All you need to read in the other general medical journals

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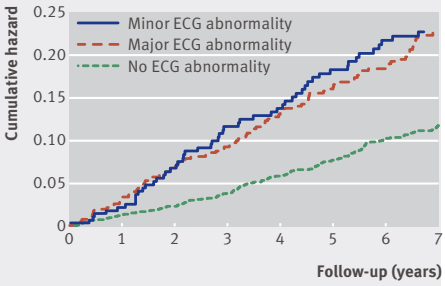
Should ECG be used to detect heart disease in asymptomatic older adults?

ECG abnormalities and hazard of coronary heart disease



Adapted from *JAMA* 2012;307:1497-505

For older people without overt heart disease, resting electrocardiographic (ECG) abnormalities help predict future coronary events beyond traditional risk factors, such as age, sex, smoking, cholesterol, hypertension, and diabetes. This was found in a population based study of 2192 older adults from the US. At baseline all participants were in their 70s and free of heart disease, but 276 (13%) had minor and 506 (23%) had major ECG abnormalities. In tune with the Minnesota code, minor ST-T changes were considered minor abnormalities, whereas major abnormalities were defined as Q-QS wave abnormalities, left ventricular hypertrophy, Wolff-Parkinson-White syndrome, complete bundle branch block or intraventricular block, atrial fibrillation or atrial flutter, or major ST-T changes.

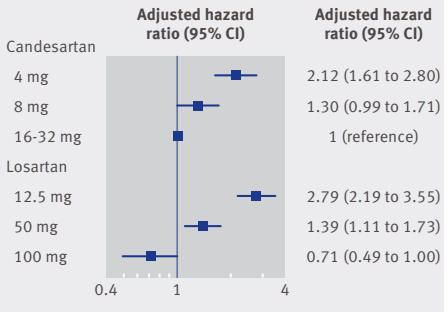
Over eight years of follow-up 351 people experienced acute myocardial infarction, death from coronary heart disease, or admission to hospital for angina or coronary revascularisation. The incidence of these outcomes was 17.2 per 1000 person years in those without ECG abnormalities at baseline, compared with 29.3 per 1000 person years and 31.6 per 1000 person years in those with minor and major abnormalities, respectively.

Beyond traditional risk factors, ECG abnormalities helped correctly reclassify 13.6% of people at intermediate risk, mainly by moving them to a lower risk category, for an overall net reclassification improvement of 7.4% (95% CI 3.1% to 19%). This is as many or more people than biomarkers such as C reactive protein or interleukin 6, but fewer than the recently developed coronary artery calcification score measured with computed tomography. In a recent study, this calcification score correctly reclassified a quarter of all participants, and more than half of those at intermediate risk.

The authors call for a trial to assess whether ECG should be done routinely in older adults. A linked editorial (p1530) points out that such a trial would need to recruit at least 60 000 people and follow them up for at least five years, and it would probably find that, rather than preventing coronary events, ECG helps reduce healthcare costs by avoiding statins in people at lower risk. The editorialist therefore argues for a good cost effectiveness analysis instead of the trial proposed by the authors.
JAMA 2012;307:1497-505

ARBs for heart failure: a class effect after all

All cause mortality in candesartan and losartan users with heart failure



Adapted from *JAMA* 2012;307:1506-12

Angiotensin II receptor blockers (ARBs) are recommended for patients with heart failure who cannot tolerate angiotensin converting enzyme inhibitors. A study published last year, from the Swedish registry of people with heart failure, suggested that losartan might be associated with increased mortality compared with other ARBs. However, a new study based on the Danish registry disproves this.

The study analysed all people with newly detected heart failure who started treatment with candesartan or losartan between 1998 and 2008. Overall, the unadjusted incidence of dying was higher with losartan (1212/4397; 10.7/100 person years) than with candesartan (330/2082; 9/100 person years). However, when propensity scoring was used to adjust for confounders such as demographics, comorbidities, and other drug use, no excess risk was seen for losartan (adjusted hazard ratio 1.10, 95% CI 0.96 to 1.25).

Losartan was associated with increased mortality only when low (12.5 mg) and medium (50 mg) doses were compared with high doses of candesartan (16-32 mg) (2.79, 2.19 to 3.55 and 1.39, 1.11 to 1.73, respectively). No excess risk of death was seen for high (100 mg) doses of losartan compared with high doses of candesartan (0.71, 0.50 to 1.00).

It may be that, rather than being a true dose dependent differential effect, the findings reflect residual confounding, whereby users of lower doses of losartan are more frail and have more severe heart failure than people who can tolerate higher doses of candesartan. In both the Swedish and the Danish studies, users of losartan were on average older and had more comorbidities than users of other ARBs.
JAMA 2012;307:1506-12

Vitamin D supplements don't prevent infant pneumonia in Kabul and may cause harm

In Afghanistan, infants are at risk of vitamin D deficiency owing to a generally low dietary intake of the vitamin, as well as women commonly wearing a burka and swaddling infants, both of which limit exposure to sunlight. Because vitamin D affects immune function, a trial tested whether quarterly oral bolus doses of vitamin D_3 (cholecalciferol) could reduce the incidence and severity of pneumonia.

Over 18 months, 1524 children aged 1-11 months were given 100 000 IU (2.5 mg) of vitamin D_3 every three months. Compared with 1522 children who were randomised to receive placebo, these children—contrary to the researchers' expectations—had a higher incidence of radiologically confirmed pneumonia, although the result wasn't significant (0.145 *v* 0.137/child/year; incidence rate ratio 1.06, 95% CI 0.89 to 1.27).

However, repeat episodes of pneumonia were more common in infants who received

"Are major and minor ECG abnormalities associated with coronary heart disease events? Yes. Does this mean that everybody should have a regular ECG? No. And why? Oh for goodness sake don't bother me—just go back to medical school or read *Overdiagnosed*
Richard Lehman's blog at www.bmj.com/blogs

vitamin D_3. No difference in this secondary outcome was seen for severe and very severe disease, but the incidence of overall (1.68, 1.28 to 2.21) and simple (1.88, 1.34 to 2.64) repeat episodes of pneumonia (confirmed by chest radiograph) was higher among children who received vitamin D_3 supplements.

Six children allocated to vitamin D_3 and four children allocated to placebo died of septicaemia or pneumonia. Of 652 children who were tested for serum concentrations of calcifediol, two were found to have concentrations that are considered toxic.
Lancet 2012;379:1419-27

Polyglutamine diseases protect patients against cancer

People with polyglutamine diseases such as Huntington's disease, spinobulbar muscular atrophy, and hereditary ataxia develop cancer less often than members of the general population, unlike their unaffected parents.

The registry linkage study comprised 1510 patients with Huntington's disease, 471 with spinobulbar muscular atrophy, and 3425 with hereditary ataxia who were diagnosed in Sweden over four decades. Standardised incidence ratios of any cancer were 0.47 (95% CI 0.38 to 0.58), 0.65 (0.45 to 0.91), and 0.77 (0.70 to 0.85), for the three diseases, respectively. Confounders such as age and sex, time and region, and socioeconomic position were taken into account.

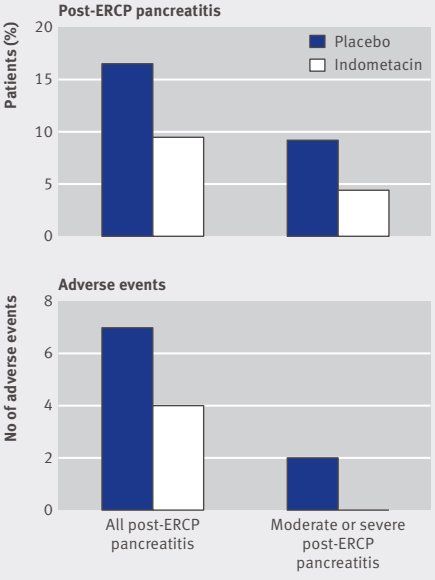
Most site specific cancers investigated were less common in people with polyglutamine disease, including cancers of the digestive system, lung, and breast. The protective effect was even more pronounced before the neurodegenerative disorders became apparent.

By contrast, patients' parents without polyglutamine disease had cancer rates similar to those seen in the general population (0.95, 0.82 to 1.10 for Huntington's disease, 0.94, 0.76 to 1.16 for spinobulbar muscular atrophy, and 1.00, 0.92 to 1.09 for hereditary ataxia).

The mechanisms behind these associations remain to be elucidated, but they almost certainly involve the expansion of CAG triplet repeats in certain genes, a common feature in all three diseases. Previous studies have shown a reduced risk of cancer in patients with Parkinson's disease, Alzheimer's disease, and schizophrenia.
Lancet 2012; doi:10.1016/S1470-2045(12)70132-8

Indometacin suppositories prevent pancreatitis after ERCP

Effect of indometacin on pancreatitis and adverse events



Adapted from *N Engl J Med* 2012;366:1414-22

A single dose of indometacin given rectally immediately after endoscopic retrograde cholangiopancreatography (ERCP) prevents pancreatitis in people at high risk of this complication.

In a randomised trial done in four US university hospitals, most (82%) people had a clinical suspicion of sphincter of Oddi dysfunction. Non-steroidal anti-inflammatory drugs inhibit phospholipase A2, cyclo-oxygenase, and neutrophil-endothelial interactions, which are all thought to play a major role in the pathogenesis of pancreatitis.

Postprocedural pancreatitis occurred in 27/295 (9.2%) of patients who received indometacin compared with 52/307 (16.9%) of those who received placebo, a relative risk reduction of 46%. Thirteen people needed to be treated with indometacin to prevent one episode of pancreatitis. A prespecified secondary outcome of moderate or severe pancreatitis also favoured the intervention (13 cases (4.4%) with indometacin *v* 27 (8.8%) with placebo), as did a post hoc secondary outcome of length of hospital stay (3.5 *v* 4.0 days). These results held in various prespecified and post hoc subgroup analyses, such as whether or not patients underwent pancreatic stenting, what subtype of sphincter of Oddi dysfunction they had, and size of the study centre.

There was some evidence that people at higher risk of pancreatitis benefited more from indometacin. For example, the number needed to treat was 21 for those with a preprocedure risk score of 1, indicating the presence of one major or two minor inclusion criteria, compared with a number needed to treat of six for people with a risk score of 5 (presence of four major and two minor inclusion criteria).

Adverse events were more common with placebo than with indometacin.
N Engl J Med 2012;366:1414-22

US tax days linked to more deaths in traffic incidents

The first study to examine the effects of US income tax days (which occur yearly round 15 April) on people's health shows that, on average, each tax day results in 13 additional deaths caused by traffic incidents. Most deaths occur in young adult men driving in the country.

Researchers compared tax days over the past three decades with control days (one week before and one week after each tax day). Analyses were further stratified by age and sex, region, decade, time of day, position (driver, passenger, or pedestrian), and initial outcome (dead or alive), but researchers had no information on things such as alcohol consumption, stress, or driving patterns.

A total of 6783 people (226/day) died in car crashes on tax days in the whole of the US during the study period, whereas 12 758 (213/day) died on control days (odds ratio 1.06, 95% CI 1.03 to 1.10). An excess of 404 people died in car crashes on tax days over the three decades, or an average of 13 extra deaths on each income tax day. The effect is a similar size to that previously shown for Super Bowl Sunday.
JAMA 2012;307:1486-8

Cite this as: *BMJ* 2012;344:e2750