

SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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"Try to put yourself in the position of a health worker trying to save the lives of hundreds of patients in an under-resourced clinic in Cambodia or India or Botswana"

Read Richard Lehman's journal blog at bmj.com/blogs

New analysis confirms the place of radiotherapy for women with early breast cancer

A new meta-analysis has confirmed that post-operative radiotherapy substantially reduces the risk of recurrence in women having breast conserving surgery for early stage breast cancer. The authors, who add new trials and longer follow-up to previous analyses, also confirmed that radiotherapy saves lives, reducing the risk of death from breast cancer from 25.2% to 21.4% over 15 years (absolute reduction 3.8%, 95% CI 1.6% to 6.0%).

The authors aimed to fine tune previous estimates and explore how well radiotherapy works for different groups of women. Absolute benefits were greatest for young women with high grade tumours. Radiotherapy also seemed to work better against tumours that were oestrogen receptor positive, and a linked editorial suggests that researchers should now evaluate whether intensifying radiotherapy can help

improve outcomes for women with oestrogen receptor negative disease (doi:10.1016/S0140-6736(11)61296-8).

Although the effects of radiotherapy on recurrences appeared quickly and were greatest in the first year after surgery, preventing deaths took half a decade and persisted for at least 15 years. Overall, radiotherapy saved one life for every four recurrences avoided.

Most of the women in these 17 trials had breast conserving surgery, usually a lumpectomy, for tumours that had not spread to local lymph nodes (7287/10801). Radiotherapy halved the risk of recurrence over 10 years in this large subgroup (15.6% v 31%; relative risk 0.49, 0.45 to 0.55) and cut deaths from breast cancer by one sixth over 15 years (17.2% v 20.5%; 0.83, 0.73 to 0.95). *Lancet* 2011; doi:10.1016/S0140-6736(11)61629-2

How and how often should women be screened for breast cancer?

There are still plenty of unanswered questions about mammography screening for breast cancer, including ongoing debates about how often women should be screened, and whether providers should be using old fashioned film or newer digital technology for mammograms. Two new observational studies from the US try to answer these questions using data from the same national surveillance consortium.

The first reports that women who have yearly mammograms for 10 years have more false alarms (61.3% have at least one, 95% CI 59.4% to 63.1%) than women screened every two years (41.6%, 40.6% to 42.5%). Women screened yearly also have more unnecessary biopsies (7.0%, 6.1% to 7.8% v 4.8%, 4.4% to 5.2%). Cancers detected by biennial screening were slightly more likely to be late stage than cancers detected by yearly screening. But the difference wasn't significant, and a linked editorial warns that proportions can be misleading (p 554). The weight of evidence remains very much against yearly mammography.

The choice between digital and film mammograms is less clear cut. In a cohort of more than 300 000 women, the two methods looked broadly comparable, except for non-significant hints that digital screening might be better (more sensitive) for women with extremely dense breasts and those with oestrogen receptor negative cancers. Digital mammography was significantly less specific than film in young women (88.0% v 89.7%; $P<0.001$)

and was associated with significantly more recalls.

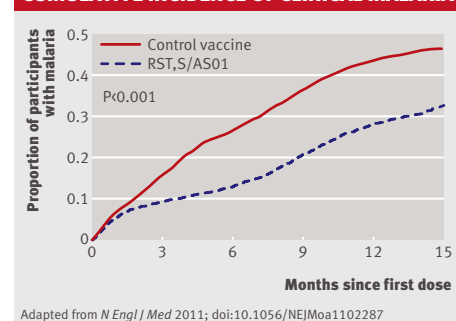
More than 70% of mammography machines in the US are already digital, an enthusiasm that was probably premature. The switch from film may well reduce the overall efficiency of breast cancer screening, says the editorial.

Ann Intern Med 2011;155:481-92

Ann Intern Med 2011;155:493-502

Finally, a vaccine against malaria

CUMULATIVE INCIDENCE OF CLINICAL MALARIA

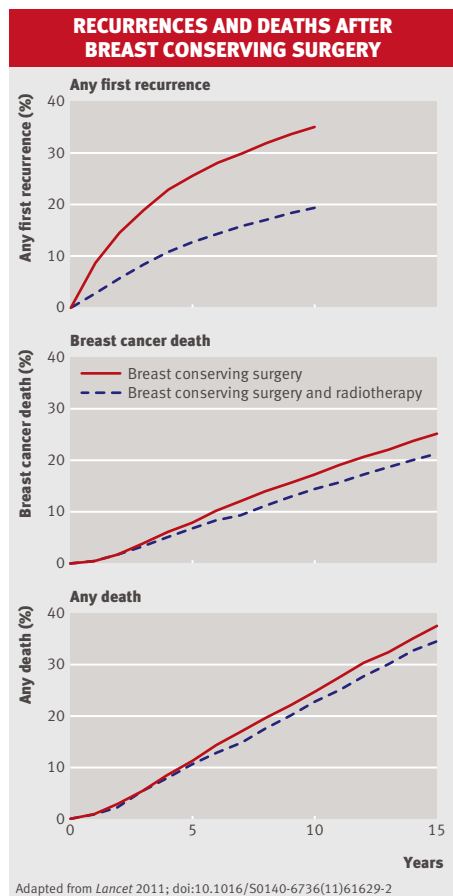


GlaxoSmithKline has developed a malaria vaccine directed against sporozoites, the parasitic stage injected into humans by feeding mosquitoes. Theirs isn't the only vaccine in the pipeline, but it is the first to reach phase III trials, and preliminary results look promising. RTS,S/AS01 was 50.4% (95% CI 45.8% to 54.6%) effective against falciparum malaria in 6000 African children aged 5-17 months. It was 45.1% (23.8% to 60.5%) effective against severe malaria.

The trial still has a long way to go, however. Researchers recruited close to 16 000 children in two age groups, and results for younger infants aged 6-12 weeks won't be available for at least another year. RTS,S/AS01 was 34.8% (16.2% to 49.2%) effective against severe malaria in an analysis combining available data from both age groups.

The older children in this report had three doses of RTS,S/AS01 over three months, with or without a booster 18 months later. Older controls received a rabies vaccine. Younger controls were vaccinated against meningococcal meningitis group C.

A malaria vaccine has been a long time coming, and we may finally be getting somewhere, says a linked editorial (doi:10.1056/nejme1111777). This vaccine looks reasonably effective so far, although results are too preliminary to inform



policy at this stage. Safety issues to watch out for in later reports include a higher risk of febrile reactions and seizures in children given the new vaccine, and a higher risk of meningitis, which is harder to explain (11/5949 v 1/2974 in older children; relative risk 5.5, 0.7 to 42.6).

N Engl J Med 2011; doi:10.1056/NEJMoa1102287

Encouraging families to move from poor neighbourhoods reduces obesity

Encouraging people to move out of poor neighbourhoods had a discernible effect on their risk of obesity and diabetes in a randomised social experiment from the US.

The experiment began in 1994 in public housing developments where more than 40% of families were living below the US government's poverty threshold. Just under 4500 women with young children agreed to take part, and roughly a third were given vouchers to subsidise their rent on the condition that they moved to a more affluent neighbourhood. Another third were given similar vouchers with no strings attached, and the final third (controls) received nothing.

Between 10 and 15 years later, 31.1% of the women encouraged to move had a body mass index of 35 or more compared with 35.5% of control women—a significant difference. Rent vouchers for more affluent neighbourhoods were also associated with a slightly but significantly lower prevalence of severe obesity (body mass index of at least 40), and diabetes (glycated haemoglobin of at least 6.5%). Women given the rent subsidy to use wherever they wanted also looked healthier than controls at the end of follow-up, but the differences were smaller and not statistically significant.

We know that being poor is a risk factor for obesity and diabetes. This novel social experiment suggests that the environment of poor neighbourhoods is probably part of the problem, and that giving families the opportunity to move out can help, say the authors. Roughly half of the families took advantage of the opportunity in this study.

N Engl J Med 2011;365:1509-19

Legal settlement details cash flow between industry and orthopaedic surgeons

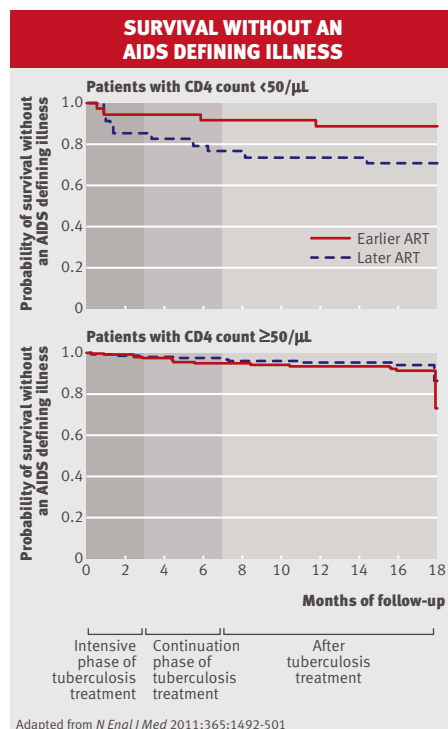
In 2007, the top five manufacturers of orthopaedic devices paid \$198m (£125m; €144m) to 939 US orthopaedic surgeons in consulting fees, research support, and royalties. The number of payments (but not the total value) fell in 2008, after a legal settlement that required manufacturers to disclose payments to the public and surgeons to disclose payments to their patients.

A close look at data released by the Department of Justice showed that the size of individual payments varied from a few thousand to several million dollars, but average payments represented roughly 25% of a typical surgeon's salary. Between a third and a half of the payments went to academically affiliated surgeons. Of the 43 payments worth more than \$1m made in 2008, 17 went to full professors at medical schools.

We don't have a particularly clear idea of what these payments were for because the word "consulting" is so poorly defined, says a linked comment (p 1765). We don't know whether the payments influenced surgeons' clinical decisions, or how much of the total was legitimate remuneration for services to research and development. But these kinds of disclosures must continue, because without them, we can't even begin to manage, minimise, and eventually eliminate the well known and serious biases associated with financial competing interests among doctors from all specialties.

Arch Intern Med 2011;171:1759-65

New trials help coordinate treatments for adults with HIV and tuberculosis



Adults with tuberculosis and HIV need complex treatment protocols for both diseases, and timing can be crucial. Starting antiretroviral therapy (ART) too early increases the risk of polypharmacy, drug interactions, side effects, and a serious complication called immune reconstitution inflammatory

syndrome. Delaying for too long increases the risk of HIV related illness and death.

Optimum timing seems to depend on the patient's CD4 cell count, according to the latest three trials. Adults with advanced immunosuppression—typically a CD4 count below 50/μL—did best when given antiretroviral drugs within two to four weeks from the start of their tuberculosis treatment, although the benefits were offset by a higher risk of immune reconstitution inflammatory syndrome. For everyone else, a later start looked safer, without compromising survival significantly. A later start meant no antiretroviral drugs for the first eight to 12 weeks of treatment for tuberculosis.

An editorial (p 1538) says that this new evidence is good enough to guide practice, but it warns that most of the patients in these studies had pulmonary tuberculosis. The optimal timing of treatment may be different for adults with tuberculosis at different sites, and particular caution is needed for those with tuberculous meningitis. Intracranial immune reconstitution inflammatory syndrome is often lethal.

N Engl J Med 2011;365:1471-81

N Engl J Med 2011;365:1482-91

N Engl J Med 2011;365:1492-501

Yoga and stretching both improve chronic low back pain

Yoga and stretching exercises are both effective treatments for chronic low back pain, and there was little to choose between them in the latest trial. Twelve weekly sessions of either form of exercise helped improve function more than a self help booklet, and the improvements—which were modest—seemed to endure for 26 weeks. Adults attending yoga classes also reported that they were less bothered by pain than self help controls after 12 weeks (1.07 points less on an 11 point scale, 95% CI 1.75 to 0.41). Yoga looked no more effective than stretching exercises for any outcome at any time in direct comparisons.

The 228 participants had a long history of chronic back pain when recruited, but they functioned reasonably well, with mild or moderate pain. Both physical treatments are reasonable options for adults with this profile, and the choice will depend on local availability of services, patient preference, and costs, say the researchers. Doctors referring to local classes need to check they are therapeutically orientated and run by well trained and experienced instructors. The yoga instructors in this trial followed the principles of viniyoga. Licensed physiotherapists took the stretching classes.

Arch Intern Med 2011; doi:10.1001/

archinternmed.2011.524

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