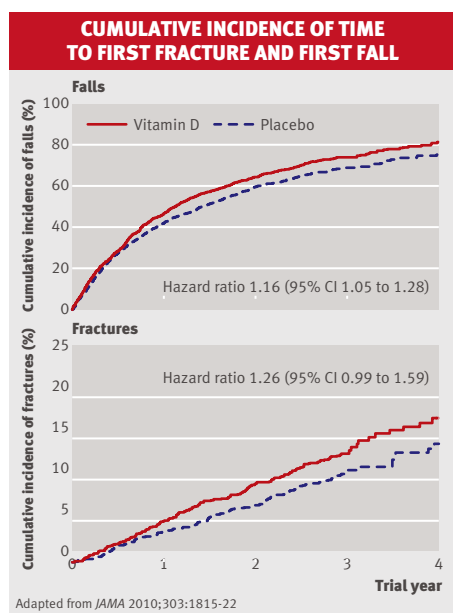


# SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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## Falls and fractures increase after high dose vitamin D

High doses of oral vitamin D may not be safe, say researchers, who found an excess of both falls (incidence rate ratio 1.15, 95% CI 1.02 to 1.30) and fractures (1.26, 1.00 to 1.59) in older women who took 500 000 international units (IU) once a year during a placebo controlled trial. The hazard looked greatest in the first three months after treatment, as serum concentrations of 25 hydroxycholecalciferol peaked before falling slowly for the rest of the year.

These women had a median age of 76, a median baseline concentration of 49 nmol/l, and a higher than average risk of fractures. They took their assigned treatment every autumn for three to five years, a practical regimen designed to offset the usual winter dip in vitamin D concentrations, and to improve adherence.

The extra falls and fractures were unexpected and hard to explain, although an editorial (p 1861) speculates that women given vitamin D might have had fewer infections, better mobility, and been more active during the winter than controls, paradoxically leading to more falls. The safety of annual high dose treatment needs further study. Meanwhile, doctors should stick to more traditional regimens using lower doses given daily, weekly, or monthly, says the editorial. Vitamin D deficiency remains widespread in this population and doctors should continue to treat it.

*JAMA* 2010;303:1815-22

## No evidence of worsening mental health in UK veterans of Afghanistan and Iraq

The mental health of UK armed forces is in reasonable shape despite prolonged operations in both Iraq and Afghanistan. A survey of 9990 regular service personnel and reservists from all three forces (response rate 56%) found a generally low prevalence of post-traumatic stress disorder (4%, 95% CI 3.5% to 4.5%) and no more symptoms of mental illness than respondents had reported in a similar survey between 2003 and 2005 (19.7%, 18.7% to 20.6%). Common mental illnesses such as anxiety and depression were not linked to deployment in either Afghanistan or Iraq. Reserves who had been deployed had more post-traumatic stress disorder than other reserves, although rates in both groups remained low.

The survey suggests that alcohol misuse is the most pressing mental health problem for UK military personnel. More than one in eight respondents scored above the threshold for harmful or hazardous drinking on a validated questionnaire (13%, 12.2% to 13.8%), an overall prevalence much higher than that reported by the general population, says a linked comment (doi:10.1016/S0140-6736(10)60716-7). Regular troops deployed to either Iraq or Afghanistan reported significantly more heavy drinking than those who had not been deployed (odds ratio 1.52, 1.30 to 1.79). Alcohol misuse was also significantly associated with direct combat during deployments (22.5% for combat troops v 14.2% for personnel in supporting roles; 1.75, 1.45 to 2.12).

*Lancet* 2010; doi:10.1016/S0140-6736(10)60672-1

## Chaotic literature is little help to people with food allergies

People with food allergies and the doctors who diagnose and treat them have little concrete evidence to support their decisions. There is no internationally recognised definition of food allergy and there are no well accepted criteria for diagnosis, so prevalence figures vary and it is hard to track trends in any meaningful way or to compare study results. Researchers recently did their best to summarise a diffuse and heterogeneous literature published since 1988. Clinically useful findings were limited to a “guesstimate” that prevalence lies somewhere between 1% and 10%, and a sug-

gestion that food challenges, skin patch testing, and serum concentrations of food specific IgE are potentially useful diagnostic tests. We don't yet know how they compare with each other or with a multitude of other unevaluated tests.

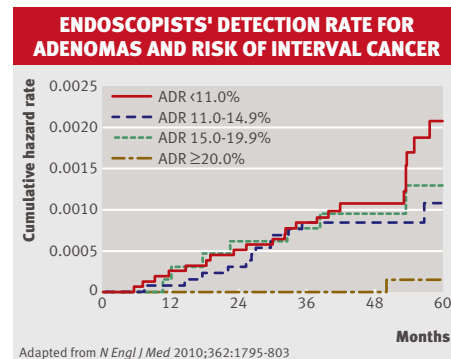
Reviewers found just one randomised trial testing an elimination diet—the mainstay of treatment for many allergies. The trial reported an improvement in atopic dermatitis for people on elimination diets. Studies evaluating immunotherapy, drug treatments, probiotics, and education weren't consistent or conclusive enough to inform clinical practice safely. Similar problems limited the evidence on prevention.

Patients risk overdiagnosis, misdiagnosis, poor treatment choices, and unnecessary dietary changes, say the authors, all of which can be harmful. Doctors need clearer guidance, urgently. This should start with a uniform definition of food allergy and a consensus on how best to diagnose it.

*JAMA* 2010;303:1848-56

## Screening colonoscopists should be judged on their detection of adenomas

The Polish national screening programme uses colonoscopy to find and treat asymptomatic colorectal cancers and adenomatous polyps. Between 2000 and 2004, 186 endoscopists did the screening tests, and some were better than others at finding adenomas. A detection rate below 20% (adenomatous lesions reported in less than one in five patients) was one of the few independent predictors of interval cancers in a study from the Polish programme. The detection rate for adenomas is already a popular quality indicator for endoscopists, say the authors. These data suggest it is a good one, unlike caecal intubation rate, which is another widely used indicator that





**“We all have our deficiencies, and in the case of people living in the British Isles, these generally include vitamin D. Correcting vitamin D deficiency is therefore a matter of national importance.”**

Richard Lehman's journal blog, [doc2doc.bmj.com](http://doc2doc.bmj.com), BMJ Group's global online clinical community, at <http://bit.ly/cd7bHr>

wasn't associated with risk of interval cancers in this study.

The authors analysed data from 45 026 men and women who were screened successfully, had adequate bowel preparation, and were cleared of all visible disease. Forty two people, screened by 32 endoscopists, developed an interval cancer between their first colonoscopy and the scheduled time of their next one, three to five years later. After multiple adjustments, the authors found a significant association between interval cancers and endoscopists with a relatively poor track record of finding adenomas—hazard ratios were greater than 10 (although confidence intervals were wide) for all categories of detection rate (ADR) below 20%. They weren't able to explore the effect of endoscopists' experience on risk of interval cancers, because experience is inaccurately recorded in the screening programme's database.

*N Engl J Med* 2010;362:1795-803

## More genetic loci linked to Alzheimer's disease

Researchers have found two new genetic loci linked to Alzheimer's disease and confirmed two others in a series of analyses that together included more than 35 000 adults. But they weren't able to improve on risk prediction models based on three traditional risk factors—age, sex, and the presence or absence of the single most powerful susceptibility gene apolipoprotein E (*APOE*). Adding the two new loci (*CLU* and *PICALM*) to the mix made little difference to the predictive power of the model, which was already high.

We shouldn't be surprised, or even disappointed, says an editorial (p 1864). Like many complex pathologies, Alzheimer's disease looks polygenic. There are probably many thousands of genetic loci, each contributing a small proportion to the overall risk of clinical disease. Even a handful, in isolation, won't be enough to help predict who will and who will not develop dementia. It is time to move away from pure genetic research and return to modifiable factors in our environment.

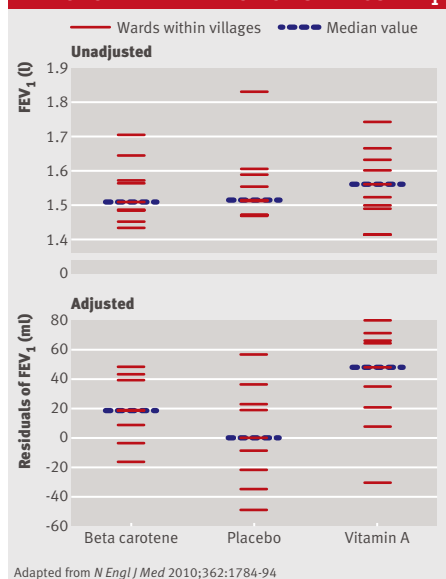
Genome-wide studies have already taught us to collaborate, combine resources, and marshal multiple cohorts to generate powerful analyses of thousands of participants. Those same cohorts can now be mined for information about how genotype and environmental factors combine to increase or decrease the risk of Alzheimer's disease. A healthy lifestyle in mid-life is already

thought to have some kind of protective effect, and doctors should carry on encouraging patients in that direction.

*JAMA* 2010;303:1832-40

## Vitamin A supplements for mothers improve lung function in children

### EFFECT OF TREATMENT ON OFFSPRINGS' FEV<sub>1</sub>



Vitamin A is essential for the development of healthy lungs in utero and early life. In one trial, supplements given to malnourished young women made a noticeable difference to their children's lung function more than a decade later. The women, from a rural part of Nepal, were all vitamin A deficient and were recruited in the 1990s to test whether supplements of preformed vitamin A or  $\beta$  carotene taken before, during, and after pregnancy could improve early outcomes for both mothers and babies. The supplements reduced maternal but not infant mortality, and researchers returned around 10 years later with portable pneumotachometers to measure lung function in 1371 of the surviving children.

Children whose mothers had taken vitamin A had a forced expiratory volume in one second (FEV<sub>1</sub>), and a forced vital capacity (FVC) 46 ml higher on average than control children whose mothers had taken a placebo (95% CI 6 to 86 for FEV<sub>1</sub> and 8 to 84 for FVC). The improvement in lung function was comparable to the known effect of preventing passive smoking in school-children, say the researchers. Supplements of  $\beta$

carotene made no significant difference to either measure of lung function, possibly because  $\beta$  carotene is a less efficient source of the active form of vitamin A.

Children's lung function at a mean age of 11 improved in line with their mothers' postpartum retinol concentrations, regardless of their assigned treatment in the original trial.

*N Engl J Med* 2010;362:1784-94

## Late thrombolysis may harm patients with ischaemic stroke

Thrombolysis with alteplase improves recovery from ischaemic stroke if it is given quickly enough. Guidelines recommend treatment within three hours, although smaller benefits are possible if treatment is given up to 4.5 hours after symptoms first appear. Beyond that, patients with ischaemic stroke have little to gain from treatment and more to lose, say researchers, who recently updated pooled analyses from eight major trials.

Patients treated within 90 minutes had the best odds of an excellent recovery (minimal or no neurological deficit) relative to placebo controls (adjusted odds ratio 2.55, 95% CI 1.44 to 4.52). Benefits decayed steadily with lengthening delays, and they disappeared between 4.5 and six hours after symptoms started (1.22, 0.92 to 1.61). The risk of serious brain haemorrhage was the same for everyone, so the balance between risk and recovery became increasingly unfavourable the longer patients waited.

The authors also noticed a trend towards increasing early mortality with longer delays. Patients given alteplase after 4.5 to six hours were more likely to die within three months than those given a placebo (1.49, 1.00 to 2.21). The difference wasn't entirely the result of large brain haemorrhages, which were rare. Statistical artefact is one possibility, says an editorial (p 1667). Others include an excess of smaller haemorrhages, or worse cerebral oedema after late thrombolysis.

The need for speed is now clearer than ever, says the editorial. We need smarter, slicker pre-hospital services, and a drive to reduce door to needle times once patients arrive. We also need a better informed public that recognises the warning signs of stroke, understands the urgency of the situation, and knows how to call for immediate help.

*Lancet* 2010;375:1695-703

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