

# SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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## Human rights treaties have no measurable impact on health

Many international treaties on human rights include statements on citizens' rights to health. In theory, countries that ratify these treaties should have healthier populations than those that don't, but it's hard to find a measurable difference. In one analysis of 170 countries, ratification of six treaties with a health element was not associated with any consistent improvement in health indicators such as infant and maternal mortality, prevalence of HIV, or life expectancy.

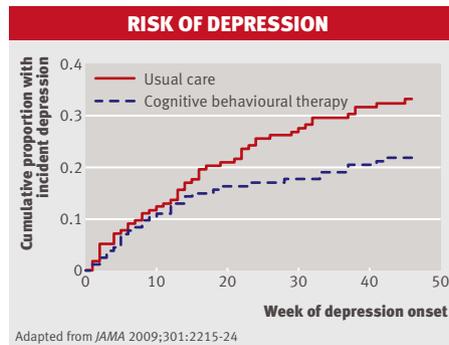
The authors did a cross sectional analysis then a before and after analysis, adjusting for important confounders. All they found was a significant and well known association between wealth and health. Overall, 65% of the countries (111/170) ratified all six treaties. Wealthy countries were no more likely to ratify all six treaties than were less wealthy countries.

The data came from widely available international sources including the World Health Organization, the United Nations, and non-governmental organisations specialising in civil liberties and human rights. Neither the cross sectional nor the before and after analysis had a complete set of data, so it's possible that significant associations were missed. The authors think a more likely explanation is that ratifying human rights treaties doesn't necessarily improve a nation's health—not because the treaties don't matter, but because they don't work without external monitoring, accountability, and a legal system with the funds and freedom to challenge the state.

*Lancet* 2009;373:1987-92

## Cognitive behavioural therapy helps prevent depression in teens at risk

Teenagers with depressed parents are more likely to become depressed themselves; however, emerging evidence indicates that cognitive behavioural therapy can reduce the risk. Researchers recently tested the effect of eight weekly sessions of group cognitive behavioural therapy followed by six monthly sessions in 316 teenagers aged 13-17 years old. All had a parent with current or past depression and had mild symptoms or a past history of depression themselves. Cognitive behavioural therapy



was better than usual care at preventing new episodes of depression over nine months of follow-up (21.4% v 32.7%; hazard ratio 0.63, 95% confidence interval 0.40 to 0.98) and helped reduce self reported symptoms. Therapy worked better in teens whose parents were not currently depressed than in those with a depressed parent (11.7% v 40.5%; 0.24, 0.11 to 0.50).

More than four fifths of the teenage participants had a history of depression, so therapy essentially helped prevent recurrences rather than new diagnoses, say the authors. They estimate that cognitive behavioural therapy would prevent one teenager out of every nine treated from developing a new episode of depression. For comparison, the number needed to treat for antidepressants as treatment (not prevention) is around 10.

*JAMA* 2009;301:2215-24

## Most Swedish babies born alive before 27 weeks now survive to one year

In the three years between 2004 and 2007, 1011 extremely premature babies were born in Sweden. Just under a third were stillborn (304/1011), but 70% (497/707) of the rest reached their first birthday, according to a national prospective study of all babies born before 27 weeks' gestation.

Survival to 1 year was dependent on gestational age and ranged from 9.8% (51/55; 95% confidence interval 4% to 23%) in babies born alive at 22 weeks to 85% (176/206; 81% to 90%) in babies born alive at 26 weeks. Use of tocolytics, antenatal steroids, and surfactants was common and all were associated with a higher chance of survival for babies who were alive at birth. Birth at a regional hospital

was also positively associated with survival. Serious morbidity was common among survivors: one third (169/493) had retinopathy of prematurity; a quarter (113/452) had severe bronchopulmonary dysplasia; and one in 10 (50/493) had an intraventricular haemorrhage of grade 3 severity or worse. Even so, almost half the live born babies (45%) reached 1 year old without any serious complications.

These figures are the best yet, says an accompanying editorial (pp 2270-1), and show what can be achieved in a country where citizens enjoy universal health insurance, free care in pregnancy, and technologically advanced, centralised perinatal services.

*JAMA* 2009;301:2225-33

## A break from hormone therapy does not reduce recall rates after mammography

Hormone therapy increases the density of breast tissue and can interfere with the accuracy of mammography for breast cancer screening. So should women take a break from hormone therapy before screening? A randomised trial suggests that this approach makes little difference to recall rates, which the authors used as a pragmatic proxy for the accuracy of screening. Very few recalled women ultimately have breast cancer.

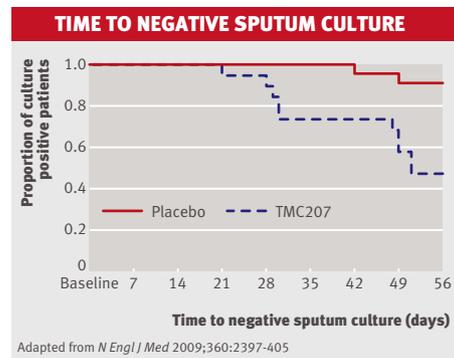
Women who took a one month or two month break from hormone therapy had small reductions in breast density, but were no less likely to be recalled after a screening mammogram than controls who continued hormone therapy (50/478 (12.3%) v 44/451 (9.8%) v 61/542 (11.3%) for one month break, two month break, and no break, respectively). The women who stopped hormone therapy experienced a significant upsurge in menopausal symptoms including hot flushes, disturbed sleep, night sweats, and mood swings.

The women were members of a single integrated health plan in the US and in general they were reluctant to give up hormone therapy, even for a short time. The researchers approached 5861 potentially eligible women aged 45-80 years old and managed to recruit just 1704. Yet more women dropped out when they were assigned a break from therapy for one (90/570 (15.8%)) or two (114/567 (20.1%)) months.

Despite the problems, the authors think their findings are reasonably secure. They don't support the practice of encouraging women to stop taking hormones before a mammogram. *Ann Intern Med* 2009;150:752-65

### New agent is potentially active against multidrug resistant tuberculosis

Drug manufacturers looking for new ways to fight drug resistant tuberculosis have devel-



oped TMC207, an agent that inhibits mycobacterial ATP synthetase. Early trials in 47 South African adults suggest the new drug might be clinically effective when added to standard second line treatments for multidrug resistant tuberculosis. Patients given TMC207 for eight weeks had infection free sputum significantly sooner than those on placebo, and more had negative sputum cultures by the end of the trial (10/21 (48%) v 2/23 (9%)). Nausea was more common in the TMC207 group than the placebo group (6/23 (26%) v 1/24 (4%)).

An accompanying editorial says these results are encouraging and validate ATP synthetase as a new target for drugs against tuberculosis (pp 2466-7). Evaluation is still at an early stage but at last there is a "refreshing sense of forward movement" in a clinical area that until recently was stuck with a few relatively ineffective and toxic treatment options. Problems with TMC207 that must be ironed out include the long term safety of the agent, a potential interaction with rifampicin, and its unusually long half life.

*N Engl J Med* 2009;360:2397-405

### Gardasil is partially effective in a mixed population of older women

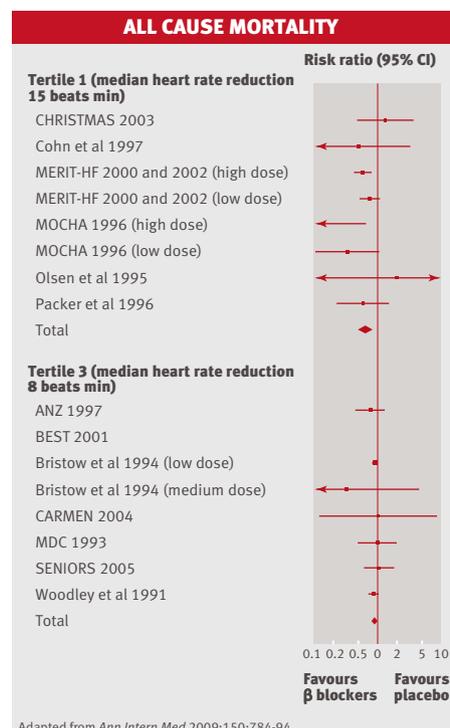
Merck's quadrivalent vaccine Gardasil reduced the risk of human papillomavirus infection among women aged 24-45 years old in a placebo controlled trial. The vaccine worked best in women who had never been infected with any relevant human papillomavirus

subtype. The trial included 3819 women aged 24-45 years old who had no history of cervical or genital disease caused by human papillomavirus. In an analysis that included the whole trial population, the vaccine had an efficacy of 30.9% (95% confidence interval 11.1% to 46.5%). In other words, there were 30.9% fewer primary outcomes among women randomised to receive the vaccine than among those on placebo. Efficacy reached 90.5% (73.7% to 97.5%) in an analysis confined to the 3222 women with no evidence of past or present human papillomavirus infection at baseline and who received all three vaccine doses. The authors used a primary outcome that combined persistent human papillomavirus infection with cervical or genital lesions caused by the virus. Most of the assessed outcomes were infections, since the trial lasted only two years and intraepithelial lesions and cancers take longer than two years to develop.

We already know that Gardasil works for teenagers who are not already infected with human papillomavirus. The same vaccine offers some protection to older women, but not as much, say the authors. Longer follow-up and cost-benefit analyses are planned. *Lancet* 2009; doi:10.1016/S0140-6736(09)60691-7

### Fall in heart rate looks more important than dose of beta blocker in heart failure

A new meta-analysis suggests that the benefits of beta blockers in people with heart failure depend not on dose, but on how much a



patient's heart rate falls during treatment. The authors analysed aggregate data from 23 placebo controlled trials and found a significant 18% reduction in mortality (95% confidence interval 6% to 29%) for every 5 beat reduction in heart rate. This mortality benefit seemed unaffected by dose or by absolute heart rate achieved during treatment. Overall, beta blockers reduced the risk of mortality by 24% (risk ratio 0.76, 0.68 to 0.84), and the evidence of benefit was strongest for metoprolol, carvedilol, and bisoprolol. Most of the 19209 participants in these trials had left ventricular systolic dysfunction: 22 of the 23 trials reported mean left ventricular ejection fractions below 0.3.

The authors were unable to calculate a "best" heart rate reduction from the data, and suggest that trials comparing different target reductions would be valuable. Most of the trials in this analysis were done before widespread use of cardiac resynchronisation therapy or implantable cardioverter defibrillators. Almost all the participants were also taking angiotensin converting enzyme inhibitors. *Ann Intern Med* 2009;150:784-94

### Rotavirus vaccine is less effective in Nicaragua

Oral vaccines against rotaviruses have been shown to work in middle and high income countries but it's still unclear how well they protect infants in the developing world, where most deaths from rotavirus diarrhoea occur. Trials are under way in Asia and Africa and will be reported soon. In the meantime, researchers looked for evidence of efficacy from a case-control study in Nicaragua, where an oral pentavalent vaccine (RV5) has been part of the childhood immunisation schedule since 2006.

The benefits were detectable but modest. The 285 cases of confirmed rotavirus diarrhoea were less likely to have been fully vaccinated than the 1530 matched controls. The researchers estimate that vaccination was 46% effective at preventing confirmed rotavirus infections needing hospital admission or intravenous rehydration (odds ratio 0.54, 95% confidence interval, 0.36 to 0.82). It was best at preventing severe (0.42, 0.26 to 0.70) and very severe (0.23, 0.08 to 0.61) disease. None of the cases died.

This vaccine seems less effective in Nicaragua than it was in trials in Finland and the US, say the researchers, possibly because most of the children in Nicaragua were infected with a relatively uncommon strain of the virus.

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