Abstracts

Prototype malaria vaccine doesn't work for children in Mali

GlaxoSmithKline's latest malaria vaccine failed to prevent clinical disease in a recent trial in Mali. Children given three doses at monthly intervals mounted a good immune response, but an estimated 48.4% still developed clinical falciparum malaria over the next six months. A comparable proportion of controls, who were given a rabies vaccine, also developed clinical malaria (54.4%; hazard ratio 0.83, 95% confidence interval (CI) 0.63 - 1.09). Four hundred children aged 1 - 6 years took part.

The authors were testing a monovalent prototype directed against the blood stage of the falciparum malaria parasite. The active ingredient (antigen) is a membrane protein called apical membrane antigen 1, from the 3D7 strain of *Plasmodium falciparum*. Although the children in this trial didn't get any useful protection from malaria in general, the vaccine did seem to protect them from the 3D7 strain. Of the 22 children with this infection, 16 were in the control group, which gives an estimated efficacy of 64.3% (0.36, 0.08 - 0.86).

Fevers were significantly more common after the malaria vaccine, and a local reaction was almost universal. Parents also reported more irritability, fussiness, and loss of appetite in children given the malaria vaccine. The authors say the safety profile looks acceptable so far, and they hope that FMP2.1/AS02$_A$ might eventually prove useful as part of a multicomponent vaccine.

Thera MA, et al. N Engl J Med 2011;365:1004-1013.

Chocolate consumption and cardiometabolic disorders

The authors of this paper evaluated the association of chocolate consumption with the risk of developing cardiometabolic disorders using a systematic review and meta-analysis of randomised controlled trials and observational studies. Their data sources were Meddline, Embase, Cochrane Library, PubMed, CINAHL, IPA, Web of Science, Scopus, Pascal, reference lists of relevant studies to October 2010, and e-mail contact with authors.

They selected randomised trials and cohort, case-control, and cross-sectional studies carried out in human adults, in which the association between chocolate consumption and the risk of outcomes related to cardiometabolic disorders were reported.

Data were extracted by two independent investigators, and a consensus was reached with the involvement of a third. The primary outcome was cardiometabolic disorders, including cardiovascular disease (coronary heart disease and stroke), diabetes, and metabolic syndrome. A meta-analysis assessed the risk of developing cardiometabolic disorders by comparing the highest and lowest level of chocolate consumption.

Of the data sources selected (4 576 references) seven studies met the inclusion criteria (including 114 009 participants). None of the studies was a randomised trial, six were cohort studies, and one a cross-sectional study. Large variation was observed between these seven studies for measurement of chocolate consumption, methods, and outcomes evaluated. Five of the seven studies reported a beneficial association between higher levels of chocolate consumption and the risk of cardiometabolic disorders. The highest levels of chocolate consumption were associated with a 37% reduction in cardiovascular disease (relative risk 0.63 (95% confidence interval (CI) 0.44 - 0.90)) and a 29% reduction in stroke compared with the lowest levels.

Based on observational evidence, levels of chocolate consumption seem to be associated with a substantial reduction in the risk of cardiometabolic disorders. Further experimental studies are required to confirm a potentially beneficial effect of chocolate consumption.

Buitrago-Lopez A, et al. BMJ 2011;343:d4488.

Popular natural remedy for men's urinary symptoms works no better than a placebo

Extract of fruit from the saw palmetto palm tree is thought to improve urinary symptoms caused by benign prostatic hyperplasia. Saw palmetto extract is popular, but there is little evidence that it works, despite a series of more than two dozen increasingly rigorous trials and at least two meta-analyses. Reasoning that the lack of effect might be the result of inadequate dosing in previous trials, researchers designed a trial that tested double, then triple, the standard dose against an identical-looking placebo in 369 men with lower urinary tract symptoms typical of benign prostatic hypertrophy.

The extract had no effect at any dose, at any time, or for any subgroup. Symptom scores fell slightly in both groups during the 72-week trial. Men given palmetto extract started on the standard dose in a single capsule, added a second capsule at week 24, and a third at week 48. Even the highest dose had no impact on quality of life, nocturia, or any other secondary outcome.

Participants had a mean age of 61 and a mean symptom score of 15 (out of a possible 35) at the start of the trial. The researchers excluded men whose serum concentrations of prostate specific antigen were more than 10 µg/l and any who had recently taken drugs for benign prostatic hypertrophy.

Barry MJ, et al. JAMA 2011;306:1344-1351.

Zoledronic acid does not prolong survival for women with early breast cancer

Intravenous zoledronic acid should not be offered routinely to women with early breast cancer, say researchers, after a large trial found it had no discernible effect on recurrence or survival over five years. The trial, which was sponsored by Novartis, tested the drug in 3 360 women with T1, T2, or T3 tumours. Almost all had axillary spread. Results were clear, and the trial stopped early after an interim analysis and a median follow-up of 59 months.

Just over 1% of the women treated with zoledronic acid developed osteonecrosis of the jaw (17/1 681), an unexpectedly high incidence of a well-known and serious side-effect. The authors blame their intensive treatment schedule – 4 mg infusions starting monthly and decreasing to twice yearly for a total of five years. No cases of osteonecrosis of the jaw were seen in controls, who had standard treatment without zoledronic acid.

Most of the women in this trial had postoperative chemotherapy. They also had radiotherapy and endocrine treatments as appropriate, according to local protocols. Almost identical proportions of women in each group were alive and disease free after five years (76.9% v. 77.1%; adjusted hazard ratio 0.98, 95% confidence interval (CI) 0.85 - 1.13).

Subgroup analyses hinted at a small but significant survival advantage for postmenopausal women given zoledronic acid. The drug's effects may depend on background values of reproductive hormones, say the authors.

Coleman RE, et al. N Engl J Med 2011;doi:10.1056/nejmoa1105195.

Bridget Farham