SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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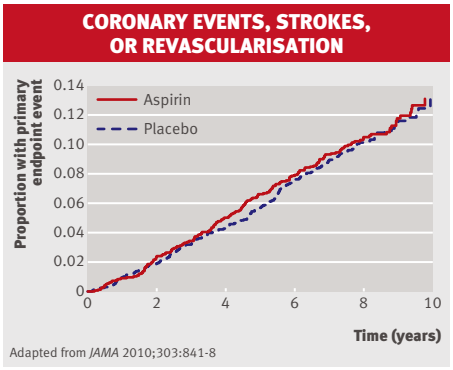
More evidence against aspirin for primary prevention



In 1998, researchers in Scotland began a large trial of low dose aspirin for adults without clinical cardiovascular disease. The results, now published, suggest that 100 mg of enteric coated aspirin a day is no more effective than placebo at preventing serious vascular events including heart attacks, strokes, and revascularisation procedures (hazard ratio 1.03, 95% CI 0.84 to 1.27). These adults had an ankle brachial index below 0.95, indicating a higher risk of cardiovascular disease than the general population of Scotland. Even so, aspirin did not save lives (hazard ratio for all cause mortality 0.95, 0.77 to 1.16) during more than eight years of follow-up, or protect participants from symptomatic disease (hazard ratio for cardiovascular events, angina, claudication, or transient ischaemic attack 1.00, 0.85 to 1.17). Aspirin caused significantly more major bleeds than placebo (1.71, 0.99 to 2.97), some of which were fatal.

The weight of evidence is now balanced against low dose aspirin for primary prevention, says an editorial (p 880). This trial had its flaws, as most trials do, but if aspirin has any prophylactic effect in this population, it is likely to be small. The harms are more obvious. These researchers screened nearly 30 000 adults aged 50-75 to find the 4914 with a reduced ankle brachial index. They managed to randomise 3350. Around 70% of participants were women.

JAMA 2010;303:841-8

The ups and downs of ECG screening for athletes

College athletes in the US must pass preparticipation screening by history and examination in an attempt to rule out undiagnosed heart disease. Some experts believe electrocardiography (ECG) should be mandatory too, and in one recent study adding ECG to history and examination improved the sensitivity of screening from 45.5% (95% CI 16.8% to 76.2%) to 90.9% (58.7% to 99.8%). Researchers compared the two strategies with a reference standard—transthoracic echocardiography—in 510 college athletes. Eleven participants had potentially significant cardiac abnormalities. History and examination alone picked up five of them, screening that also included ECG picked up 10. ECG was particularly good at finding ventricular abnormalities (hypertrophy or dilation) thought to be responsible for most sudden deaths. ECG cost an extra $42 900 (£28 180; €31 395) per life year saved ($21 200 to $71 300) in an economic analysis.

The downside to screening with ECG was a large number of false positives and a low positive predictive value of just 10.4% (5.1% to 18.3%). Overall, 16% (83/510) of the athletes had at least one ECG abnormality. Most of them had no structural heart disease but had ECG changes that were consistent with the remodelling that goes with physical fitness. Still, an abnormal ECG in inexperienced hands could easily lead to worry, overinvestigation, additional costs, and overcautious exclusion from competition, say the authors. ECG criteria specific to athletes would help. For now, there are too many doubts, too many remaining questions, and too many logistical problems for US authorities to consider mandating ECG screening for all young athletes, says an editorial (p 324).

Ann Intern Med 2010;152:269-75, 276-86

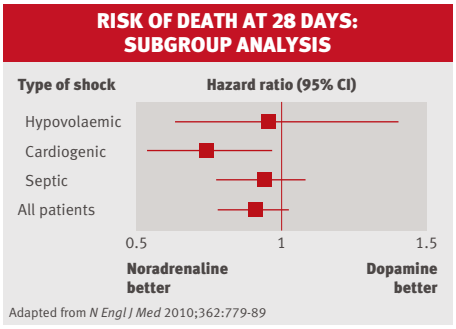
Room for one more trial of vitamin D for cardiovascular health

Vitamin D is a popular dietary supplement, partly because of the common perception that supplements can improve cardiovascular health. Evidence is patchy, however, and two recent systematic reviews found little to suggest that vitamin D supplements prevent or delay cardiovascular disease. Both teams of reviewers took a close look at data from published observational studies and randomised trials. Some observational analyses hinted at a link between low serum concentrations of vitamin D and poor cardiovascular health, particularly hypertension. But the main trials of vitamin D supplements were negative. The biggest trial, the Women's Health Initiative, tested a supplement of oral vitamin D and calcium in more than 36 000 women. The combined supplement was no more effective than placebo at preventing ischaemic heart disease or stroke.

So far, it doesn't look good for vitamin D as a cardiovascular tonic. But it is too early to write it off completely, says a linked editorial (p 327). There are good biological reasons why vitamin D might help protect the cardiovascular system and good methodological reasons—such as too low doses—why trials have failed to show an effect. We still have room for at least one more. The next trial should be big and it should test a high dose of vitamin D in a diverse population of men and women. It must also look carefully for harms as well as benefits.

Ann Intern Med 2010;152:307-14, 315-23

Researchers challenge guidelines recommending dopamine for shock



The vasopressor dopamine may not be safe for patients in shock, say researchers. Intensive care patients given the drug to restore blood pressure and tissue perfusion had more arrhythmias, usually atrial fibrillation, than those given noradrenaline in a recent trial (24.1% (207/858) *v* 12.4% (102/821); P<0.001). Dopamine was also associated with a significantly higher risk of death at 28 days in a preplanned subgroup analysis of 280 patients with cardiogenic shock. Consensus guidelines that recommend dopamine as the first line vasopressor should be revisited, they say.

"The authors of this study based on ARIC suggest that we may need to redefine the term 'diabetes' using gHb. No! no! Bin the term diabetes until patients become symptomatic"
Richard Lehman's journal blog, doc2doc.bmj.com

The 1679 participants had a mean age of 68. Two thirds had septic shock. Overall, 52.5% of patients treated initially with dopamine and 48.5% of those treated initially with noradrenaline died within 28 days (odds ratio 1.17, 95% CI 0.97 to 1.42). The difference wasn't significant, but an editorial (p 841) agrees that the subgroup analysis combined with a more favourable side effect profile for noradrenaline tips the balance away from dopamine as a first line agent. The trial's findings are broadly consistent with observational studies.

More work needs to be done, however. The editorial questions whether trial doses of dopamine (20 µg/kg/min) and noradrenaline (0.19 µg/kg/min) were equivalent. It is also unclear how many patients were resuscitated adequately with intravenous fluids. Subgroup analyses can be unreliable, and the extra deaths from cardiogenic shock associated with dopamine in this trial need to be confirmed.

N Engl J Med 2010;362:779-89

Mortality remains high for older adults who survive ICU

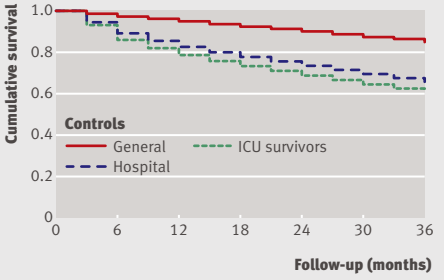
Adults over 65 make up about half of all admissions to US intensive care units (ICUs). More and more are surviving to discharge, but what happens to them in the months and years after they go home? An analysis of data from Medicare (government funded care for people over 65) reports high mortality: 14.1% (4961/35 308) during the first six months and 39.5% (13 950/35 308) by the end of three years.

These survivors did slightly but significantly worse than matched controls who were admitted to hospital but not to ICU (adjusted hazard ratio for death within three years 1.07 (95% CI 1.04 to 1.10)). They did far worse than a second control group representative of the general population over 65 (2.39, 2.31 to 2.48). Death rates were highest for the minority of adults who needed mechanical ventilation during intensive care (57.6% (1234/2141) over three years).

A third of ICU survivors were discharged to a nursing home (33% (11 634/35 308)). Needing nursing home care was a powerful and independent predictor of death in this analysis (adjusted hazard ratio for three year mortality 1.77, 1.72 to 1.82), second only to a diagnosis of metastatic cancer (3.02, 2.87 to 3.18). A third of the whole cohort also went back into hospital in the six months after their first discharge (36.1% (12 753/35 308)).

JAMA 2010;303:849-56

SURVIVAL FOR ICU COHORT AND CONTROLS



Adapted from *JAMA* 2010;303:849-56

Ethosuximide is best for children with absence epilepsy

Ethosuximide, a drug from the 1950s, came out on top in a head to head trial of three widely used drug treatments for absence epilepsy in childhood. Ethosuximide and valproic acid both worked significantly better than lamotrigine, but ethosuximide was associated with a significantly lower risk of attention problems during treatment.

The trial, paid for by the US National Institutes of Health, looked at 453 children with newly diagnosed absence epilepsy. The authors were primarily interested in treatment failure after 16-20 weeks, an outcome that included continuing absence attacks, any tonic clonic seizure, intolerable toxicity, or withdrawal by the child's parents or doctor. Treatment succeeded ("freedom from treatment failure") for 53% (81/154) of children given ethosuximide, 58% (85/146) of children given sodium valproate, and just 29% (43/146) of those given lamotrigine as first line treatment (odds ratio for ethosuximide *v* lamotrigine 2.66, 95% CI 1.65 to 4.28; odds ratio for valproic acid *v* lamotrigine 3.34, 2.06 to 5.42). Clinically relevant attention problems occurred in 49% of children treated with valproic acid (52/106) and 33% (35/106) of those treated with ethosuximide (1.95, 1.12 to 3.41). A similar proportion of each group stopped treatment because of intolerable toxicity.

The authors and a linked editorial (p 843) agree that ethosuximide is a sensible first choice for children with absence epilepsy. There is plenty of room for improvement, however. The best drug in this trial worked for only around half the children who took it.

N Engl J Med 2010;362:790-9

Bystanders should stick to conventional CPR for children

Between 2005 and 2007, 5758 Japanese children had a cardiac arrest outside hospital. Of these, 5170 had the arrest before emergency medical services arrived and were eligible for a study of cardiopulmonary resuscitation (CPR) by bystanders. Overall, 9.2% (476/5170) of all children survived for at least a month after their arrest. Only 3.2% (163/5170) survived with a good neurological outcome.

Bystanders attempted to resuscitate almost half the children (47% (2439/5170)). After careful adjustment for case mix and other factors, these children were significantly more likely to have a good neurological outcome than those who were not resuscitated by bystanders (4.5% (110/2439) *v* 1.9% (53/2719); adjusted odds ratio 2.59, 95% CI 1.81 to 3.71). Conventional resuscitation with both chest compressions and rescue breathing was associated with better outcomes than compression only resuscitation in children who had cardiac arrest after a non-cardiac event such as trauma, hanging, drowning, drug overdose, or asphyxiation (5.54, 2.52 to 16.99).

Because most children belong to this subgroup (71% (3664/5158) in this study), public health authorities should continue to recommend and to teach conventional cardiopulmonary resuscitation for children, says an editorial (doi:10.1016/S0140-6736(10)60316-9).

Infants under 1 year old did uniformly badly after an out of hospital cardiac arrest. Only 1.7% (36/2082) survived to 1 month without serious neurological impairment.

Lancet 2010; doi:10.1016/S0140-6736(10)60064-5

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