Abstracts

China's excess males, sex-selective abortion and one-child policy

Wei Zing Zhu and colleagues, publishing in the *British Medical Journal*, examined current trends and geographical patterns in the sex ratio at birth and in the population aged under 20 in China to determine the roles played by sex-selective abortion and the one-child policy. They used an analysis of a household-based cross-sectional population survey done in November 2005. This was carried out in all of China's 2 861 counties, comprising 1% of the total population, selected to be broadly representative of the total.

The main outcome measure was sex ratio defined as males per 100 females. They included 4 764 512 people under the age of 20. Overall sex ratios were high across all age groups and residency types, but they were highest in the 1- 4-year age group, peaking at 126 (95% confidence interval 125 - 126) in rural areas. Six provinces had sex ratios of over 130 in the 1 - 4-year age group. The sex ratio at birth was close to normal for first-order births but rose steeply for second-order births, especially in rural areas, where it reached 146 (143 - 149). Nine provinces had ratios of over 160 for second-order births. The highest sex ratios were seen in provinces that allow rural inhabitants a second child if the first is a girl. Sex-selective abortion accounts for almost all the excess males. One particular variant of the one-child policy, which allows a second child if the first is a girl, leads to the highest sex ratios.

In 2005 males under the age of 20 exceeded females by more than 32 million in China, and more than 1.1 million excess births of boys occurred. China will see very high and steadily worsening sex ratios in the reproductive age group over the next two decades. Enforcing the existing ban on sex-selective abortion could lead to normalisation of the ratios.

Wei Zing Zhu *et al. BMJ* 2009; 338: b1211.

Neonatal vitamin A supplementation not justified

Siddhartha Gogia and Harshpal Singh Sachdev from New Delhi evaluated the effect of neonatal vitamin A supplementation on infant mortality, morbidity and early adverse effects. They used a systematic review, meta-analysis, and meta-regression of randomised controlled trials. The sources were electronic databases and hand search of reviews, abstracts and proceedings of conferences.

They analysed randomised, quasi-randomised or cluster randomised placebo-controlled trials evaluating the effect of prophylactic, neonatal (<1 month) supplementation with synthetic vitamin A on mortality or morbidity in infancy (<1 year), and early adverse effects (7 days).

The 6 included trials were from developing countries. There was no convincing evidence of a reduced risk of mortality during infancy (relative risk 0.92, 95% confidence interval 0.75 - 1.12, p=0.393 random effect; I^2=54.1%) or of an increase in early adverse effects, including a bulging fontanelle (1.16, 0.81 - 1.65, p=0.418; I^2=65.3%). No variable emerged as a significant predictor of mortality, but data for important risk groups (high maternal night blindness and low birth weight) were restricted. Limited data (from 1 to 4 trials) did not indicate a reduced risk of mortality during the neonatal period (0.90, 0.75 - 1.08, p=0.270; I^2=0%), or cause-specific mortality, common morbidities (diarrhoea and others), and admission to hospital. There was, however, evidence of an increased risk of acute respiratory infection and a reduced risk of clinic visits.

There is no convincing evidence of a reduced risk of mortality and possibly morbidity or of increased early adverse effects after neonatal supplementation with vitamin A. There is therefore no justification for initiating such supplementation as a public health intervention in developing countries for reducing infant mortality and morbidity.

Gogia S, Sachdev HS. *BMJ* 2009; 338: b919.

Nicotine replacement and smoking cessation

Nicotine replacement therapy is commonly assumed to be effective in smoking cessation and has been confirmed by numerous trials. However, all these trials include regular behavioural support and monitoring. The authors of this study published in the *British Medical Journal* carried out a systematic review of randomised controlled trials to determine the efficacy and safety of nicotine replacement in smoking cessation.

Eligible studies were published or unpublished randomised controlled trials that enrolled smokers who declared no intention to quit smoking in the short term, and compared nicotine replacement therapy (with or without motivational support) with placebo, no treatment, other pharmacological therapy, or motivational support, and reported quit rates. Two reviewers independently applied eligibility criteria. One reviewer assessed study quality and extracted data – these processes were checked by a second reviewer. The primary outcome, 6 months sustained abstinence from smoking beginning during treatment, was assessed by individual patient data analysis. Other outcomes were cessation and reduction at end of follow-up, and adverse events.

Seven placebo-controlled, randomised controlled trials were included (4 used nicotine replacement therapy gum, 2 nicotine replacement therapy inhaler, and 1 free choice of therapy). These were reduction studies that reported smoking cessation as a secondary outcome. The trials enrolled a total of 2 767 smokers, gave nicotine replacement therapy for 6 - 18 months, and lasted 12 - 26 months. Furthermore, 6.75% of smokers receiving nicotine replacement therapy attained sustained abstinence for 6 months, twice the rate of those receiving placebo (relative risk (fixed effects) 2.06, 95% confidence interval 1.34 - 3.15; (random effects) 1.99, 1.01 - 3.91; 5 trials). The number needed to treat was 29. All other cessation and reduction outcomes were significantly more likely in smokers given nicotine replacement therapy than those given placebo. There were no statistically significant differences in adverse events (death, odds ratio 1.00, 95% confidence interval 0.25 - 4.02; serious adverse events 1.16, 0.79 - 1.50; and discontinuation because of adverse events 1.25, 0.64 - 2.51) except nausea, which was more common with nicotine replacement therapy (8.7% v. 5.3%; odds ratio 1.69, 95% confidence interval 1.21 - 2.36).

The authors concluded that available trials indicate that nicotine replacement therapy is an effective intervention in achieving sustained smoking abstinence for smokers who have no intention or are unable to attempt an abrupt quit. Most of

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the evidence, however, comes from trials with regular behavioural support and monitoring and it is unclear whether using nicotine replacement therapy without regular contact would be as effective.

Moore D, *et al. BMJ* 2009; 338: b1024.

The polypill and risk factors in healthy people

This article in the *Lancet* comes from the India Polycap study, which examined the effects of the polypill – a combined statin, aspirin and folic acid with three blood pressure-lowering drugs (ramipril, atenolol and hydrochlorothiazide) – in middle-aged people without known cardiovascular disease. The authors point out that this combination could potentially reduce cardiovascular events by 80%. The study examined the effect of the Polycap on blood pressure, lipids, heart rate, and urinary thromboxane B_2, and assessed its tolerability.

In a double-blind trial in 50 centres in India, 2 053 individuals without cardiovascular disease, aged 45 - 80 years, and with 1 risk factor (type 2 diabetes; blood pressure >140 mmHg systolic or 90 mmHg diastolic, but <160/100 mmHg; smoker within past 5 years; increased waist-to-hip ratio (>0.85 for women and >0.90 for men); or abnormal lipids (LDL cholesterol >3.1 mmol/l or HDL cholesterol <1.04 mmol/l)) were randomly assigned, by a central secure website, to the Polycap (*N*=412) consisting of low doses of thiazide (12.5 mg), atenolol (50 mg), ramipril (5 mg), simvastatin (20 mg), and aspirin (100 mg) per day, or to 8 other groups, each with about 200 individuals, of aspirin alone, simvastatin alone, hydrochlorothiazide alone, three combinations of the two blood pressure-lowering drugs, three blood pressure-lowering drugs alone, or three blood pressure-lowering drugs plus aspirin. The primary outcomes were LDL for the effect of lipids, blood pressure for antihypertensive drugs, heart rate for the effects of atenolol, urinary 11-dehydrothromboxane B_2 for the antiplatelet effects of aspirin, and rates of discontinuation of drugs for safety. Analysis was by intention to treat.

Compared with groups not receiving blood pressure-lowering drugs, the Polycap reduced systolic blood pressure by 7.4 mmHg (95% CI 6.1 - 8.1) and diastolic blood pressure by 5.6 mmHg (4.7 - 6.4), which was similar when three blood pressure-lowering drugs were used, with or without aspirin. Reductions in blood pressure increased with the number of drugs used (2.2/1.3 mmHg with 1 drug, 4.7/3.6 mmHg with 2 drugs, and 6.3/4.5 mmHg with 3 drugs). The Polycap reduced LDL cholesterol by 0.70 mmol/l (95% CI 0.62 - 0.78), which was less than that with simvastatin alone (0.83 mmol/l, 0.72 - 0.93; p=0.04); both reductions were greater than for groups without simvastatin (p<0.0001). The reduction in heart rate with the Polycap and other groups using atenolol was similar (7.0 beats per min), and both were significantly greater than that in groups without atenolol (p<0.0001). The reduction in 11-dehydrothromboxane B_2 was similar with the Polycap (283.1 ng/mmol creatinine, 95% CI 229.1 - 337.0) compared with the three blood pressure-lowering drugs plus aspirin (350.0 ng/mmol creatinine, 294.6 - 404.0), and aspirin alone (348.8 ng/mmol creatinine, 277.6 - 419.9) compared with groups without aspirin. Tolerability of the Polycap was similar to that of other treatments, with no evidence of increasing intolerability with increasing number of active components in one pill.

This Polycap formulation could be conveniently used to reduce multiple risk factors and cardiovascular risk.

The India Polycap Study (TIPS). *Lancet* 2009; doi:10.1016/S0140-6736(09)60611-5.

BRIDGET FARHAM

Single Suture

Lots of red meat shortens life

Eating large amounts of red and processed meats apparently shortens your life, according to Rashmi Sinha and colleagues at the US National Cancer Institute in Rockville, Maryland. The team looked at overall death rates among 545 000 volunteers aged between 50 and 71, who were asked about their diet over the past year. This information was used to estimate their meat intake. The volunteers were then monitored for 10 years.

During that time, more than 71 000 of the group died. After controlling for factors such as age, weight, smoking history and total food intake, the reseaerchers found that women who ate the most red meat – 66 g per 1 000 calories – were 36% more likely to have died than women who ate the least – 9.1 g. Men who ate large quantities of red meat were 31% more likely to have died.

Consumption of processed meats such as sausage, salami and hot dogs was lower, but still had a significant effect on the rate of deaths.

Sinha R, *et al. Arch Intern Med* 2009; 169: 562-571.

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