New drug combination shows promise for weight loss

A phase III trial tested two dose regimens of phentermine plus topiramate against placebo as an addition to modification of lifestyle for weight loss and reduction of metabolic risk. Participants were 2487 overweight or obese people, aged 18-70 years, with a body mass index of 27-45 and two or more of the following comorbidities—high blood pressure, unfavourable lipid profile, diabetes or prediabetes, and abdominal obesity. Less than a third made it to the end of the trial at 56 weeks.

Average weight loss with placebo, the low dose drug combination, and the high dose combination was 1.4 kg, 8.1 kg, and 10.2 kg, respectively. Compared with placebo, people who took the low dose combination had 6.3-fold better odds of losing at least 5% of body weight, and participants allocated to the high dose regimen had a 9-fold improved odds. For weight loss of 10% of body weight or more, this was 7.6-fold and 11.7-fold for the low dose and high dose drug regimens, respectively, compared with placebo. Improvements were also seen in blood pressure, waist circumference, blood lipids, blood glucose, and inflammatory biomarkers.

Adverse events were many, however, and many of them escalated with increasing drug doses. Events included dry mouth, paraesthesia, constipation, insomnia, dizziness, impaired sense of taste, anxiety, irritability, and impaired attention. Increases in heart rate, lowering of blood potassium and bicarbonate, and increased risk of kidney stones were also seen with treatment. *Lancet* 2011; doi: 10.1016/S0140-6736(11)60205-5

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**Room for flexibility in scheduling HPV vaccination**

Different dosing schedules for quadrivalent vaccine against human papillomavirus (HPV) were tested in 903 girls aged 11-13 years in Vietnam. The standard schedule (0, 2, and 6 months) was compared with three other schedules: 0, 3, and 9 months; 0, 6, and 12 months; and 0, 12, and 24 months.

Mean antibody concentrations as measured one month after the final jab were not inferior to those seen with standard scheduling in the 9 month and 12 month schedules. In the 24 month schedule, however, immunogenicity was inferior, because the lower bound of the confidence interval for the HPV-16 serotype was just below 0.5, a prespecified margin. Antibody titres were lowest in this group but still higher than previously reported for women aged 16-26 years, so it is not clear how differences seen in titres might translate to differences in clinical outcomes, such as precancerous lesions.

The study is ongoing and will examine antibody response in the longer term. Another study in adolescent girls in Canada is currently comparing two jab schedules against three jab ones. *JAMA* 2011;305:1424-31

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**Ex vivo perfusion of donor lungs may improve usability for transplantation**

Eight of 10 donor lungs are not transplanted because they have been damaged after brain death or by complications of treatment in intensive care units. Ex vivo lung perfusion is a procedure where lungs are perfused and ventilated at body temperature after harvesting, to mimic normal body conditions. In a non-randomised study, lungs that had been assessed as at high risk for non-use were transported to the study centre and perfused ex vivo for four hours.

Of the 23 lungs that underwent ex vivo perfusion, 20 were deemed suitable for transplantation after the procedure. Outcomes of patients who received these lungs compared well with those of the 116 patients who received standard lung transplantation in the study centre over the same period. A non-significant difference was seen in the primary outcome—primary graft dysfunction 72 hours after transplantation—which was 15% (3/20) in patients who received perfused lungs compared with 30% (35/116) with standard transplantation. No difference was seen between the groups in secondary outcomes and no adverse events were attributed to ex vivo perfusion. *N Engl J Med* 2011;364:1431-40

Cite this as: BMJ 2011;342:d2469