# SHORT CUTS

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

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## Secondhand smoke causes 1% of all deaths

Secondhand cigarette smoke caused an estimated 1% of all deaths worldwide in 2004, according to a pooled analysis of multiple data sources covering 192 countries. Ischaemic heart disease was the leading cause of death, followed by lower respiratory tract infections in children, asthma, and lung cancer. Children were hardest hit, losing 6.6 (61%) of the estimated 11 million disability adjusted life years lost overall in 2004. An estimated 40% of all children worldwide are exposed regularly to someone else's tobacco smoke, say the authors. Usually a close relative, and usually at home.

Almost half the attributable deaths in this analysis occurred in women (47%), who are exposed at home, at work, and in other public places. Women must be encouraged to take a more active role in local tobacco control, says a linked comment (doi:10.1016/S0140-6736(10)61922-8). They are best placed to protect themselves and their children.

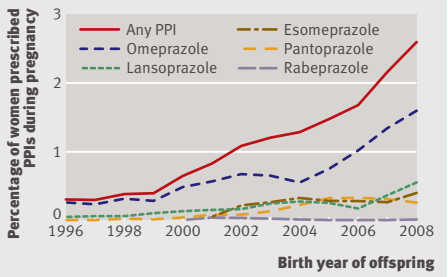
Smoke-free legislation is also important. Only 7.4% of the world's population currently live in jurisdictions covered by comprehensive smoking bans, despite well established benefits, including rapid falls in tobacco related death and disease. Banning smoking in all indoor public spaces encourages smokers to quit and reduces the number of cigarettes smoked. The 17 countries that have already done it report net economic gains and minimal cost to governments. Campaigners are pushing for legislation in many other countries, says the comment. The aim should be to eliminate this damaging indoor pollutant completely.

***Lancet*** 2020; doi:10.1016/S0140-6736(10)61388-8

## Proton pump inhibitors look to be low risk for pregnant women

Gastro-oesophageal reflux is common in pregnancy. But is it safe for women to take proton pump inhibitors (PPIs)—the most effective treatment? Probably, say researchers from Denmark. They found no evidence of a link between major birth defects and exposure to proton pump inhibitors during the first trimester in a study of 840 968 live births (adjusted prevalence odds ratio 1.10, 95% CI 0.91 to 1.34).

**USE OF PPIs DURING PREGNANCY IN DENMARK**




Adapted from *N Engl J Med* 2010;363:2114-23

The answer isn't entirely clear cut, however, thanks to an unexpected increase in major birth defects in women who took proton pump inhibitors in the month before conception (1.39, 1.10 to 1.76). The researchers dug deeper to try to explain the effect and found that the increase was confined to lansoprazole. Omeprazole, the most popular drug, was exonerated. More puzzling still, women who had taken too little of any proton pump inhibitor before conception to have any chance of exposure during the first trimester still had an increased risk of birth defects. The authors blame chance or statistical artefact, probably some sort of confounding. They had no information about the indications for treatment, for example, and no data on folic acid intake.

An editorial (p 2161) agrees that confounding is the most likely explanation. Still, more work needs to be done before women can be completely reassured. These drugs are popular and available over the counter in some countries. Use among pregnant women is likely to increase.

***N Engl J Med*** 2010;363:2114-23

## Combined aerobic and resistance training achieves better glycaemic control

Adults with type 2 diabetes should take plenty of exercise, and national guidelines now recommend both aerobic activity, such as brisk walking or cycling, and resistance exercise, such as lifting weights. A new trial confirms that exercise programmes combining the two have a greater effect on glycaemic control than programmes focusing on just one or the other.

The trial lasted nine months. Glycated haemoglobin ($HbA_{1c}$) fell by 0.34% more in participants prescribed the combined programme (95% CI −0.64% to −0.03%) than in controls prescribed stretching and relaxation. $HBA_{1c}$ did not change significantly relative to controls during nine months of aerobic exercise alone or resistance exercise alone. The three active groups spent roughly the same time exercising (140 minutes a week). Only the combined group lost weight, although the resistance group lost fat mass. The aerobic group lost neither.

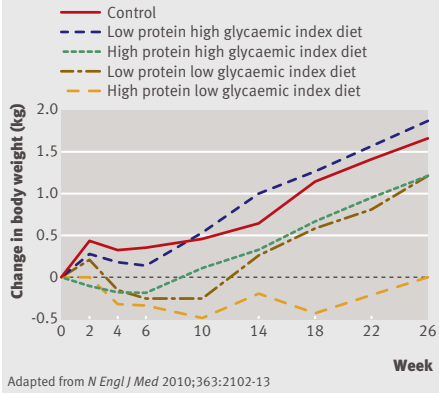
The results achieved by combined exercise were modest, says an editorial (p 2298), and they may be even more modest in the real world, where patients often exercise without supervision and support. It is now clear, however, that patients with type 2 diabetes should divide their exercise time between the treadmill and the weights for maximum hypoglycaemic effect.

These participants started with a mean $HbA_{1c}$ of 7.7% and a mean body mass index of 34.9. Just under one in five needed insulin.

***JAMA*** 2010;304:2253-62

## High protein, low GI diets help maintain weight loss

**CHANGES IN BODY WEIGHT**




Adapted from *N Engl J Med* 2010;363:2102-13

Weight regain is one of the biggest challenges facing successful dieters. Eating less and exercising more is hard to sustain long term, partly because the body responds to weight loss by increased hunger and reduced energy expenditure at rest.

Maintenance diets are more likely to be successful if they have a low glycaemic index, a high protein content, or both, according to a recent trial. The 773 participants followed one of four experimental diets or a control diet for up to 26

**"One reason that long serving general practitioners like me are reluctant to intrude into serious emergency situations is that we might be called on to do something that only real doctors can do, like intubate"**
Richard Lehman's journal blog at www.bmj.com/blogs

weeks. Those on the high protein diets regained 0.93 kg less (95% CI 0.31 to 1.55) than those on low protein diets. Participants on diets with a low glycaemic index (GI) regained 0.95 kg (0.33 to 1.57) less than those on diets with a high glycaemic index.

All participants had lost weight during a calorie controlled diet before randomisation (average loss 11 kg), and the maintenance diets did not restrict energy intake. Still, only 29% managed to stick to their diet for the full 26 weeks. Again, those on diets with a high protein content or a low glycaemic index were more successful than others.

These diets may work because they help minimise the hunger and metabolic changes that follow weight loss, says an editorial (p 2159). A higher protein content and a lower glycaemic index at least caused no harm. Four participants developed abdominal pain during the trial. The two who needed a cholecystectomy were both assigned a diet with a low protein content and a high glycaemic index.

***N Engl J Med*** 2010;363:2102-13

## Active surveillance for low risk prostate cancer?

Men have a difficult decision to make when faced with a diagnosis of low grade, low risk, localised prostate cancer. Treat aggressively now and risk serious side effects, such as impotence or incontinence, or agree to active surveillance with repeated blood tests, repeated biopsies, and the anxiety caused by living with uncertainty?

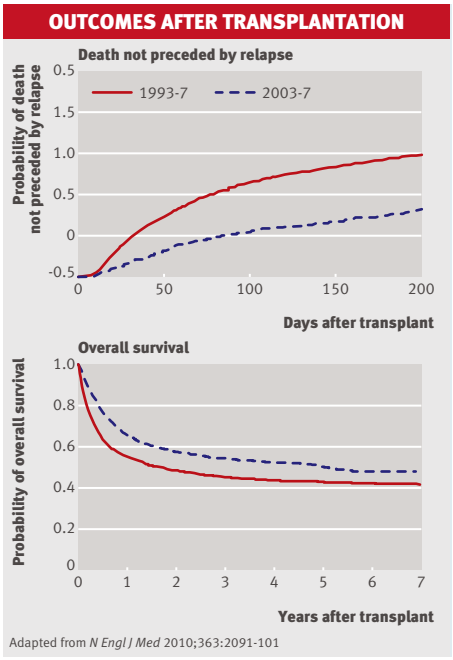
Careful modelling of the likely outcomes after various treatment options suggests that active surveillance is a reasonable approach, at least for 65 year old men. In a decision analysis, men of this age opting for active surveillance had an extra six months of quality adjusted life expectancy, compared with the next best option—early treatment with brachytherapy. Initial treatment with radiotherapy or radical prostatectomy trailed third and fourth. In this analysis, 61% of men under active surveillance eventually needed definitive treatment, a median of 8.5 years after diagnosis.

What comes out of a statistical model always depends on what goes in. So the authors did sensitivity analyses varying key inputs, such as likelihood of disease progression, to see what would happen. The findings remained essentially the same. Active surveillance was associated with the highest quality adjusted life expectancy. Radical prostatectomy was associated with the lowest.

The absolute difference between active surveillance and the other options depended crucially on patient preference, however. Clearer information and reassurance would help, says an editorial (p 2411). Or perhaps we should stop using the word cancer for low risk lesions. One observer has already suggested an alternative—"indolent lesions of epithelial origin" or IDLE.

***JAMA*** 2010;304:2373-80

## Better survival for patients having haematopoietic cell transplants




Adapted from *N Engl J Med* 2010;363:2091-101

The mortality associated with transplanting allogeneic haematopoietic cells has fallen significantly during the past decade at one centre in the US. Patients treated in Seattle between 2003 and 2007 had a lower overall mortality (47% *v* 63%; hazard ratio 0.59, 95% CI 0.52 to 0.67), a lower risk of death without relapse (16% *v* 30%; 0.40, 0.32 to 0.49), and a lower risk of serious complications than patients treated between 1993 and 1997. Researchers tracked numerous outcomes among more than 2500 patients, including graft versus host disease, infections, jaundice, renal damage, and respiratory failure. All fell significantly between the two time periods, after accounting for changes in disease severity (which got worse), age (which increased), and other factors. Patients treated later were more likely to have an unrelated donor than those treated earlier. They also had less intensive pretreatment conditioning and better prophylaxis against infections and graft versus host disease.

Other changes that may have contributed to better outcomes include a shift from using bone marrow cells to using haematopoietic cells from peripheral blood, and a change in the distribution of cancers treated with transplantation. Fewer patients in the later period had chronic myeloid leukaemia. A greater proportion had acute myeloid leukaemia or myelodysplastic syndromes.

***N Engl J Med*** 2010;363:2091-101

## Statins are not hepatotoxic

Many doctors are afraid to prescribe statins to people with moderately abnormal liver function tests. They shouldn't be, says one observer: "statin induced hepatotoxicity is a myth." There is no good evidence of serious or lasting harm to the liver associated with statins, he writes, and a recent reanalysis of data from one trial suggests that statins can even improve liver function (doi:10.1016/S0140-6736(10)61272-X).

The trial was originally designed to compare atorvastatin with usual care in adults with dyslipidaemia and coronary heart disease. Participants given atorvastatin had significantly fewer serious cardiovascular events over three years. The cardiovascular benefits were greatest for those with abnormal liver function at baseline. Most of this subgroup had metabolic syndrome, diabetes, or both, complicated by non-alcoholic fatty liver disease. They had raised alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations, which fell significantly during treatment with a statin. Mean ALT fell from 57 IU/l to 37 IU/l (35% decrease). ALT concentrations among controls rose from 56 IU/l to 63 IU/l (P=0.003 for the difference between the groups).

Subgroup analyses always need independent prospective confirmation. But these findings added to other evidence convince this observer that statins are safe and should not be withheld from adults with a fatty liver or moderately raised concentrations of liver enzymes. Both are common. He declares a shared patent application for use of statins in viral hepatitis.

***Lancet*** 2010; doi:10.1016/S0140-6736(10)62142-3

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