselling were actually less likely to quit within a year of their heart attack than those without one (50.1% *v* 60.7%; adjusted relative risk of quitting at one year 0.76, 95% CI 0.61 to 0.94).

Records of cessation counselling look like a poor way to judge a hospital's quality of care for these patients, say the researchers. It is a process measure that isn't clearly associated with the desired outcome, possibly because notes don't accurately reflect what goes on at the bedside. In this study, 70.8% of patients without documented counselling remembered being advised to quit.
Arch Intern Med 2008;168:2111-7

Routine insulin therapy may harm premature babies

Hyperglycaemia is common in premature infants, and many are given insulin therapy to control it. Routine treatment from soon after birth did not improve outcomes in one trial, however, and the authors report a suspicious increase in deaths in babies given insulin from day one. Controls had standard care, and about a third needed insulin within the first week (36% (69/192)). Mortality by the expected date of delivery was comparable in both groups. But routine insulin was associated with significantly more deaths by day 28 (11.9% (23/194) *v* 5.7% (11/192); P=0.04).

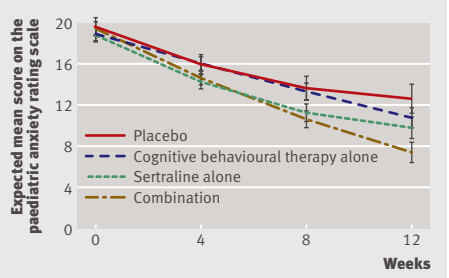
Hypoglycaemia was significantly more common in babies given routine insulin. The trial was finally suspended when the safety monitoring committee noticed an increased incidence of brain parenchymal lesions in the same group.

The trial was smaller and therefore weaker than planned. Even so, the researchers and a linked editorial (p 1951) agree that tight glycaemic control using insulin from birth cannot be recommended for very low birthweight infants. The babies in this trial weighed just over 1000 g on average.
N Engl J Med 2008;359:1873-84

Combined treatment works best for children with anxiety

Combination treatment with cognitive behavioural therapy and sertraline gives children with anxiety disorders the best chance of a good outcome, say researchers, at least in the short term. In their head to head trial, 80.7% (95% CI 73.3 to 86.4) of children given both treatments were much or very much improved after 12 weeks, compared with 54.9% (46.4 to 63.1) given sertraline alone, 59.7% (51.4 to 67.5) given cognitive behavioural therapy alone, and 23.7% (15.5 to 34.5) given placebo medication. Both active treatments worked equally well and significantly better than placebo when used alone, but the combination worked best on all outcome measures and against all comparators, with a number needed to treat of only 1.7 (1.7 to 1.9). Participating children had a mean age between 10 and 11

ANXIETY SCORES DURING TREATMENT



Adapted from *N Engl J Med* 2008;doi:10.1056/NEJMoa0804633

and at least one moderately severe anxiety disorder including social phobia, generalised anxiety disorder, or separation anxiety. Over a third had all three.

Serious side effects were uncommon, and only one serious event was thought to be related to treatment—one child's behaviour deteriorated substantially during treatment with sertraline. Children treated with sertraline alone reported more insomnia, fatigue sedation, and restlessness than those treated with cognitive behavioural therapy alone. The researchers found no evidence of suicidal ideation associated with sertraline in this trial.
N Engl J Med 2008;359 doi:10.1056/NEJMoa0804633

Malaria deaths fall in east and west Africa

Two new studies show that the burden of disease caused by malaria has fallen in recent years on both sides of Africa. Researchers from Kenya in the east report a substantial decrease in hospital admissions for malaria between 2003 (18.43/1000 children) and 2007 (3.42/1000 children), accompanied by a similar reduction in deaths from confirmed disease. Hospital data from the Gambia in the west also indicate dramatic reductions since 2003 in hospital admissions for malaria (as a proportion of all admissions), deaths attributable to malaria, and cases confirmed by blood slide. The average age of children with malaria has risen in both regions, suggesting that the youngest children have benefited most from the trends.

International efforts to control malaria have been scaled up recently and widespread distribution of treated bed nets is probably responsible for some of the improvement in the Gambia, say researchers. The picture is less clear in Kenya, where the biggest changes occurred before bed nets and effective drugs were widely available.
Lancet 2008;372:1545-54, 1555-62

Cite this as: *BMJ* 2008;337:a2391