Probiotics prevent *C. difficile* diarrhoea in people taking antibiotics

Diarrhoea associated with *Clostridium difficile* is a potentially fatal complication of antibiotic treatment, particularly in older people. Probiotics are an effective prophylactic, according to the latest meta-analysis of clinical trials. In pooled analyses, patients given probiotics were 66% less likely to develop *C. difficile* diarrhoea than were controls given a placebo or no treatment (relative risk 0.34, 95% CI 0.24 to 0.49).

The new meta-analysis updates previous reviews with the inclusion of six extra trials, adding power and precision to previous estimates. The 20 trials had problems with missing data, but results were consistent. The authors say we can be at least moderately confident that probiotics work and prevent an estimated 33 (25 to 38) episodes of *C. difficile* diarrhoea for every 1000 people treated. We can also be moderately confident that they are safe. Controls had significantly more adverse events than patients given probiotics in a pooled analysis of the 17 trials that reported harms.

Most trials tested probiotics in adults who were taking a variety of antibiotics for acute infections. Probiotic preparations included *Bifidobacterium, Lactobacillus, Saccharomyces,* and *Streptococcus* spp, alone or in combination. Patients in intervention groups took probiotics for the duration of their antibiotic treatment and for up to two weeks longer. *Ann Intern Med* 2012; published online 13 November

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**Ten valent vaccine prevents most invasive pneumococcal disease**

GlaxoSmithKline have confirmed that their 10 valent pneumococcal vaccine prevents invasive disease in vaccinated infants. The vaccine was licensed in 2009, on the basis that it generated a good immune response. A new trial from Finland shows that it also prevents 92-100% of invasive pneumococcal disease when given alongside routine infant vaccinations.

The company tested two or three primary doses followed by a booster. Both schedules worked well, but the trial wasn’t designed or powered to compare the two directly. Control children received hepatitis vaccines. Just 16 cases of invasive disease were reported in 30 528 infants who were enrolled before 7 months of age. Fourteen cases had received control vaccines. No infants died.

Pneumococcal vaccines are already offered to infants in 88 countries, says a linked comment (doi:10.1016/S0140-6736(12)61957-6). The new trial adds more clinical data from Europe and also fills a gap in the evidence on the less intensive schedule. Two primary doses followed by a booster (2+1) prevented 92% (95% CI 58% to 100%) of invasive pneumococcal disease in this trial, and this result strengthens the World Health Organization’s recent endorsement of the lighter schedule.

GlaxoSmithKline’s vaccine contains polysaccharides from 10 pneumococcal serotypes conjugated to three carrier proteins (*Haemophilus influenzae* protein D, tetanus toxoid, and diphtheria toxoid). The authors report nine serious adverse events associated with study vaccines. They were equally distributed between children given the pneumococcal vaccine and controls.

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**Survival after cardiac arrest in hospital improves in the US**

Survival after cardiac arrest in hospital improved significantly between 2000 and 2009 in a study from the US. A large group of well motivated hospitals saw overall survival rise from 13.7% to 22.3% (P<0.001 for trend), while the prevalence of neurological disability in survivors fell from 32.9% to 28.1% (P=0.02).

The authors report significant improvements in survival for adults with asystole or ventricular fibrillation, for men and women, and for adults under and over 65 years.

The positive trends remained significant through extensive adjustments for changes in patient and hospital characteristics, including a shift in initial rhythm (proportion with asystole or pulseless electrical activity 68.7% in 2000 and 82.4% in 2009).

By 2009, more people were surviving their initial arrest, and more of those survivors were making it home. The authors suspect that improvements in care before, during, and after an arrest are responsible and call for further work to find out. They analysed data from a register of cardiac arrests that did not record response times, quality of resuscitation techniques, or specific treatments such as hypothermia.

In all, 374 hospitals across the US contributed data to the register, which was set up as part of a quality improvement initiative. These findings may not extend to hospitals outside the network or to patients who arrest in emergency departments, procedure suites, and operating theatres, say the authors. All 86 625 adults in this study had their cardiac arrest on wards and intensive care units.


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**Mental health deteriorates in economically successful Taiwan**

Taiwan’s economy has grown rapidly since the early 1990s, and this has been accompanied by profound social change. The country is richer, but is it any happier? Researchers have been surveying the adult population every five years since 1983. They added a screening tool for common mental disorders in 1990, when a representative sample reported a prevalence...
of 11.5% (95% CI 10.2% to 12.8%). By 2010, prevalence of common mental disorders had more than doubled to 23.8% (21.9% to 25.7%). The increase wasn’t explained by shifts in demographic or social variables, but rates of divorce, suicide, and unemployment all rose during the same period.

Other countries can learn from Taiwan’s experience, says a linked comment (doi:10.1016/S0140-6736(12)61602-X). Taiwan is an economic and political success story. But the transformation has not helped the population feel happier or worry less, just the opposite. Widen ing inequality and job insecurity have probably contributed to these trends.

We know that gross national product is a crude indicator of progress, but it dominates political thinking and discourse around the world. Governments have rich economic data at their disposal but poor data tracking the impact of their policies on population health, says the comment. These few Taiwanese surveys are the best available data in Asia. They show us why we need a much more holistic approach to progress, which can measure health and well-being as well as economic productivity. Credible measures are already available, and we should encourage politicians to use them.

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Increased incidence of hip fracture after first prescription for antihypertensive drugs

Just over 300 000 older adults started drug treatments for hypertension in Ontario, Canada, between 2000 and 2009. Researchers identified 1463 hip fractures in the same cohort during the same period. They also identified a significantly increased risk of fracture in the 45 days immediately after a first prescription (incidence rate ratio 1.43, 95% CI 1.19 to 1.72). Angiotensin converting enzyme inhibitors, β blockers, and thiazide diuretics were the three most prevalent treatments, followed by calcium channel blockers and angiotensin receptor blockers. Researchers combined all drug classes for their main analyses, which compared fracture incidence in the 45 days immediately after the start of treatment with control periods both before and after the first 45 days of treatment. Individuals acted as their own controls. Mean age at hip fracture was 80.8 years. Most fractures occurred in women (80.7%).

Other researchers have already reported a higher risk of falls after drug treatments for hypertension, say the authors. So an association with hip fractures isn’t unexpected. Nine out of 10 hip fractures are preceded by falls, and orthostatic hypotension caused by antihypertensive drugs is a plausible culprit for both. Doctors should be aware of the possibility of early falls and fractures in older people who start taking these drugs, say the authors, and they should exercise caution until we know more.

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Job losses linked to myocardial infarction in US cohort

Unemployment has often been linked to poor mental and physical health, and the latest study reports a significant association between a disrupted employment history and risk of myocardial infarction in middle aged US adults. Risk rose steadily as the number of job losses accumulated, so that adults who had lost at least four jobs were 63% more likely to report a new myocardial infarction during eight years of follow-up than adults who had lost none (hazard ratio 1.63, 95% CI 1.29 to 2.07). Risk was particularly high in the first year of unemployment in analyses adjusted for more than a dozen social, demographic, and clinical variables including symptoms of depression.

The new study analysed data from more than 13 000 adults, who were interviewed every two years between 1994 and 2010. It adds power and a dose response dimension to previous analyses, says a linked comment (doi:10.1001/jama.2013.1835). The study also looked at myocardial infarctions occurring after job losses, to help rule out reverse causation. The evidence linking unemployment and poor health is now compelling, and it may be time to stop looking for associations and start exploring why this happens, says the comment. If losing a job or losing multiple jobs causes poor health (and it probably does), then what are the mechanisms and can we do anything to modify them? We don’t yet know, although there are many theories. Poverty, social withdrawal, risky behaviours such as smoking, raised cortisol concentrations, and chronic anxiety are all possible contributors.

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Reviewers question the use of antibiotics for uncomplicated diverticulitis

Antibiotics are a standard treatment for uncomplicated diverticulitis, recommended by guidelines. A careful search for supporting evidence found just three randomised trials. Only one—the best and most recent—compared antibiotics with no antibiotics in a big sample of adults. The antibiotics made no difference to complications, length of stay, need for surgery, or recurrence. Two smaller trials compared different drugs or different durations of treatment, and they found no clinically useful differences between treatment groups.

Uncomplicated diverticulitis is common, say the authors. Patients are given antibiotics because of presumed infection with *Escherichia coli* and other microbes. Doctors hope treatment will prevent progression to something more serious, such as abscess formation, perforation, or fistulas. They hope to stop the condition bouncing back, which it often does. This preliminary review isn’t conclusive enough to change well established practice, but it does suggest that antibiotics may not work as well as we think they should.

High quality trials are now needed to find out whether antibiotics are really necessary for these patients, say the authors. Antibiotics can cause life threatening superinfection with *Clostridium difficile*, and unnecessary use fuels the spread of antibiotic resistance through populations. One more trial is currently under way and due to report in 2014.

Cochrane Database Syst Rev 2012;11:CD009092
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