

SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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Screening doesn't prevent cardiac events in people with type 2 diabetes

Coronary artery disease kills or disables many people with type 2 diabetes and it often has a silent course, but it has been unclear whether screening for asymptomatic disease can identify people with high risk and improve cardiac outcomes. A multicentre randomised trial of 1123 people with diabetes (mean age 60 years) and no history of ketoacidosis or symptoms of coronary artery disease, who were randomly assigned to screening with adenosine stress radionuclide myocardial perfusion imaging or no screening, suggests that screening is not beneficial.

During a mean follow-up of 4.8 years, the cumulative rate of death from a cardiac cause or non-fatal myocardial infarction was 2.9%; 2.7% in the screened group and 3% in the non-screened group (hazard ratio 0.88, 95% CI 0.44 to 1.88). Among those screened, people with normal results and small defects had lower event rates than people with moderate or large defects, but the positive predictive value of a moderate or large defect was only 12%. Few people underwent coronary revascularisation—5.5% in the screened group and 7.8% in the non-screened group (0.71, 0.45 to 1.1).

Because of a lower than anticipated cardiac event rate, possibly as a result of high standards of contemporary diabetes care, the trial

had only 14% power to detect a 20% difference between the groups. However, the authors suggest that a reduction in cardiac events from 0.6% to 0.5% a year, even if proved, would not justify cardiac screening of people with type 2 diabetes *JAMA* 2009;301:1547-55

Hypoglycaemia increases risk of dementia in type 2 diabetes

Episodes of hypoglycaemia severe enough to need admission to hospital are associated with a subsequent increased risk of dementia in older people with type 2 diabetes. Among 16667 members of the Kaiser Permanente Northern California diabetes registry who in 2003 had no diagnoses of dementia, mild cognitive impairment, or memory problems, severe episodes of hypoglycaemia between 1980 and 2002 were linked with the incidence of dementia in the four subsequent years.

Compared with patients who had no recorded episodes of hypoglycaemia requiring admission to hospital, patients with one episode had an increased risk for dementia (adjusted hazard ratio 1.26, 95% CI 1.10 to 1.49); this increased to 1.80 (1.37 to 2.36) for two episodes and 1.94 (1.42 to 2.64) for three or more episodes. The excess risk amounted to 2.39% per year (1.72% to 3.01%), and the association was robust after adjustment for age, sex, ethnicity, education, body mass index, duration of diabetes, seven year mean glycated haemoglobin, diabetes treatment, duration of insulin use, hyperlipidaemia, hypertension, cardiovascular disease, stroke, transient cerebral ischaemia, and end stage renal disease. The excess risk remained when use of medical services, length of health plan membership, and time since initial diagnosis of diabetes were added to the model.

Admissions to the emergency department for severe hypoglycaemia showed a similar association with the risk of dementia.

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ities to provide adequate medical care even as it dramatically increases healthcare needs, say the authors of an analysis that assessed the nature and effects of various weapons on civilians in Iraq.

Using data from the Iraq Body Count (www.iraqbodycount.org), a non-governmental organisation that has monitored civilian violent deaths daily since the beginning of the war in 2003, the authors report that 91 358 civilians were killed in the first five years of the conflict. When specific events of armed violence were investigated, 60 481 civilian deaths were identified in 14 196 events. Of these, 19 706 (33%) people were killed by execution after abduction or capture, 5760 (29%) of whom showed marks of torture, such as bruises, drill holes, or burns.

One in five civilians were killed by small arms gunfire in open shootings and fire fights, 14% in executions by gunfire, and 14% from suicide bombs. Women and children made up the highest proportions of civilian deaths as a result of weapons fired indiscriminately from a distance—air attacks and mortars. Execution with torture, on the other hand, was mostly used against men and adults.

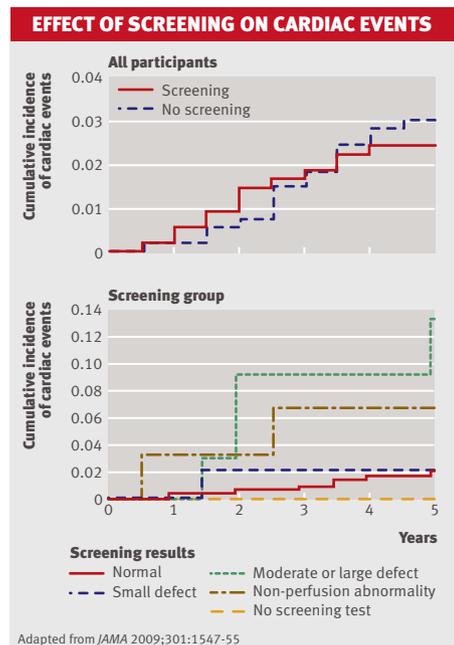
The authors say that the patterns they found convince them that documenting the particular causes of violent civilian deaths during armed conflict is essential, both to prevent civilian harm and to monitor compliance with international humanitarian law.

N Engl J Med 2009;360:1585-8

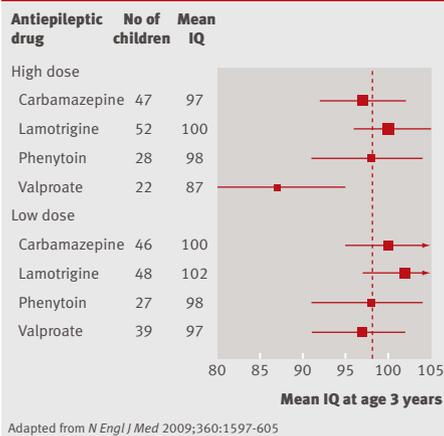
Valproate reduces IQ in offspring

Valproate shouldn't be used as the drug of first choice in women with epilepsy who may become pregnant. A multicentre prospective cohort study enrolled 303 pregnant women with epilepsy who were taking monotherapy with carbamazepine, lamotrigine, phenytoin, or valproate. At 3 years of age, children born to these women were assessed for cognitive outcomes by blinded assessors who used the mental developmental index of the Bayley scales of infant development (2nd edition) or differential ability scales. Results were adjusted for mother's IQ and age, dose of antiepileptic drug, gestational age at birth, and maternal use of folate before conception.

Mean IQs in children whose mothers were



IQ SCORES OF CHILDREN EXPOSED TO ANTIPILEPTICS IN UTERO



taking lamotrigine, phenytoin, carbamazepine, or valproate during pregnancy were 101, 99, 98, and 92, respectively. In children exposed in utero to valproate, IQ was on average 9 points lower than in children exposed to lamotrigine (95% CI 3.1 to 14.6), 7 points lower than in children exposed to phenytoin (0.2 to 14.0), and 6 points lower than in children exposed to carbamazepine (0.6 to 12.0). The association between exposure to valproate and IQ was dose dependent, and children's IQs were significantly related to maternal IQs in all children except for those exposed to valproate.

For some women, valproate is the only drug that controls seizures. These women should be informed of the potential risks associated with the use of this drug in pregnancy. But the authors say that women taking valproate who are already pregnant should not stop taking the drug without consulting their doctor, because this could lead to seizures and serious consequences for both the woman and her fetus.

N Engl J Med 2009;360:1597-605

Polymorphism rs12425791 increases risk of stroke

A genome-wide association study of 19 602 white people (mean age 63 years), with 1544 incident strokes over an average follow-up of 11 years, identified two single nucleotide polymorphisms on chromosome 12p13 (rs12425791 and rs11833579) that were associated with stroke ($P < 5 \times 10^{-8}$). The sequences were located close to the *NIN2* gene. This gene encodes an adhesion molecule expressed in glia that shows increased expression after nerve injury.

Direct genotyping found that rs12425791 was associated with an increased risk of any type of stroke (hazard ratio 1.30, 95% CI 1.19 to 1.42) and ischaemic stroke (1.33, 1.21 to 1.47), with population attributable risks of 11% and 12% in this cohort. The finding

was confirmed in two independent cohorts—one of 2430 black people with 215 incident strokes and the other of 652 Dutch people with ischaemic stroke and 3613 unaffected people. The association of rs11833579 with the risk of stroke was poorly confirmed outside the discovery cohort.

N Engl J Med 2009;360:1718-28

Valsartan doesn't prevent recurrent atrial fibrillation

Contrary to previous reports that angiotensin II receptor blockers might influence atrial remodelling and prevent atrial fibrillation, a randomised placebo controlled multicentre trial of valsartan shows that this is not the case. The 1442 participants were in sinus rhythm at baseline, but they had had either two or more episodes of atrial fibrillation in the previous six months or successful cardioversion for atrial fibrillation in the previous two weeks. In addition, all participants had underlying cardiovascular disease, diabetes, or left atrial enlargement.

In the year after randomisation, atrial fibrillation recurred in 371 of the 722 people (51.4%) who were randomised to valsartan and 375 of 720 (52.1%) of those randomised to placebo (adjusted hazard ratio 0.97, 96% CI 0.83 to 1.14). More than one episode of atrial fibrillation occurred in 194 of 722 patients (26.9%) in the valsartan group and in 201 of 720 (27.9%) in the placebo group (0.89, 0.64 to 1.23).

N Engl J Med 2009;360:1606-17

Glucose control after myocardial infarction seems safe

Control of blood glucose with insulin is recommended for patients with high blood glucose who are being treated for myocardial infarction, but concerns exist over possible harms from episodic hypoglycaemia as a result of this treatment. A study analysed the records of 7820 people who were treated for acute

myocardial infarction and hyperglycaemia in 40 hospitals across the US over six years. It found that hypoglycaemia was associated with an increased risk of dying in patients with acute myocardial infarction, but only in people who developed hypoglycaemia spontaneously. Iatrogenic hypoglycaemia after treatment with insulin bore no excess risk.

In the group not treated with insulin, 18.4% (25/136) of those with hypoglycaemia died, compared with 9.2% (425/4639) of those without hypoglycaemia. However, in the group treated with insulin, 10.4% (36/346) died after hypoglycaemia compared with 10.2% (276/2699) who did not have hypoglycaemia. Hypoglycaemia was a predictor of higher mortality in people who were not treated with insulin (odds ratio 2.32, 95% CI 1.31 to 4.12 *v* people without hypoglycaemia), but not in people treated with insulin (0.92, 0.58 to 1.45 *v* people without hypoglycaemia). *JAMA* 2009;301:1556-64

The artificial pancreas may be just around the corner

In a few years, the advent of an artificial pancreas could transform diabetes care. The crucial step in developing such a device is to close the loop between the continuous glucose monitor and the insulin pump with a computer algorithm that calculates the need for delivery of insulin. Preclinical testing of such closed loop systems became feasible last year with the approval of a computer simulation environment, which—on the basis of 10 years of data from 300 people with type 1 diabetes—mimics a human metabolic system and reduces years of animal experiments to minutes of laboratory based “in silico modelling.”

Once the artificial pancreas reaches us, the nanotechnology of glucose responsive insulin won't be far behind, and results of stem cell research—the ultimate biological solution for people with diabetes—may also soon follow.

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ASSOCIATION BETWEEN HYPOGLYCAEMIA AND MORTALITY

