SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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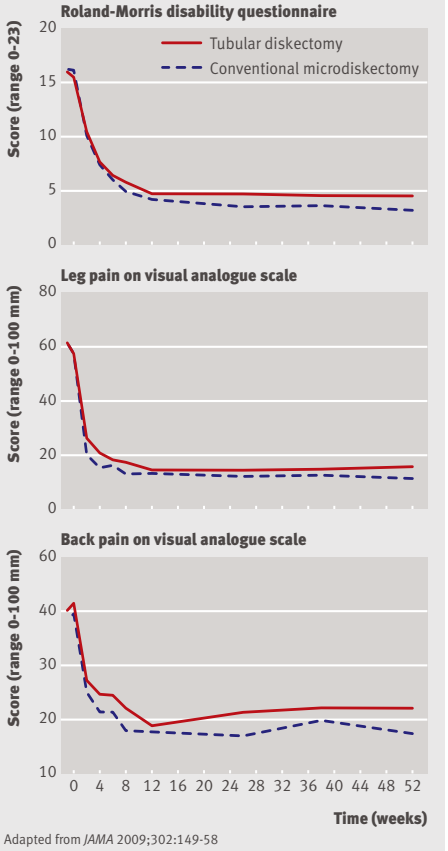
Surgical refinements to microdiscectomy make little difference to patients

In 1997, surgeons refined traditional microdiscectomy to reduce tissue damage during surgery and potentially speed recovery. Initial trials looked promising, but the latest and largest shows that tubular discectomy may be associated with worse, not better, outcomes after a year. Three hundred and twenty eight adults with persistent leg pain from a herniated disc had a traditional microdiscectomy or a tubular discectomy. Both groups made a good recovery in the first two weeks. By the end of one year, those who had had a tubular discectomy reported slightly but significantly worse functional recovery, and slightly but significantly more back pain and leg pain than controls. The patients did not know which group they were in, nor did the researchers assessing outcomes.

OUTCOMES OVER TIME



Adapted from *JAMA* 2009;302:149-58

The authors say the differences they found were too small to be clinically important, and that neither technique is conclusively better than the other. Both operations were associated with comparable rates of complications and recurrence. Tubular discectomy took 11 minutes longer (47 *v* 36 minutes; P<0.001), possibly because surgeons have to dilate a small working channel through the muscle. During traditional microdiscectomy the muscle is simply retracted.

JAMA 2009;302:149-58

Cervarix protects against high grade cervical lesions

Human papillomavirus (HPV) types 16 and 18 cause around 70% of cervical cancers worldwide, and GlaxoSmithKline's bivalent vaccine against both types is already being given to teenage girls in several countries. Final analyses from the company's large efficacy trial suggest that Cervarix prevents 70.2% (96.1% CI 54.7% to 80.9%) of high grade cervical intraepithelial neoplasia (CIN grade 2 or worse) lesions in young women who have no evidence of current or past infection when vaccinated. They analysed around 9000 participants aged 15-25. All had at least one dose of Cervarix or a control hepatitis A vaccine, and they were meant to represent the target population for primary vaccination—teenage girls who haven't yet had sex.

So called "catch-up" vaccination programmes are also a possibility, so the authors did further analyses in a broader population that included sexually active women, one quarter of whom had already been infected with HPV. Cervarix prevented 30.4% (16.4% to 42.1%) of CIN 2 or worse lesions during a follow-up of nearly three years.

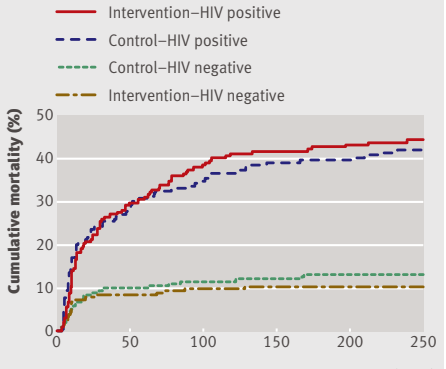
The authors estimate that their vaccine also prevents between 37% and 54% of high grade cervical lesions caused by HPV types other than 16 or 18.

All well and good, says a linked comment (doi:10.1016/S0140-6736(09)61247-2), but these lethal viruses will never be eradicated until we also vaccinate boys and men.

Lancet 2009; doi:10.1016/S0140-6736(09)61248-4

Severely malnourished African children need more than probiotics

DEATHS BY TREATMENT GROUP AND HIV STATUS



Adapted from *Lancet* 2009;374:136-44

Between 13 million and 19 million children worldwide are acutely and severely malnourished. High calorie therapeutic foods are part of the treatment, and researchers recently tested the value of adding prebiotic elements and probiotic bacteria to standard therapeutic food for children admitted to one hospital in Malawi. It didn't work. The children given enriched therapeutic food were no more likely to reach weight for height targets than controls (53.9%, (215/399) *v* 51.3% (203/396); relative risk 1.06, 95% CI 0.93 to 1.21). They were no more likely to survive either—more than a quarter of all the children died during the study (27.1% (108/399) *v* 30.0% (119/396); 0.90, 0.72 to 1.12).

These children were extremely sick when admitted. Almost half had HIV. Few received life saving antiretroviral drugs because of a waiting list, although they did get prophylactic co-trimoxazole. Perhaps we shouldn't be surprised that they did worse than children in other trials of treatments for acute severe malnutrition, says a linked comment (p 94). Clearly, adding prebiotics and probiotics to therapeutic food doesn't save lives in countries where weak public health policy and inadequate governance deny many malnourished children timely access to treatments for pneumonia, malaria, diarrhoea, and HIV as well as food. International agencies should focus on these basic failings first.

Lancet 2009;374:136-44

Changes to abortion protocols in the US linked to dramatic fall in infections

Changes to medical abortion protocols in the US were associated with a 93% fall in serious infections, according to a before and after study of abortions carried out in planned parenthood health centres across the country. Between March 2006 and July 2007, 78 centres made a series of changes starting with a switch from vaginal to buccal misoprostol, and ending with a mandatory regimen of oral doxycycline for all women. The rate of serious infections after a medical abortion fell from 0.93 per 1000 abortions before the changes to 0.06 per 1000 abortions in the first six months of 2008. The authors defined serious infections as fever and pelvic pain requiring intravenous antibiotics, or an inpatient episode with documented sepsis or death. During the whole study period 227 823 women had a medical abortion in one of the participating centres. Ninety two had a serious infection and one died—she developed *Clostridium perfringens* infection in early 2006 before any improvements were introduced.

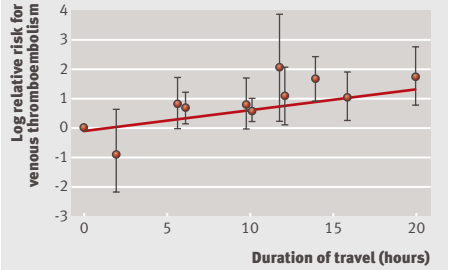
The authors think it unlikely that reporting of infections changed much during the study. They are fairly confident that the drop in infections was caused by the switch to buccal misoprostol and increased use of antibiotics. It is hard to know which had the bigger effect.

N Engl J Med 2009;361:145-51

New analysis supports stronger link between travel and VTE

We know that long distance travel is linked to an increased risk of venous thromboembolism (VTE). The size of the risk varies from study to study, however, so pooling estimates is difficult and potentially inaccurate. Researchers did a systematic review to look for and eliminate the source of the variation. It turned out to be a methodological problem with the case-control studies that dominate this field—studies with biased control samples reported lower risks than those with more representative control samples. An analysis confined to the "best" eight observational studies found that travel was associated with an almost threefold increase in risk of VTE, compared with no travel (relative risk 2.8, 95% CI 2.2 to 3.7). The selected analysis was not limited by heterogeneity, and the researchers think the resulting estimate is the most robust so far.

DURATION OF TRAVEL AND RISK OF VENOUS THROMBOEMBOLISM (FROM FOUR STUDIES)



Adapted from *Ann Intern Med* 2009;151;August 4

They used the same eight studies to look for a dose-response effect. Four studies reported risks according to duration of travel. In a pooled analysis, each extra two hours spent travelling was associated with an 18% (4% to 33%) increase in risk of venous thromboembolism. In the three studies confined to air travel, each extra two hours was associated with a 26% increase in risk (7% to 48%).

Ann Intern Med 2009;151 www.annals.org/cgi/content/full/0000605-200908040-00129v1

Angiotensin receptor blockade has little effect on renal function, again

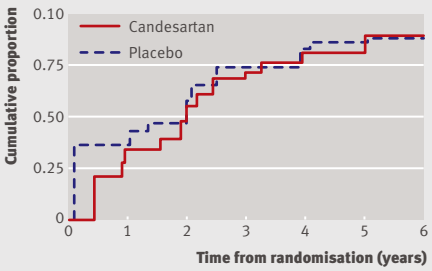
Further evidence has emerged that blocking the renin-angiotensin system doesn't necessarily protect renal function in people with diabetes or vascular disease.

Two analyses tested the renal effects of an angiotensin receptor blocker in different but complementary populations. In the first, pooled data from a trio of related placebo controlled trials showed that candesartan did not prevent new microalbuminuria in people with type 1 or type 2 diabetes. Most of the 5231 participants had normal blood pressure. All had normal albumin secretion at baseline.

In the second, telmisartan had no consistent effects on renal function in people with cardiovascular disease or diabetes. These 5926 participants also had good renal function at the start of the trial and only 10% had microalbuminuria. Telmisartan reduced the risk of new microalbuminuria, macroalbuminuria, or both (11.4% *v* 14.8%). But, more importantly, telmisartan did not prevent worsening renal function or dialysis (combined end point reached by 1.96% (58/2954) *v* 1.55% (46/2972) of patients; hazard ratio 1.29, 95% CI, 0.87 to 1.89). Microalbuminuria may be a poor marker for renal function in people with vascular disease, says an editorial (p 63).

Both analyses used data from trials that were not set up primarily to look at renal outcomes. Even so, they are an important contribution to an ongoing debate about

PROPORTION OF PATIENTS WITH MICROALBUMINURIA



Adapted from *Ann Intern Med* 2009;151:11-20

blockade of the renin-angiotensin system in people with normal but vulnerable kidneys, says the editorial. Good control of blood pressure, lipids, and serum glucose is probably more important than angiotensin receptor blockers for people with diabetes.

Ann Intern Med 2009;151:1-10, 11-20

Clozapine has a better risk benefit profile than other antipsychotic drugs

People with schizophrenia have a shorter life expectancy than the general population. Second generation antipsychotic drugs such as clozapine and olanzapine have been blamed for at least some of the difference, because of associated metabolic side effects, including weight gain. A large database study from Finland has overturned this prevailing wisdom by reporting that the mortality gap between people with schizophrenia and everyone else has not widened, despite a sharp increase in the use of second generation agents. They also say that clozapine looks like one of the safest antipsychotic drugs available.

In a cohort of nearly 67 000 people with schizophrenia, current use of clozapine was associated with a lower overall mortality, and a lower risk of suicide, than all other first or second generation agents (hazard ratio for death 0.74, 0.60 to 0.91 for clozapine *v* perphenazine; P<0.0001 for clozapine *v* all other antipsychotic drugs). Current use of quetiapine, risperidone, and haloperidol was associated with a significantly higher mortality than use of perphenazine. But long term treatment with any agent was associated with lower mortality than no treatment. The authors found no evidence of a link between any particular drug and death from heart disease, which surprised both the study's authors and the authors of a linked comment (doi:10.1016/S0140-6736(09)61072-2). The study was funded by the Ministry of Health for Finland.

Lancet 2009; doi:10.1016/S0140-6736(09)60742-X

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