



Bigger babies for women given antimalarial prophylaxis during pregnancy

Updated guidelines from the World Health Organization recommend boosting malaria prophylaxis for pregnant women in sub-Saharan Africa. The new policy could help increase average birthweights and reduce the number of babies born weighing less than 2 500 g, according to a meta-analysis of seven trials from the region.

In pooled analyses, women given 3 or more doses of sulfadoxine pyrimethamine in mid-to late pregnancy had babies that were 56 g (95% CI 29 - 83) heavier at birth than women given the standard 2 doses. They also had significantly fewer low-birthweight babies (134 v. 167/1 000; relative risk 0.8, 0.69 - 0.94; number needed to treat 31). Treatment with 3 or more doses was associated with a lower risk of both maternal malaria at delivery and placental malaria. Babies exposed to 3 or more doses had no more jaundice than those exposed to 2.

About a quarter of the women in these trials used bed nets treated with insecticide. The authors were surprised that an extra dose of sulfadoxine pyrimethamine made such a difference to outcomes. Women with and without HIV seemed to benefit, as did regions with a higher and lower prevalence of molecular resistance to the drug.

These findings add weight to the new guidelines, which recommend that eligible

women receive preventive treatment at every antenatal visit in the second and third trimesters.

Kayentao K, et al. *JAMA* 2013;309(6):594-604. [<http://dx.doi.org/10.1001/jama.2012.216231>]

Long-term outcomes of treatment for prostate cancer

Men who had a radical prostatectomy for localised prostate cancer reported worse urinary incontinence and worse sexual function 5 years later than similar men treated with external beam radiotherapy in a cohort study from the USA. Compared with radiotherapy, surgery was associated with double the odds of serious erectile dysfunction at 5 years (75.7% v. 71.9%; adjusted odds ratio 1.96, 95% CI 1.05 - 3.63) and 5 times higher odds of frequent urinary leakage or worse (13.4% v. 4.4%; 5.10, 2.29 - 11.36).

Survivors were still reporting worse urinary incontinence 15 years after prostatectomy, although by then the difference was not significant (18.3% v. 9.4%; 2.34, 0.88 - 6.23). Erectile dysfunction was almost universal among men who survived for 15 years after either treatment (87% v. 93.9%).

Prostatectomy was associated with a lower odds of bowel urgency than radiotherapy 5 years after treatment (16.3% v. 31.3%; 0.47, 0.26 - 0.84), but the difference was no longer significant after 15 years (21.9% v. 35.8%; 0.98, 0.45 - 2.14).

The authors tracked a selected cohort of 1 655 men treated for localised prostate cancer in the mid-1990s, when they were 55 - 74 years of age. Most (1 164) had surgery. Comparisons between prostatectomy and radiotherapy were adjusted extensively in an attempt to compare similar men who simply had different treatments. A quarter of those who had surgery (322/1 164; 27.7%) and a half of those who had radiotherapy (247/491; 50.3%) died during the long follow-up.

Resnick NJ, et al. *N Engl J Med* 2013;368:436-445. [<http://dx.doi.org/10.1056/NEJMoa1209978>]

Reduction in preterm birth – a public health benefit of smoking restriction

We know that smoking during pregnancy affects fetal growth and raises the incidence of preterm birth – and that second-hand

smoke also affects birth outcomes. The authors of this study published recently in the *British Medical Journal* investigated the incidence of preterm delivery in the Belgian population after the three-phase implementation of smoke-free legislation between January 2006 and January 2010.

They found reductions in the risk of preterm birth after the introduction of each phase of the smoking ban. No decreasing trend was evident in the years or months before the bans. We observed a step change in the risk of spontaneous preterm delivery of -3.13% (95% CI -4.37% to -1.87%; $p < 0.01$) on 1 January 2007 (ban on smoking in restaurants), and an annual slope change of -2.65% (-5.11% to -0.13%; $p = 0.04$) after 1 January 2010 (ban on smoking in bars serving food). The analysis for all births gave similar results: a step change of -3.18% (-5.38% to -0.94%; $p < 0.01$) on 1 January 2007, and an annual slope change of -3.50% (-6.35% to -0.57%; $p = 0.02$) after 1 January 2010. These changes could not be explained by personal factors (infant sex, maternal age, parity, socio-economic status, national origin, level of urbanisation); time-related factors (underlying trends, month of the year, day of the week); or population-related factors (public holidays, influenza epidemics, and short-term changes in apparent temperature and particulate air pollution).



The study shows a consistent pattern of reduction in the risk of preterm delivery with successive population interventions to restrict smoking. This finding is not definitive but it supports the notion that smoking bans have public health benefits from early life.

Cox B, et al. *BMJ* 2013;346. [<http://dx.doi.org/10.1136/bmj.f441>]

The end for PUFAs?

We have had 50 years of advice to substitute vegetable oils rich in polyunsaturated fatty acids (PUFAs) for animal fats, rich in saturated fatty acids (SFAs). The advice originated in the 1960s, when PUFAs were thought to be a uniform molecular category with one relevant biological mechanism – reduction in blood cholesterol. The best-known PUFA at the time was omega 6 (n-6) linoleic acid (LA), and PUFA and LA were often used interchangeably when reporting clinical trial results and giving advice on diet. However, we now recognise that there are several different categories of PUFA – each with unique biochemical properties and possibly different cardiovascular effects.

The authors of this paper evaluated the effectiveness of replacing dietary SFA with omega 6 linoleic acid for the secondary prevention of coronary heart disease and death. They used recovered data from the Sydney Diet Heart Study, a single blinded, parallel group, randomised controlled trial conducted between 1966 and 1973. They also did an updated meta-analysis including these previously missing data. The participants were 458 men aged 30 - 59 with a recent coronary event.

The intervention was replacement of dietary saturated fats (from animal fats, common

margarines and shortenings) with omega 6 linoleic acid (from safflower oil and safflower oil polyunsaturated margarine). Controls did not get any specific instruction on diet or study foods. All non-dietary aspects were designed to be equivalent in both groups. Outcomes were all-cause mortality (primary outcome), cardiovascular mortality and mortality from coronary heart disease (secondary outcomes).

The intervention group ($n=221$) had higher rates of death than controls ($n=237$) (all-cause 17.6% v. 11.8%, hazard ratio 1.62 (95% confidence interval 1.00 - 2.64), $p=0.05$; cardiovascular disease 17.2% v. 11.0%, 1.70 (1.03 - 2.80), $p=0.04$; coronary heart disease 16.3% v. 10.1%, 1.74 (1.04 - 2.92), $p=0.04$). Inclusion of these recovered data in an updated meta-analysis of linoleic acid intervention trials showed non-significant trends toward increased risks of death from coronary heart disease (hazard ratio 1.33 (0.99 - 1.79); $p=0.06$) and cardiovascular disease (1.27 (0.98 - 1.65); $p=0.07$).

Advice to substitute polyunsaturated fats for saturated fats is a key component of worldwide dietary guidelines for coronary heart disease risk reduction. However, clinical benefits of the most abundant polyunsaturated fatty acid, omega 6 linoleic acid, have not been established. In this

cohort, substituting dietary linoleic acid in place of saturated fats increased the rates of death from all causes, coronary heart disease and cardiovascular disease. An updated meta-analysis of linoleic acid intervention trials showed no evidence of cardiovascular benefit. These findings could have important implications for worldwide dietary advice to substitute omega 6 linoleic acid, or polyunsaturated fats in general, for saturated fats.

Ramsden CE, et al. *BMJ* 2013;346. [<http://dx.doi.org/10.1136/bmj.e8707>]

