

No evidence that vitamin A supplementation reduces pregnancy-related mortality

A trial in Nepal showed that supplementation with vitamin A or its precursor (beta-carotene) in women of reproductive age reduced pregnancy-related mortality by 44%. The authors of this paper, published in the *Lancet*, assessed the effect of vitamin A supplementation in women in Ghana.

ObapaVitA was a cluster-randomised, double-blind, placebo-controlled trial undertaken in 7 districts in Brong Ahafo Region in Ghana. The trial area was divided into 1 086 small geographical clusters of compounds with fieldwork areas consisting of 4 contiguous clusters. All women of reproductive age (15 - 45 years) who gave informed consent and who planned to remain in the area for at least 3 months were recruited. Participants were randomly assigned by cluster of residence to receive a vitamin A supplement (25 000 IU retinol equivalents) or a placebo capsule orally once every week. Randomisation was blocked and based on an independent, computer-generated list of numbers, with 2 clusters in each fieldwork area allocated to vitamin A supplementation and 2 to placebo. Capsules were distributed during home visits undertaken every 4 weeks, when data were gathered on pregnancies, births, and deaths. Primary outcomes were pregnancy-related mortality and all-cause female mortality. Cause of death was established by verbal post mortems. Analysis was by intention to treat (ITT) with random-effects regression to account for the cluster-randomised design. Adverse events were synonymous with the trial outcomes.

A total of 104 484 women were randomly assigned to vitamin A supplementation and 103 297 women to placebo. The main reason for participant drop-out was migration out of the study area. In the ITT analysis, there were 39 601 pregnancies and 138 pregnancy-related deaths in the vitamin A supplementation group (348 deaths per 100 000 pregnancies) compared with 39 234 pregnancies and 148 pregnancy-related deaths in the placebo group (377 per 100 000 pregnancies). A total of 1 326 women died in 292 560 woman-years in the vitamin A supplementation group (453 per 100 000 years) compared with 1 298 deaths in 289 310 woman-years in the placebo group (449 per 100 000 years).

The body of evidence, although limited, does not support inclusion of vitamin A supplementation for women in either safe motherhood or child survival strategies.

Kirkwood BR, *et al. Lancet* 2010; early online publication 4 May (doi:10.1016/S0140-6736(10)60311-X).

RSV and the global burden of acute lower respiratory infections

The global burden of disease attributable to respiratory syncytial virus (RSV) remains unknown. This study, recently published in the *Lancet*, aimed to estimate the global incidence of and mortality from episodes of acute lower respiratory infection (ALRI) due to RSV in children younger than 5 years in 2005.

The authors estimated the incidence of RSV-associated ALRI in children younger than 5 years, stratified by age, using data from a systematic review of studies published between January 1995 and June 2009, and 10 unpublished population-based studies. They estimated possible boundaries for RSV-associated ALRI mortality by combining case fatality ratios with incidence estimates from hospital-based reports from published and unpublished studies and identifying studies with population-based data for RSV seasonality and monthly ALRI mortality.

In 2005, an estimated 33.8 million new episodes of RSV-associated ALRI occurred worldwide in children younger than 5 years (22% of ALRI episodes), with at least 3.4 million episodes representing severe RSV-associated ALRI necessitating hospital admission. We estimated that 66 000 - 199 000 children younger than 5 years died from RSV-associated ALRI in 2005, with 99% of these deaths occurring in developing countries. Incidence and mortality can vary substantially from year to year in any one setting.

Globally, RSV is the most common cause of childhood ALRI and a major cause of admission to hospital as a result of severe ALRI. Mortality data suggest that RSV is an important cause of death in childhood from ALRI, after pneumococcal pneumonia and *Haemophilus influenzae* type b. The development of novel prevention and treatment strategies should be accelerated as a priority.

Nair H, *et al. Lancet* 2010; 375: 1545-1555 (doi:10.1016/S0140-6736(10)60206-1).

Sugar in processed foods linked to poor lipid profiles

Adults in the USA eat a lot of sugar, much of it added to their food by manufacturers. New figures from national surveys suggest that added sugars comprise roughly one-sixth (15.8%, 95% CI 15.3 - 16.4) of an average adult's daily energy intake, possibly more given the well-known tendency for people to under-report their intake of unhealthy food. These are essentially wasted calories, with no

nutritional value other than energy. Weight gain is one obvious consequence. A cross-sectional analysis of the survey data suggests that foods containing added sugars are also associated with adverse lipid profiles and an increased risk of cardiovascular disease. The link was independent of body mass index and a score calculated from other factors, including age and sex, intake of fats, dieting, smoking, drinking habits, total energy intake, poverty, physical activity, and blood pressure.

The authors analysed data from 6 113 adults who took part in National Health and Nutrition Examination Surveys (NHANES) between 1999 and 2006. Serum concentrations of high-density lipoprotein (HDL) cholesterol decreased, and concentrations of triglycerides increased with increasing consumption of added sugars. The link was strongest for HDL cholesterol. Adults in the top fifth of added sugar consumption were 3 times more likely to have a pathologically low concentration than adults in the bottom fifth (odds ratio 3.1, 2.3 - 4.3). Concentrations of low-density lipoprotein cholesterol went up in line with sugar consumption in women, but not in men.

Welsh JA, *et al. JAMA* 2010; 303: 1490-1497.

WHO guidelines for treatment in areas of intense *P. falciparum* transmission inadequate

The authors of this study, published in the *British Medical Journal*, assessed the performance of WHO 'Guidelines for care at the first-referral level in developing countries' in an area of intense malaria transmission and identified bacterial infections in children with and without malaria.

They used a prospective study in a district hospital in Muheza, north-east Tanzania. The participants were children aged 2 months - 13 years admitted to hospital for febrile illness.

The authors looked at the sensitivity and specificity of the WHO guidelines in diagnosing invasive bacterial disease - susceptibility of isolated organisms to recommended antimicrobials.

Over 1 year 3 639 children were enrolled and 184 (5.1%) died; 2 195 (60.3%) were blood-slide positive for *Plasmodium falciparum*, 341 (9.4%) had invasive bacterial disease, and 142 (3.9%) were seropositive for HIV. The prevalence of invasive bacterial disease was lower in slide-positive children (100/2 195, 4.6%) than in slide-negative children (241/1 444, 16.7%). Non-typhi *Salmonella* was isolated in 52/100 slide-positive children

(52%) and in 108/241 slide-negative children (45%). Mortality among children with invasive bacterial disease was significantly higher (58/341, 17%) than in children without invasive bacterial disease (126/3 298, 3.8%), and this was true regardless of the presence of *P. falciparum* parasitaemia. The sensitivity and specificity of WHO criteria in identifying invasive bacterial disease in slide-positive children were 60.0% and 53.5% (51.4 - 55.6%) compared with

70.5% (68.2 - 72.9%) and 48.1% (45.6 - 50.7%) in slide-negative children. In children with WHO criteria for invasive bacterial disease, only 99/211 (47%) of isolated organisms were susceptible to the first recommended antimicrobial agent.

In an area exposed to high transmission of malaria, current WHO guidelines failed to identify almost one-third of children with invasive bacterial disease, and more

than half of the organisms isolated were not susceptible to currently recommended antimicrobials. Improved diagnosis and treatment of invasive bacterial disease are needed to reduce childhood mortality.

Nadjm B, *et al.* *BMJ* 2010; 340: c1350 (doi:10.1136/bmj.c1350).

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