SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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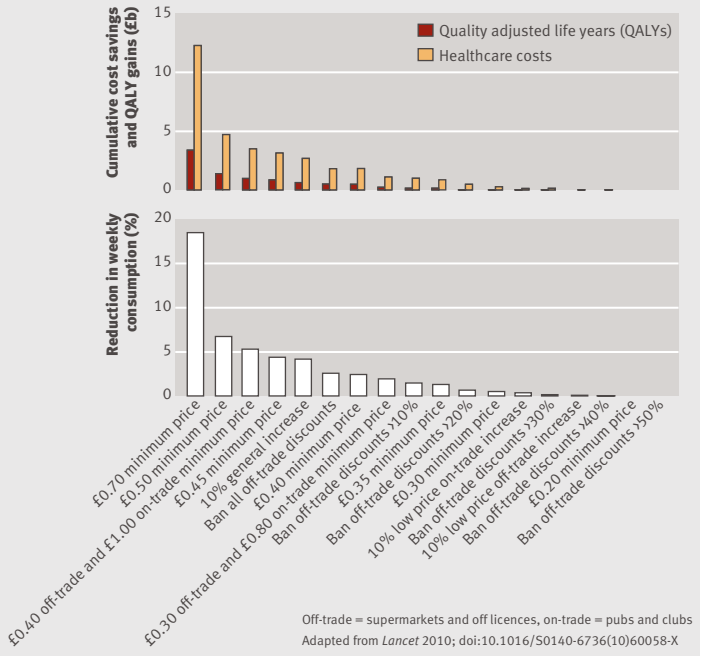
"This week's *Lancet* is largely devoted to the health of the Chinese people, but right in the middle of this veritable Brighton Pavilion of chinoiserie, they stage a fight between two drug eluting stents."
Richard Lehman's journal blog, doc2doc.bmj.com

ESTIMATED EFFECTS OF VARIOUS ALCOHOL POLICIES



Off-trade = supermarkets and off licences, on-trade = pubs and clubs
Adapted from *Lancet* 2010; doi:10.1016/S0140-6736(10)60058-X

Alcohol policies that cut consumption save money and save lives

The UK's NHS spends £2.7bn (€3bn; $4bn) a year treating ill health caused by alcohol, and the government is under increasing pressure to regulate the price of alcohol in pubs, clubs, off licences, and supermarkets. Minimum pricing looked like one of the best options in a study commissioned by the Department of Health. The authors estimate that a legal threshold of 50 pence a unit would cut consumption by close to 7%, save 2930 lives a year, and accrue £6.2bn of health economic benefits over 10 years. Minimum pricing had its biggest effect on problem drinkers in this model, making it an attractive policy option for legislators keen to avoid penalising responsible drinkers.

A 10% increase in overall prices cut alcohol consumption (by 4.4%) and saved lives (1460 a year), but had no preferential effect on harmful drinkers. Banning all discounting by supermarkets and off licences was also effective.

Policy makers in England and Scotland are already looking seriously at a minimum price for alcohol, says a linked comment (doi:10.1016/S0140-6736(10)60276-0). This study shows what might be achieved, and why politicians must fight and win through inevitable challenges from commercial interests and possibly also from European competition laws. Public health comes first, it says, and we could all do more to encourage political will in that direction.

Lancet 2010; doi:10.1016/S0140-6736(10)60058-X

Truncated trials overestimate benefits

Stopping trials early is controversial. Results tend to fluctuate in the early stages of trials, and interim analyses can truncate trials at a random high point that overestimates the benefits of the treatment under study. One team of researchers recently compared trials stopped early because the treatment seemed to work with completed trials on the same research question. Most truncated trials reported lower relative risks (greater benefits) than their matched completed trials. The overall ratio of relative risks across 63 different research questions was 0.71 (95% CI 0.65 to 0.77). So, for treatments that don't work in completed trials (relative risk 1.0), a truncated trial would overestimate the benefit by 29% on average (relative risk 0.71).

The bias seemed worse in trials with relatively few outcome events, and the researchers urge data monitoring committees to wait until substantial numbers of events have accrued before suggesting an early end to a trial. Formal statistical rules, now commonly used to guide these committees, didn't help prevent bias in this analysis.

The potential for misleading patients and doctors is clear, say the researchers. Results from truncated trials are published and widely disseminated. Although an early end to recruitment or follow-up can be justified on the grounds that patients need speedy access to treatments that work, authors, sponsors, and editors must be clear about the risks, which include a false positive result, an overoptimistic result, a less convincing result, or a missed opportunity to gather essential data on side effects.

JAMA 2010;303:1180-7

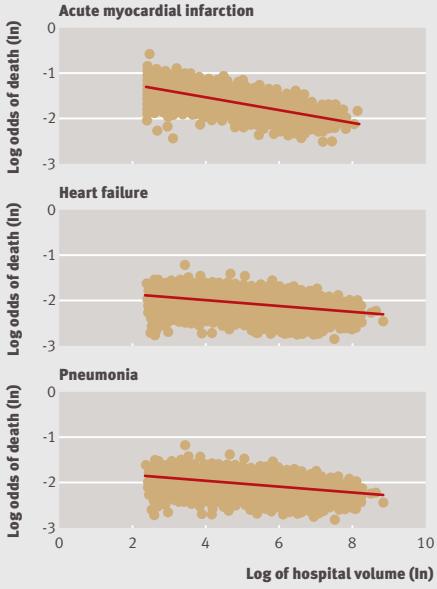
Acute medical patients do better in large volume hospitals

Older adults with pneumonia, heart failure, or heart attack do better in hospitals that treat large volumes of similar patients, according to an analysis of Medicare data from the US. The analysis, which was extensively adjusted for case mix and important hospital characteristics, found a clear link between larger yearly throughput and lower mortality at 30 days for all three acute illnesses. Each additional 100 patients treated per year reduced the odds of death by 11% for heart attack (adjusted odds ratio 0.89, 95% CI 0.88 to 0.90), 9% for heart failure (0.91, 0.90 to 0.92), and 5% for pneumonia (0.95, 0.94 to 0.96).

The advantage associated with large volumes was evident only up to a certain threshold, however. The authors found no additional benefit above a threshold of 610 patients a year for heart attack, 500 patients a year for heart failure, and 210 patients a year for pneumonia.

They had data on more than three million adults aged at least 65 treated in hospitals across the US

HOSPITAL VOLUME AND ODDS OF DEATH AT 30 DAYS



Adapted from *N Engl J Med* 2010;362:1110-8

between 2004 and 2006. Most were admitted to large volume hospitals—those in the top quarter of throughput for each condition—which treat several hundreds of patients a year. Small volume hospitals treated just a few dozen on average.

The law of diminishing returns may encourage policy makers to increase throughput at small volume hospitals, say the authors. This makes more sense than wholesale regionalisation of services for three common acute conditions that could be clinically difficult, politically unpopular, and disruptive for patients.

N Engl J Med 2010;362:1110-8

Diabetes reaches epidemic proportions in China

One in 10 (9.7%) Chinese adults had diabetes, and a further 15.5% had prediabetes, in the latest national survey. Researchers questioned a representative sample of 46 239 adults across China, before screening for diabetes with a fasting plasma glucose concentration and an oral glucose tolerance test. The response rate was 87.3%. Around 60% of participants with fully fledged diabetes were unaware of their condition. Those with prediabetes had a either a high fasting glucose concentration or impaired glucose tolerance in isolation. The researchers used World Health Organization definitions.

Male sex, urban residence, older age, family history, and poor education were among the factors independently associated with diabetes in fully adjusted analyses.

This survey, conducted between 2007 and 2008, reveals an epidemic, say the researchers: an estimated 92.4 million adults in China already have diabetes, and another 148.2 million have high risk prediabetes. The prevalence of both has risen sharply in recent decades. In 1994, surveys reported a prevalence of around 2.5% in China. Prevalence had reached 5.5% by 2001.

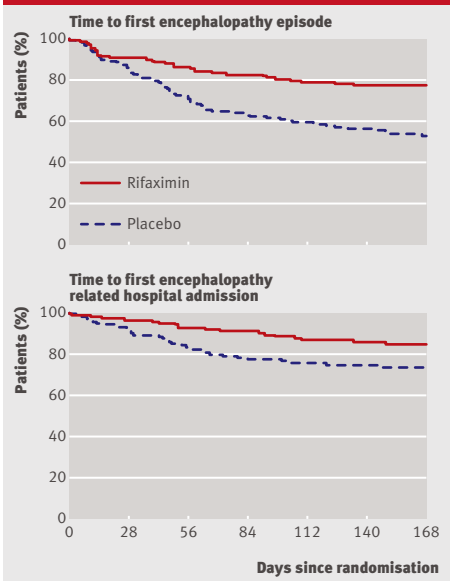
High levels of undiagnosed disease are particularly worrying, they add. Diabetes is now a serious challenge to public health and is crying out for national strategies targeted at prevention, diagnosis, and treatment.

N Engl J Med 2010;362:1090-101

An oral prophylactic against hepatic encephalopathy?

Hepatic encephalopathy is thought to be caused by a build up of gut derived neurotoxins including ammonia produced by some gut flora. Antibiotics are an established part of treatment, and the oral agent rifaximine is under evaluation as a prophylactic, to be taken between episodes. In a placebo controlled trial, six months of treatment with

TIME TO END POINTS



Adapted from *N Engl J Med* 2010;362:1071-81

rifaximine helped prevent breakthrough episodes of encephalopathy in adults with liver cirrhosis (22.1% (31/140) *v* 45.9% (73/159); hazard ratio 0.42, 95% CI 0.28 to 0.64) and reduced hospital admissions (13.6% (19/140) *v* 22.6% (36/159); 0.5, 0.29 to 0.87). Participants had a history of two or more episodes of encephalopathy related to cirrhosis. They were in remission when randomised. The trial was paid for, designed, and analysed by the manufacturers, Salix Pharmaceuticals. More than 90% of both groups were taking lactulose at baseline and continued to take it alongside the study drug.

Rifaximine is an oral antibiotic with a broad spectrum. It is poorly absorbed and remains within the gastrointestinal tract. Rifaximine looked reasonably safe in this trial. Adverse events were almost universal in both groups, but participants taking rifaximine had no more serious events than controls. Two people taking rifaximine developed *Clostridium difficile* infections, but both had many other risk factors. It is unclear whether the rifaximine contributed to the infections.

N Engl J Med 2010;362:1071-81

Antithrombotic treatment doesn't prevent recurrent miscarriage

Antithrombotic treatment with aspirin, subcutaneous heparin, or both didn't help prevent recurrent miscarriage in a recent trial from the Netherlands. Many women with unexplained miscarriages receive these treatments, on largely theoretical grounds, say the authors. It may be time to think again.

Women in the trial had experienced at least two unexplained miscarriages and were trying to conceive again. They took aspirin alone (equivalent to 80 mg acetylsalicylic acid), aspirin plus additional subcutaneous low molecular weight heparin started during early pregnancy, or a placebo. Live birth rates were statistically comparable in all three groups (50.8% (61/120), 54.5% (67/123), and 57.0% (69/121)). Neither active treatment prevented miscarriage in the 299 women who became pregnant (relative risk of live birth 0.92, 95% CI 0.75 to 1.13 for aspirin alone and 1.03, 0.85 to1.25 for combination treatment). The trial was reasonably well powered, but it was stopped early when it became clear that treatment was probably futile.

An editorial agrees that practice has raced ahead of the evidence, and that brakes should be applied (doi:10.1056/NEJMe1002592). Antithrombotic treatment doesn't work for unselected women with two or more unexplained miscarriages. These women had experienced a median of three miscarriages, 40% (144/364) had had at least one baby, and 16% (47/302) had an inherited thrombophilia.

N Engl J Med 2010; doi:10.1056/NEJMa1000641

Childhood mortality is falling fast in some parts of China

Childhood mortality in China has fallen sharply since 1990. New analyses including publicly available data from multiple sources within China suggest decreases of more than 70% for neonatal mortality (from 34.0 to 10.2 per 1000 live births), infant mortality (from 53.5 to 14.9 per 1000 live births), and overall mortality in children under 5 years (from 64.6 to 18.5 per 1000 live births). These data help to fill a well documented hole in previous global estimates, say the authors. They searched online databases of more than 1000 Chinese medical journals and mined national and local surveillance systems to paint a picture of disease and death among China's under 5s, who now account for 15% of children worldwide.

Pneumonia remains the leading cause of death overall (17% of deaths), followed by birth asphyxia (16%) and the complications associated with preterm birth (15%). Only 3% of deaths were caused by diarrhoea in 2008, an unexpectedly low proportion that may have something to do with the improvements in water treatment and sanitation accompanying rapid economic development, says an editorial (p 1058).

The overall figures disguise wide variations between rural and urban populations and between the less developed and more developed provinces, say the authors. In large cities such as Shanghai, only 1% of babies die before their 5th birthday, compared with 6.4% in the least developed rural areas.

Lancet 2010;375:1083-9

Cite this as: *BMJ* 2010;340:c1735