SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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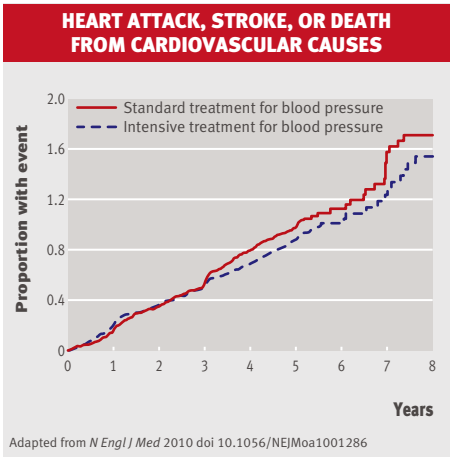
"Millions of parents worldwide are still panicked by this nonsense [asthma] and encouraged to give their children continuous inhaled corticosteroids for no reason whatever"
Richard Lehman's journal blog, doc2doc.bmj.com

Tighter lipid and blood pressure control has few cardiovascular benefits in type 2 diabetes



Adapted from *N Engl J Med* 2010 doi 10.1056/NEJMoa1001286

The hat trick of trials collectively known as ACCORD compared intensive control with standard control of blood sugar, blood lipids, and blood pressure in people with type 2 diabetes and a high risk of cardiovascular disease. Results just in do not support more intensive treatment of blood pressure or lipids.

Researchers were mainly interested in preventing cardiovascular events including heart attacks, strokes, and death. Participants treated to a target systolic blood pressure below 120 mm Hg had no fewer events over nearly five years than those treated to a target below 140 mm Hg (1.87% (208/2363) *v* 2.09% (237/2371) per year; hazard ratio with intensive treatment 0.88; 95% CI 0.73 to 1.06), although they did have fewer strokes (0.32% (36/2363) *v* 0.53% (62/2371) per year; 0.59, 0.39 to 0.89). In the lipid trial, those treated with fenofibrate and simvastatin had the same risk of cardiovascular events as controls given simvastatin alone (2.2% (291/2765) *v* 2.4% (310/2753) per year; 0.92, 0.79 to 1.08).

Tighter control of blood pressure exposed participants to more antihypertensive drugs and more side effects, including hypotension and bradyarrhythmias. They also had worse renal function at the end of the trial. Subgroup analyses from the lipid trial hinted at different effects for men and women. Men seemed to benefit from the extra fenofibrate, whereas women may have been harmed (women in this group had more cardiovascular events).

It is now clear from these and other landmark trials, that people with type 2 diabetes need a flexible approach, says an editorial (doi:10.1056/nejme1002498). There are no "one size fits all" targets for blood pressure, lipids, or blood sugar in this population—men and women with at least 7.5% glycated haemoglobin, plus clinical cardiovascular disease or at least two risk factors. Inevitably, further trials must be done to help doctors fine tune treatment according to each individual's clinical profile.

N Engl J Med 2010; doi:10.1056/NEJMoa1001286, doi:10.1056/NEJMoa1001282

A market in kidneys could be ethical—in theory

When researchers asked 409 people on Philadelphia's trains and trolley buses under what circumstances they would donate a kidney, respondents' willingness to donate went up in line with the payment offered. They were more likely to donate to a relative than a stranger on a waiting list, and more likely to donate if their own risk of renal failure was low.

The researchers did further analyses to explore whether donor payments would influence poor people more than rich people (unjust inducement), and whether payments would encourage donors to take greater personal risks (undue inducement). They found no evidence of either. The link between payment value and willingness to donate looked the same regardless of income. The link between higher personal risk and reduced willingness to donate was similar at all levels of payment. The survey had a response rate of nearly 75%. In a well regulated market, paying donors may not be as unethical as previously feared, say the authors.

Maybe, says an editorial (p 396), but there are no guarantees that a market in body parts could be regulated tightly enough to prevent at least some exploitation of poor donors for the benefit of richer recipients. The US system already encourages a bias towards wealthy recipients. Paying kidney donors could also harm the doctor-patient relationship and devalue human dignity in general.

Ann Intern Med 2010;152:358-65

Relax heart rate targets for people with atrial fibrillation

Heart rate control is now an accepted strategy for people with atrial fibrillation, and international guidelines suggest that doctors should aim for a resting heart rate below 80 beats/min. A new trial finds that a more relaxed strategy aiming for below 110 beats/min works just as well and is easier to achieve.

The researchers used β blockers, digoxin, verapamil, and diltiazem alone or in combination to achieve the assigned target. Patients managed with the relaxed strategy did no worse over three years than those treated more aggressively—a comparable proportion of each group reached a combined end point that included stroke, hospital admission for heart failure, systemic embolism, bleeding, life threatening arrhythmia, and death (12.9% for the relaxed control group *v* 14.9% for the tight control group; adjusted hazard ratio 0.80, 90% CI 0.55 to 1.17). Patients given the higher target needed fewer drugs, lower doses, and far fewer clinical visits than controls. They were also more likely to reach their target heart rate (97.7% (304/311) *v* 75.2% (228/303); P<0.001). A higher heart rate had no discernible effect on breathlessness, fatigue, or palpitations.

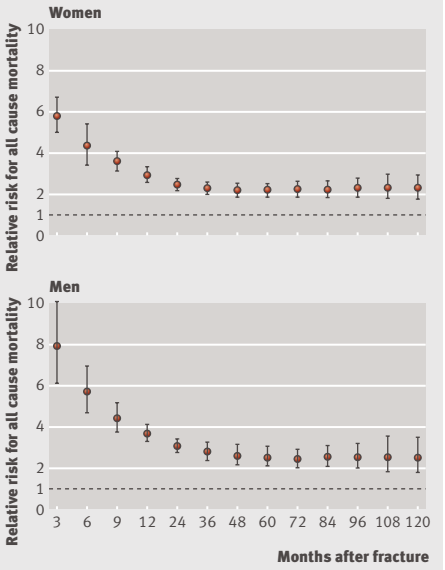
Guideline developers may want to revisit their pragmatic recommendation to drive resting heart rate below 80 beats/min in these patients, says an editorial (doi:10.1056/nejme1002301). This trial provides reasonable evidence that it isn't right for everyone.

N Engl J Med 2010; doi:10.1056/NEJMoa1001337

High mortality persists for years after a hip fracture

Mortality is high for the first few months after a hip fracture. One meta-analysis reported a hazard ratio for all cause death during the first three months of 5.75 (95% CI 4.94 to 6.67) for women and 7.95 (6.13 to 10.30) for men, relative to adults of the same age without hip fracture. Excess risk fell sharply during the next two years, but never made it to zero. Annual mortality remained higher than normal for up to 15 years after a fracture (relative hazard after 15 years 3.00 (1.10 to 8.18) for women and 3.52 (0.99 to 12.5) for men).

EXCESS RISK OF DEATH AFTER A HIP FRACTURE



Adapted from *Ann Intern Med* 2010;152:380-90

The authors pooled data from 24 published studies of survival after hip fracture—22 separate cohorts of women and 17 cohorts of men. The studies were heterogeneous and had other limitations including a variety of populations, control groups, and adjustments for confounding. Even so, the authors are fairly confident that the enduring risk after hip fracture is real, and a new finding. What they can't confirm is that hip fracture is directly responsible for the extra deaths long term. People who sustain fractures are generally more frail than those who don't. Differences in comorbidities before the injury could explain at least some of the excess deaths. In this analysis, men had higher mortality than women at all ages.

Ann Intern Med 2010;152:380-90

Cancer isn't beaten yet, but neither are we

Cancer is a complex biological phenomenon made up of more than 100 anatomical subtypes, many of which are further divided into variants with differing histology, prognosis, and response to treatment. Like viruses, cancers can be hard to pin down as they mutate and clone, developing resistance and other effective defences against treatment. Meanwhile, close to half of all men and a third of all women will experience cancer at some point in their lives. So, are we losing the battle against one of the word's biggest killers?

Although progress has been slower than expected by some (US president Richard Nixon, for example, declared war on cancer in 1971), we have plenty of reasons to be cheerful about what has been achieved, write two experts. People with cancer are surviving longer, and incidence is falling, by around 1% a year between 1999 and 2006 in the US alone. Tobacco control and cervical cancer screening have both been successful at preventing cancer. Rapid progress continues in the treatment of many childhood cancers, testicular cancer, some leukaemias, and Hodgkin's disease. Prognosis is now better than ever for many common cancers—including breast cancer, colorectal cancer, and prostate cancer—particularly when detected early.

Highly lethal cancers (such as cancer of the pancreas, liver, and lung) and metastatic diseases of all kinds are among the crucial challenges remaining. But 40 years of progress and insights gained from many hundreds of billions of research dollars leave us well placed to meet them, they conclude.

JAMA 2010;303:1084-5

The case for public access defibrillators, from Japan

During the three years between 2005 and 2007, 12 631 Japanese adults collapsed from ventricular fibrillation in front of bystanders. One in seven (14.4% (1815/12 631)) survived to one month without serious neurological impairment. This proportion increased to 31.6% (146/462) for the lucky few initially resuscitated by bystanders with access to a public automated external defibrillator.

An analysis of data from a national register suggests that a sharp rise in publicly accessible defibrillators between 2005 and 2007 contributed to improvements in survival for people with a witnessed arrest from ventricular fibrillation. In 2005 there were 7.8 defibrillators per 100 000 population, and this had increased to 69 per 100 000 population by 2007. More people with ventricular fibrillation were given their first shock by bystanders in 2007 than in 2005 (1.2% (45/3841) *v* 6.2% (274/4402); P<0.001). Response times to first shock were slightly but significantly faster, and the chances of survival to one month when given a shock by a bystander were significantly higher (24.4% (11/45) *v* 41.6% (114/274); P=0.01).

Overall survival after a witnessed arrest from ventricular fibrillation also improved between 2005 and 2007, as bystanders got better at initiating any kind of cardiopulmonary resuscitation (CPR). In fully adjusted analyses, both conventional CPR (odds ratio 1.67, 95% CI 1.4 to 2.0) and compression only CPR (1.65, 1.40 to 1.96) were associated with better short term survival than no CPR.

N Engl J Med 2010;362:994-1004

Cite this as: *BMJ* 2010;340:c1599

Latest study suggests no harm in combining clopidogrel with a PPI

US regulators warn doctors that clopidogrel may be less effective when given with proton pump inhibitors (PPI), such as omeprazole, because the two drugs share a common metabolic pathway. The evidence isn't clear cut, however, and the latest study suggests that the standard practice of combining clopidogrel with a PPI doesn't increase the risk of heart attack, stroke, or cardiovascular death in people who already have serious cardiovascular disease.

The authors analysed Medicare data from 20 596 older US adults given clopidogrel for indications such as coronary revascularisation. Serious cardiovascular outcomes were similar for those who did and did not take a PPI (hazard ratio 0.99, 95% CI 0.82 to 1.19). As expected, significantly fewer gastrointestinal bleeds occurred in those who took both drugs (0.50, 0.39 to 0.65).

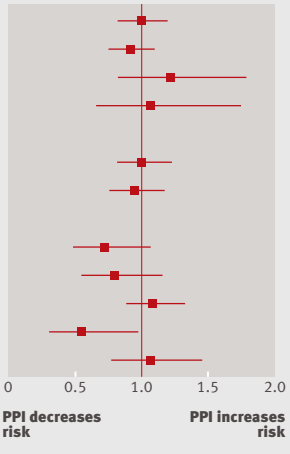
The authors adjusted extensively to try and minimise the bias caused by doctors selecting sicker patients for combination treatment. They also did sensitivity analyses. The results stayed the same.

A retrospective look at routinely collected data can never be the final word, and statisticians commenting on the study say the safety of this combination is still an open question (p 393). Most of the 7953 adults on combination treatment in this cohort took pantoprazole (62%).

Ann Intern Med 2010;152:337-45

PPI USE AND RISK OF CARDIOVASCULAR DISEASE

Type of disease	Hazard ratio (95% CI)
All	0.99 (0.82 to 1.19)
Heart attack/sudden cardiac death	0.91 (0.75 to 1.09)
Stroke	1.21 (0.82 to 1.78)
Other cardiovascular death	1.06 (0.65 to 1.74)
PPI dose	
Low	1.00 (0.81 to 1.22)
High	0.94 (0.75 to 1.17)
Individual PPIs	
Esomeprazole	0.71 (0.48 to 1.06)
Omeprazole	0.79 (0.54 to 1.15)
Pantoprazole	1.08 (0.88 to 1.32)
Rabeprazole	0.54 (0.30 to 0.97)
Lansoprazole	1.06 (0.77 to 1.45)



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