SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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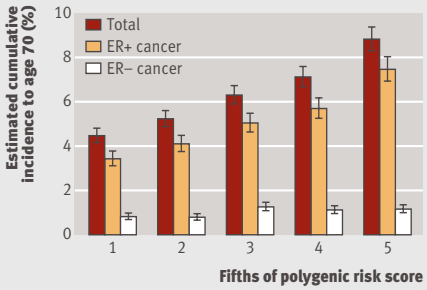
"It is a solemn sight to see the great medical journals gathering to pronounce that rosiglitazone is dead. Like the bird of loudest lay in Shakespeare's *The Phoenix and the Turtle*, *JAMA* leads the troop of mourners"

Richard Lehman's blog, now back at www.bmj.com/blogs

CUMULATIVE INCIDENCE OF BREAST CANCER TO AGE 70



Adapted from *JAMA* 2010;304:426-34

Genetic risk score helps predict breast cancer but is no better than family history

A case-control study of more than 20 000 UK women and a review of other published studies confirmed that seven low penetrance single nucleotide polymorphisms, out of 14 studied, affect the risk of breast cancer. The association is strongest for *FGFR2*-rs2981582, *TNRC9*-rs3803662, and 2q35-rs13387042, which increase the risk of breast cancer 1.23, 1.20, and 1.16 times, respectively, in carriers of one high risk allele compared with two wild-type alleles.

Links with tumour characteristics were also seen: both *FGFR2* and *TNRC9* were more strongly associated with oestrogen receptor (ER) positive tumours than with oestrogen receptor negative tumours, whereas 2q35 showed a greater odds ratio for bilateral than unilateral disease (1.39, 95% CI 1.21 to 1.60 *v* 1.15, 1.11 to 1.20) and for lobular rather than ductal tumours.

Several polygenic risk scores that the authors constructed on the basis of these results help determine the risk of breast cancer: women who score in the top fifth are twice as likely to get breast cancer than those who score in the bottom fifth. Similarly, when the cumulative incidence of breast cancer before age 70 is estimated, on the basis of the frequencies of high risk alleles in Western populations, the risk scores predict breast cancer, and more so for oestrogen receptor positive tumours. However, the genetic risk score does not seem to improve prediction beyond established risk factors, such as family history.

JAMA 2010;304:426-34

Immunotherapy improves survival for people with prostate cancer

A phase III trial tested sipuleucel-T—a new type of immunotherapy that stimulates a host response based on tumour recognition—against placebo in people with metastatic prostate cancer resistant to castration (formerly known as hormone refractory prostate cancer) who were expected to survive for at least six months. The treatment was given intravenously in three biweekly infusions.

Men randomised to sipuleucel-T had a median survival of 25.8 months, compared with 21.7 months in those who received placebo (hazard ratio adjusted for baseline levels of prostate specific antigen and lactate dehydrogenase 0.78, 95% CI 0.61 to 0.98). The probability of survival to three years was 31.7% with sipuleucel-T versus 23.0% with placebo. The results persisted after adjustment for treatments received after the studied intervention, which included docetaxel. The treatment was well tolerated, with most adverse events occurring within a day after infusion and subsiding within the next two days. Cerebrovascular events were more common with the intervention though (2.4% (8/338) *v* 1.8% (3/168)).

A better control group would have allowed for more insight into whether the key component of the treatment is the tumour antigen, argues the editorialist (p 479). Still, the trial helped convince the Food and Drug Administration to approve sipuleucel-T for clinical use. The cost of one month's treatment is $93 000 (£59 340; €71 000).

N Engl J Med 2010;363:411-22

School based programme might reduce risk of diabetes

Schools seem like a great place to focus preventive efforts against risk factors for diabetes in children. But this approach has had little success to date. However, a cluster trial now reports moderate improvements with a complex intervention delivered over three years. The nutritional component of the intervention controlled the quantity and quality of foods available at school; the physical activity component aimed to increase time spent in moderate to vigorous activity; the behavioural component taught knowledge and skills related to self awareness, self monitoring, and goal setting; and finally, communication strategies and social marketing integrated and supported the intervention. More than 4500 students participated. Those attending the control schools received assessments only.

No effect was seen on the primary outcome—the combined prevalence of overweight and obesity—which dropped in the intervention and control schools by 4.5% and 4.1%, respectively. But the intervention did result in some improvements: in the body mass index z score, the proportion of students with abdominal obesity, and the mean concentration of insulin. Changes seen in the subgroup of students who were overweight or obese at baseline (about half of participating children) were encouraging. Among them, the combined prevalence of overweight and obesity decreased by 16.5% in the intervention schools and by 15.9% in the control schools, and the effect of the intervention on the prevalence of obesity reached significance (odds ratio 0.79, 95% CI 0.63 to 0.98, P=0.04). The researchers could not offer an explanation for the marked reductions in obesity indices in the control schools.

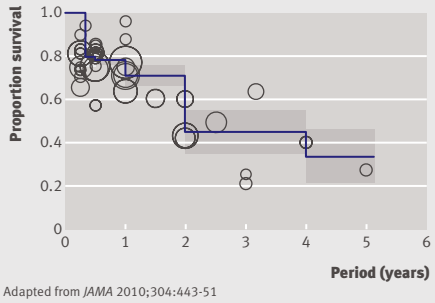
N Engl J Med 2010;363:443-53

Aim to avert delirium in elderly people in hospital

We know that delirium in elderly people in hospital is often followed by poor outcomes, but how much of this is the result of confounding factors? A review of observational studies tried to disentangle this.

In the primary analysis of 21 high quality studies, which were reported according to the "strengthening the reporting of observational

META-ANALYTICAL SURVIVAL CURVE FOR PATIENTS WITH DELIRIUM



Adapted from *JAMA* 2010;304:443-51

studies in epidemiology" (STROBE) statement, delirium while in hospital in people aged 65 years or more was associated with double the risk of death over the subsequent 22 months (271/714 people with delirium *v* 616/2243 controls; hazard ratio 1.95, 95% CI 1.51 to 2.52), more than double the risk of admission to an institution over 14 months (176/527 people with delirium *v* 219/2052 controls; odds ratio 2.41, 1.77 to 3.29), and nearly a 13-fold increased risk of dementia in the next four years (35/56 people with delirium *v* 15/185 controls; 12.52, 1.86 to 84.21).

The findings were independent of age, sex, comorbidities, illness severity, and dementia at baseline. Secondary analyses, based on 62 lower quality studies, supported the results. High mortality, coupled with high rates of subsequent dementia and admission to institution, make these people especially vulnerable, argue the authors. Efforts should be aimed at preventing delirium. Little can be done to avert poor outcomes after it occurs.

JAMA 2010;304:443-51

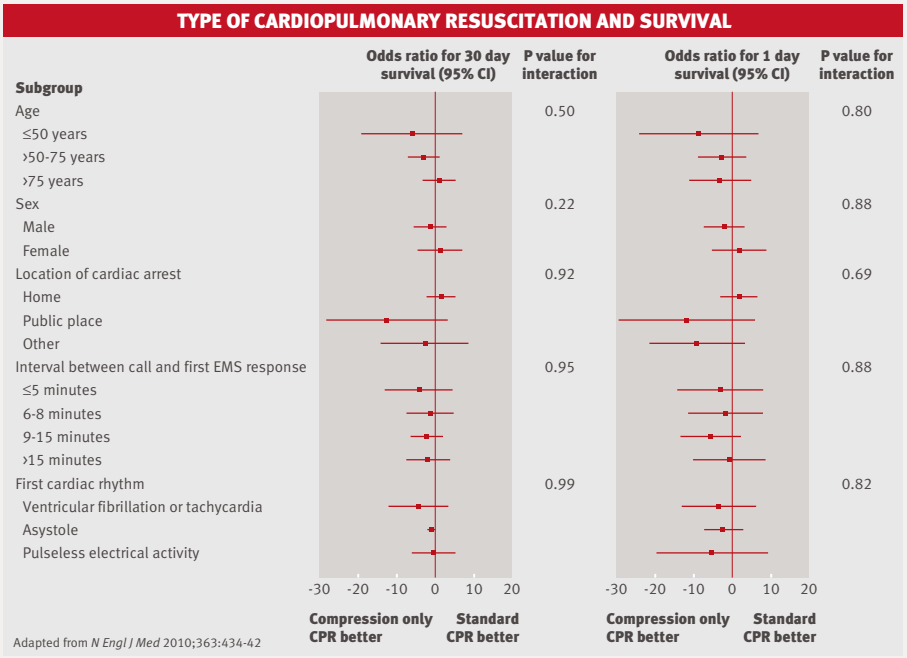
A step towards self grown joints

In a proof of concept study, researchers removed the proximal humeral joints of 23rabbits then in 20 of them installed bioscaffolds in their place. These scaffolds were designed with the help of computers and made out of a composite of poly-ε-caprolactone and hydroxyapatite. Bioscaffolds were infused with collagen hydrogel in all 20 rabbits, but in 10 rabbits this was combined with transforming growth factor β3.

Although no stem cells or any other cells were added to the bioscaffolds at implantation, the 10 rabbits that received bioscaffolds infused with growth factor all resumed normal weight bearing and locomotion within three to four weeks of surgery. Four months after the procedure, the whole joint surface was covered in cartilage, which had similar properties to those of normal cartilage. Only partial improvements in function and histological build were seen in rabbits that were randomised to bioscaffolds not infused with the growth factor. The three rabbits that did not receive bioscaffolds after their healthy joints were excised limped throughout the duration of the study.

The re-creation of the entire joint cartilage and the subchondral bone resulted from endogenous cell homing, local tissue response, and functional stimulation (doi:10.1016/S0140-6736(10)60931-2). We are yet to see biological joint replacement in humans though.

Lancet 2010; online July 29; doi:10.1016/S0140-6736(10)60668-X



Should CPR include rescue breathing?

Evidence is accumulating to challenge the 50 year old standard procedure for out of hospital cardiopulmonary resuscitation (CPR), which currently includes chest compressions and rescue breathing. Animal models and observational studies have suggested that chest compressions alone may result in better outcomes, including survival.

Two large trials of CPR performed by bystanders and led by emergency dispatchers randomised instructions to standard CPR or chest compressions alone. One trial comprised nearly 2000 people and found no difference between the groups in survival to hospital discharge, or in survival without severe cerebral disability. The study also found a non-significant difference in survival to hospital discharge in favour of compressions alone (15.5% *v* 12.3%, P=0.09).

In the other trial, which comprised 1276 people with out of hospital cardiac arrest, no difference was seen between the groups across the examined outcomes. This included the primary outcome—survival to 30 days—which was 8.7% (54/620) in those who received compression only compared with 7.0% (46/656 patients) with standard CPR.

The editorialist (p 481) discusses how different subgroups of patients may benefit more from the different methods of CPR. Chest compressions alone may be optimal for people whose arrest has cardiac causes and for those with ventricular tachycardia or fibrillation, rather than asystole or electromechanical dissociation. However, rescue breathing may be essential when cardiac arrest is caused by respiratory failure. Further trials might include testing of compression only in emergency settings on arrival to hospital.

N Engl J Med 2010;363:423-33

N Engl J Med 2010;363:434-42

Homeless people are willing to do advanced end of life planning

When given the chance, homeless people in the US fill in advance directives at similar rates to those seen in the general population. A trial compared a minimal self guided intervention (advance directive forms plus written educational information) with a face to face advance planning intervention delivered by a social worker, during which advance directive forms were filled in. In the general population, the completion rates are known to range from 15% to 30%. In the trial, which looked at 262 homeless people, the overall completion rate was 26.7% (95% CI 21.5% to 32.5%)—12.8% in the self guided group and 37.9% in the intervention group.

Interestingly, homeless people's end of life preferences differed somewhat from those seen in the general population—37% and 31% of homeless people said that they would choose to forgo treatment if in a coma or dying, compared with 78% and 94% in the general population. In addition, 61 of 70 participants who completed advance directives named a family member as a surrogate decision maker.

Ann Intern Med 2010;153:76-84

Cite this as: *BMJ* 2010;340:c4185