SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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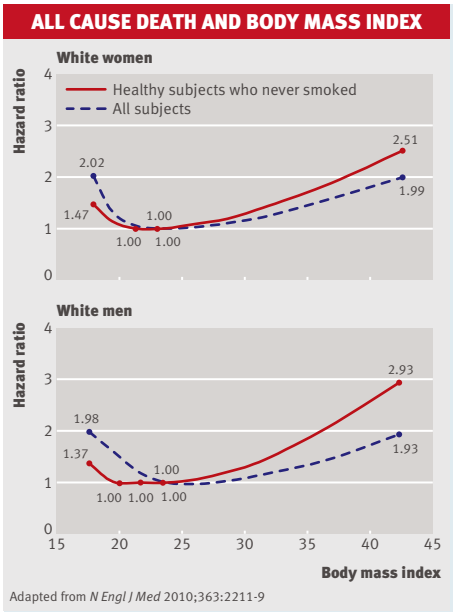
"Phlegm is important stuff: think of what happens to the lungs in cystic fibrosis, or in severe asthma when plugs of rubbery mucus can block enough of the airways to cause rapid death"

Richard Lehman's journal blog at www.bmj.com/blogs

Higher body mass index, higher mortality



Adapted from *N Engl J Med* 2010;363:2211-9

A fresh look at published data from nearly one and a half million adults has confirmed that being overweight or obese can significantly shorten your life. Researchers found an association shaped like a flattened J between body mass index and death from any cause. Adults with a body mass index between 22.5 and 24.9 had the lowest risk of death over 10 years of follow-up. Both bigger and smaller adults had a higher risk, although the link was strongest for increasing rather than decreasing body mass.

The researchers focused on men and women who were without cancer or heart disease at baseline and had never smoked. The ideal body mass index for this subgroup was 20-24.9. Risk of death rose by around 30% (hazard ratio 1.31, 95% CI 1.29 to 1.33) for every 5 unit increase in body mass index over the range 25-49.9. Even moderately overweight adults (body mass index 25-29.9) were significantly more likely to die than those in the ideal category. The excess risk for women was 13% (1.13, 1.09 to 1.17) and similar for men. The main analyses were adjusted for age, alcohol consumption, physical activity, educational level, and marital status.

The data came from 19 cohort studies of 1.46 million white adults aged 19-84. Researchers had enough statistical power to fine tune previous estimates of the association between body mass index and mortality. Overweight and obesity were linked to death from both cardiovascular disease and cancer. Cardiovascular disease looked the bigger hazard.

N Engl J Med 2010;363:2211-9

Artesunate suppositories can be a cost effective first line treatment for children with malaria

Every year many thousands of children die from falciparum malaria in rural parts of Africa because they have no access to life saving parenteral drugs. Artesunate suppositories can buy time, say researchers. They are relatively easy to administer, and they get to work while a sick child is taken to the nearest health facility for definitive treatment. Suppositories reduce mortality from malaria and look cost effective in rural settings. Recent estimates suggest this early intervention costs somewhere between 77 and 1173 international dollars for each disability adjusted life year saved. The lower figure emerged from analyses assuming that all children were given suppositories then taken to hospital. The higher figure came from analyses assuming just 25% compliance for both.

So artesunate suppositories can be a life saving strategy in some communities, says a linked comment (doi:10.1016/S0140-6736(10)61969-1). Suppositories are probably most useful where transport to a hospital is feasible, but slow; where a network of community health workers is already in place; and where malaria is the most likely diagnosis for a very sick child. Effectiveness and cost effectiveness will vary between settings, says the comment. Rectal artesunate is no substitute for rapid transfer to a nearby hospital, definitive diagnosis, and the right treatment where that can be achieved. Suppositories take six to 12 hours to reduce parasitaemia.

Lancet doi:10.1016/S0140-6736(10)61460-2

Newer faecal occult blood tests work fine for people taking aspirin

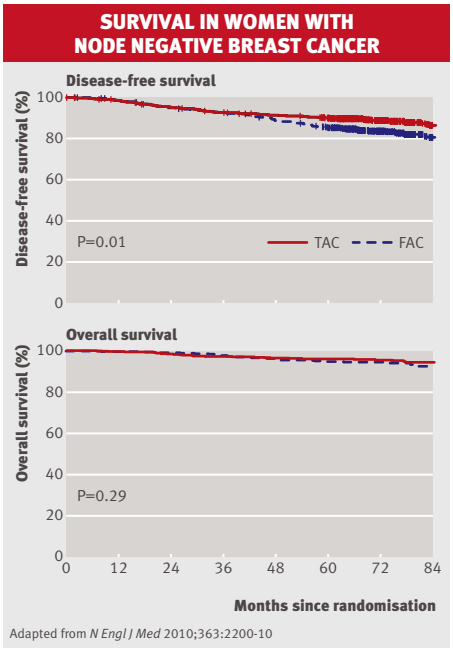
More and more adults are taking low dose aspirin, and experts worry about the effect of any gastrointestinal bleeding on faecal occult blood tests for colorectal cancer. Newer tests that use immunochemical methods to detect blood in stool seemed immune to interference from aspirin in a study grounded in Germany's screening programme.

Researchers compared the performance of two immunochemical tests in adults who did and did not use low dose aspirin. Their performance on some measures, including sensitivity, was better in aspirin users (70.8% *v* 35.9% and 58.3% *v* 32.0% for detecting cancer or advanced adenoma). The tests were slightly less specific for aspirin users, although the difference was significant for only one of the two tests. Analyses included 1979 adults with a mean age of 62. All were scheduled for a screening colonoscopy, and 233 (mostly men) reported taking low dose aspirin regularly.

Older guaiac based tests for faecal occult blood react to the heme moiety of haemoglobin, whereas the newer tests react to globin, which is degraded as it passes down the gastrointestinal tract, say the researchers. Immunochemical tests are no good at detecting blood from sources in the upper gut, which could explain why aspirin doesn't interfere with their performance.

JAMA 2010;304:2513-20

Taxanes for node negative breast cancer?



Adapted from *N Engl J Med* 2010;363:2200-10

Chemotherapy that includes a taxane is already standard for women with node positive breast cancer. Women with node negative disease may also benefit, according to a new trial. Chemotherapy with doxorubicin and

cyclophosphamide plus the taxane docetaxel (TAC) significantly prolonged disease-free survival in women with early breast cancer and no positive nodes but at least one high risk feature. Controls had fluorouracil instead of docetaxel (FAC).

After six years of follow-up, 87.8% (473/539) of women given the taxane and 81.8% (426/521) of those given fluouracil instead were alive and free from recurrence. Docetaxel based chemotherapy reduced the risk of recurrence by about a third (hazard ratio 0.68, 95% CI 0.49 to 0.93). It had no effect on overall survival. The trial was paid for by Sanofi Aventis. Just over 1000 women took part.

The taxane based chemotherapy looked more toxic than the control treatment. Women who had docetaxel reported significantly more diarrhoea, myalgia, arthralgia, other pain, amenorrhoea, and skin problems than controls. They also had more grade 3 or 4 neutropenia, (50.8% (270/532) *v* 39.5% (205/519); P<0.001). The authors were so concerned about neutropenia that they changed the protocol to allow women prophylaxis with granulocyte colony stimulating factor (G-CSF) before they started taxane based chemotherapy. The strategy seemed to work. Risk of febrile neutropenia fell from 25.2% to 5.5% after the switch.

N Engl J Med 2010;363:2200-10

Small particle pollution linked to narrowing of retinal arterioles

Researchers from the US have found a link between fine particle pollution and narrowing of the retinal arterioles in older adults. Retinal photographs showed a narrowing of 0.8 µm (−1.1 µm to −0.5 µm) for each 3 µg/m^3 increase in fine particle pollution near home—changes equivalent to seven years of ageing, or a 3 mm Hg increase in diastolic blood pressure. Exposures were measured for the two years before the photograph.

Short term exposure to pollution, measured on the day of the retinal photograph, was also associated with arteriolar narrowing, but to a lesser extent. Both analyses were adjusted for multiple personal, health, and lifestyle characteristics including blood pressure. The researchers think the observed associations are real, independent, and could help explain previous observations linking air pollution with cardiovascular disease. Narrowing of the retinal arterioles is a risk factor for heart attack, stroke, hypertension, and death from cardiovascular disease.

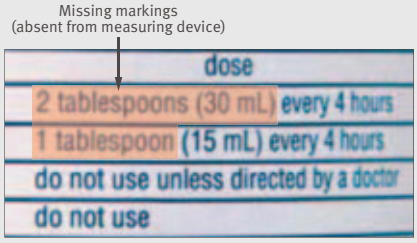
More than 4000 US adults aged 46-87 took part in the study. None had cardiovascular disease when recruited. The researchers estimated concentrations of fine particles around each participant's home, using federal monitoring stations. They were particularly interested in particles measuring 2.5 µm in diameter—around a 30th of the diameter of human hair. Particles of this size can interfere with endothelium dependent dilation of small blood vessels. Exhaust fumes from road traffic are a leading source. Living near a major road was also associated with arteriolar narrowing in this study.

PLoS Med 2010; doi:10.1371/journal.pmed.1000372

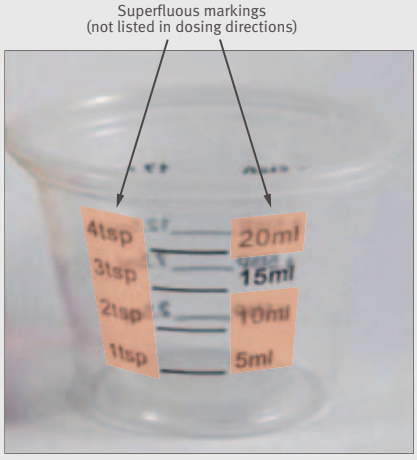
Chaotic dosing directions on over the counter drugs for children

INCONSISTENCIES BETWEEN LISTED DOSES AND MARKINGS ON MEASURING DEVICE

Dosing directions from packaging



Measuring device (one view)



Adapted from *JAMA* 2010; doi:10.1001/jama.2010.1797

When researchers from the US examined 200 best selling over the counter drugs for children they found a litany of omissions, inconsistencies, and inaccuracies in the dosing directions. Fifty two (26%) of the drugs did not have a measuring device. Almost all the others had devices (usually a cup) marked up differently from the dosing directions given in product packaging. The authors found extra markings (81% of measuring devices), missing markings (24%), different units (89%), and general confusion. The 200 products gave doses in millilitres, cubic centimetres, fluid ounces, teaspoons, tablespoons, and even drams. Abbreviations were non-standardised and often unexplained.

Dosing errors hurt children, say the authors. Many adults have poor health literacy, and even more struggle with numbers. Regulation and reform are urgently needed. The US Food and Drug Administration issued guidance at the end of 2009, but this study of liquid remedies for coughs, colds, allergies, and tummy upsets shows just how far the industry still has to go.

It is ironic that so many healthcare dollars are invested in developing, testing, and retesting drugs in expensive trials, says an editorial, when all is then thrown away in such a chaotic handover to the patient (doi:10.1001/jama.2010.1844). The solutions for over the counter drugs are obvious: provide a standard dosing device with every product, make sure it is calibrated clearly with the doses given on the packaging, and consider getting rid of popular measures such as teaspoons. Parents should be discouraged from reaching for the cutlery drawer. Flatware is notoriously inaccurate.

JAMA 2010; doi:10.1001/jama.2010.1797

Rivaroxaban prevents recurrence after acute thromboembolism

Rivaroxaban is an oral anticoagulant that directly inhibits activated factor X. It is already approved as a prophylactic against venous thromboembolism after orthopaedic surgery. The manufacturers are now evaluating rivaroxaban as a treatment for acute deep vein thrombosis, more specifically as an alternative to initial treatment with enoxaparin followed by a vitamin K antagonist.

In the first of two trials, rivaroxaban was as good as the control treatment at preventing recurrent thromboembolism over three, six, or 12 months (2.1% (36/1731) in the rivaroxaban group *v* 3.0% (51/1718) in the control group; hazard ratio 0.68, 95% CI 0.44 to 1.04) and caused no more clinically relevant bleeds. In the second trial, the same researchers compared rivaroxaban with placebo in patients who had already completed six to 12 months of anticoagulation. Those given rivaroxaban for a further six or 12 months had significantly fewer recurrent events (1.3% (8/602) *v* 7.1% (42/594); 0.18, 0.09 to 0.39) but significantly more "major or clinically relevant non major" bleeds (6.0% (36/598) *v* 1.2% (7/590); 5.19, 2.3 to 11.7). The authors consider this an acceptable risk-benefit balance. Oral rivaroxaban is also more convenient for patients than vitamin K antagonists, they write. Monitoring of international normalised ratio (INR) is unnecessary.

The first trial was open, the second double blind. Both were paid for by companies responsible for the manufacture or marketing of rivaroxaban.

N Engl J Med 2010; doi:10.1056/NEJMoa1

Cite this as: *BMJ* 2010;341:c7019