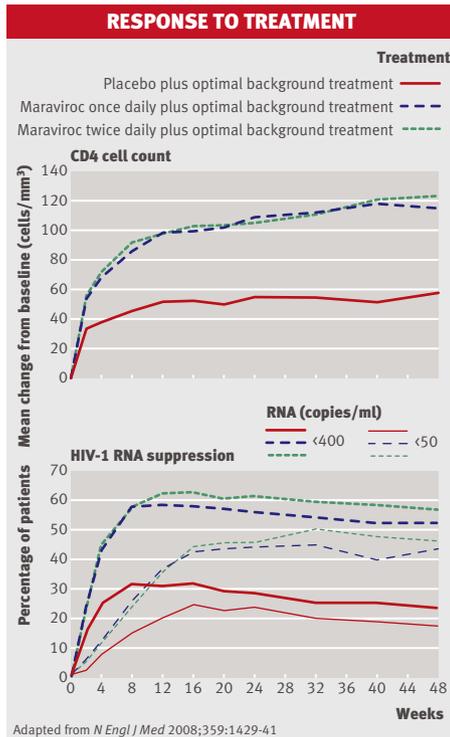


# SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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## New antiretroviral agent for patients with drug resistant HIV



Maraviroc is a new antiretroviral agent that prevents HIV from binding to CD4 cells. The phase III drug trials supporting maraviroc's approval by the US Food and Drug Administration have now been published and show that it suppresses viral replication significantly better than placebo in people with late stage disease. The 1049 participants in two identical trials had already been treated unsuccessfully with three other classes of antiretroviral or had developed resistance. All participants continued with the best available background therapy during the trial, which lasted 48 weeks. People who took maraviroc developed no more side effects than controls.

Maraviroc looks like an effective new weapon against HIV, although it is active against only one particular viral phenotype. Patients must be tested for the R5 type before they begin treatment, which adds logistical complications not shared by previous drug classes, says an editorial (p 1509). Since R5 viruses tend to predominate earlier rather than later in HIV infection, it might make sense to test the new agent at an early stage. Maraviroc blocks a host protein—a receptor

on CD4 cells—rather than attacking HIV directly. But the usual cautions about resistance still apply, says the editorial. More than a third of patients in both trials discontinued their maraviroc early. The most common reason was that it had stopped working.

*N Engl J Med* 2008;359:1429-41, 1442-55

## One reader or two for screening mammograms?

In general, two experts read mammograms more accurately than one, although new research suggests that a single reader armed with a computer aid can be an effective alternative. In a large trial from the UK, a single reader helped by a computer program detected as many breast cancers as two readers. Twenty eight thousand women were screened with both reading regimens. Double reading detected 199 of 227 cancers (87.7%). Single reading aided by computer detected 198 (87.2%). The two methods were statistically equivalent ( $P=0.89$ ).

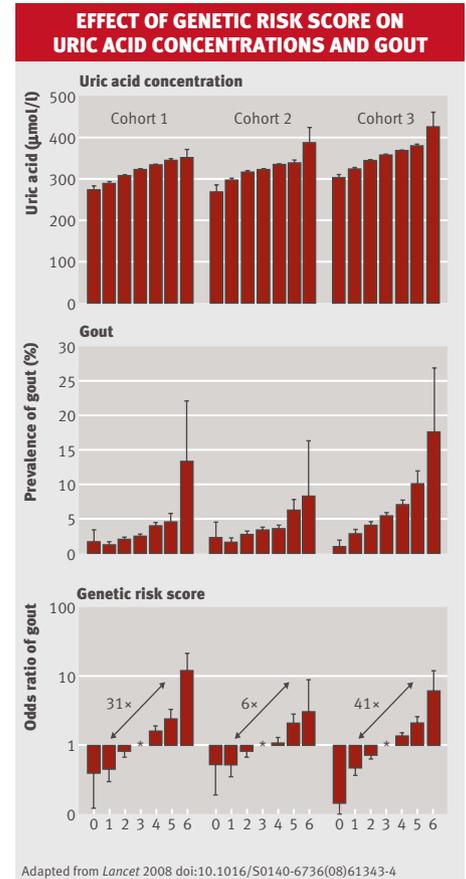
Single reading aided by computer led to slightly but significantly more recalls than double reading (3.9% (1100/28204) v 3.4% (947/28204); absolute difference 0.5%, 95% CI 0.3% to 0.8%), a result the authors say is in line with previous trials and at least one meta-analysis.

Many European countries already use two readers to screen mammograms for cancer. A single reader is the norm in the US, with or without a computer aid. The choice between two readers and one with a computer will in the end come down to cost effectiveness, say the authors. Computer aids are probably cheaper than an extra human reader, but any savings will be offset by the costs associated with recalling more women for further investigation.

*N Engl J Med* 2008;359:1675-84

## Two new genetic loci associated with gout

Researchers have discovered two new genetic loci associated with high serum concentrations of uric acid and gout. Both loci encode transporter proteins in the renal tubules, where exchange helps balance urate production with



excretion. The new genetic loci came out of a genome wide association study, which also confirmed the link between hyperuricaemia and mutations in a gene encoding a third renal transporter.

The researchers combined all three polymorphisms to compute a genetic risk score for gout that gave individuals a point for every risk allele they had (from 0 to 6). Concentrations of uric acid and risk of gout increased in line with scores in three separate cohorts—two from the US and one from Rotterdam in the Netherlands. The prevalence of gout was 1-2% in people with no risk alleles, and it rose to 8-18% in those with six.

These new discoveries should help us understand more about the role of renal transport in hyperuricaemia and gout, says an editorial (doi:10.1016/S0140-6736(08)61344-6). Current treatments such as allopurinol are effective but not perfect, and they seem to be operating a long way from the site of the problem. *Lancet* 2008; doi:10.1016/S0140-6736(08)61343-4

## Meta-analysis supports long term psychodynamic therapy for complex mental disorders

Patients with complex mental health problems, such as personality disorders and multiple comorbid disorders, may not respond well to brief forms of psychotherapy, and long term psychodynamic psychotherapy (LTPP) can be an appealing alternative. Hard evidence of effectiveness is hard to find, however, because standardisation is hard and workable placebos are lacking.

A meta-analysis has now found qualified evidence that LTPP works and is better than shorter treatments for some patients.

Analysis of improvements in target problems, general psychiatric symptoms, and personality and social functioning across 11 randomised controlled trials and 12 observational studies indicated that psychodynamic psychotherapy can have a large and positive effect. Only eight of the 23 studies compared one treatment with another. Pooled results again suggested that psychodynamic therapy could work better for people with complex mental illnesses than briefer alternatives, such as cognitive behavioural therapy or family therapy.

A linked editorial (p 1587) notes that despite relatively small numbers of patients (1053 treated with LTPP and 257 in comparison groups), the overall results support the effectiveness of LTPP at a time when psychiatrists in the US are turning away from long term psychoanalysis—probably because of cost pressures.

*JAMA* 2008;300:1551-65

## News media lag behind journals on reporting drug firms' sponsorship of studies

Medical journals have become increasingly interested in the role of drug company sponsors in research, a trend concurrent with wider concerns in the medical profession about the influence of the pharmaceutical industry. But this heightened scrutiny at the point of publication does not seem to have translated consistently into thorough reporting by the mainstream news media, as shown by an analysis of 306 news articles about drug trials.

The authors searched seven top US news websites and 45 US newspapers for all articles relating to sponsored drug trials that were published in five prominent general medical journals over the past four years.

Of the 306 identified news pieces, 130 (42%, 95% CI 37% to 48%) did not report the drug

company funding mentioned in the original research paper. Of a subgroup of 277 articles about drugs with brand and generic names, 186 (67%, 61% to 73%) used the brand name at least half of the time.

Newspaper editors seemed to be unaware of this issue. Of 93 US newspaper editors responding to a survey, 82 (88%, 80% to 94%) said their publication always or often mentioned drug company funding, and 71 of 92 (77%, 67% to 85%) said it always or often used generic names. Only 2% or 3% of newspapers had written policies on either, however.

*JAMA* 2008;300:1544-50

## Tiotropium fails to slow the decline in lung function in COPD

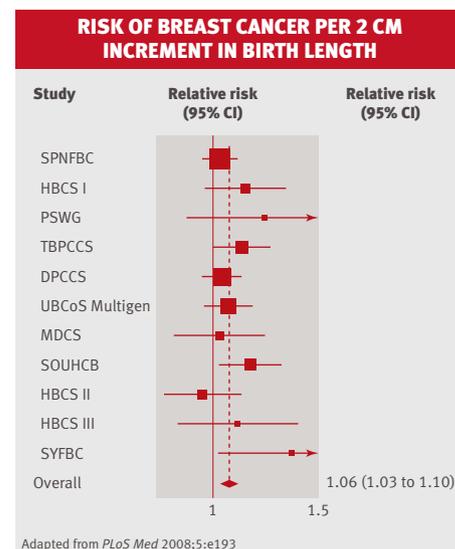
Researchers are still searching for a treatment to help slow the progression of chronic obstructive pulmonary disease (COPD) rather than simply alleviate symptoms. They had high hopes for tiotropium, but this short acting anticholinergic failed to slow the inexorable decline in lung function among participants in a recent large trial. People given tiotropium had significantly better lung function than controls given placebo throughout the four year trial, but both groups lost function at about the same rate—an average of 30 ml a year in forced expiratory volume in one second (FEV<sub>1</sub>) before bronchodilation and 41 ml a year in FEV<sub>1</sub> after bronchodilation.

Tiotropium once a day did not modify the course of the disease, and neither did it seem to save lives. Mortality was similar in both groups in the main analysis (14.9% v 16.5%; hazard ratio 0.89, 95% CI 0.79 to 1.02), although this result was complicated by the large number of patients who stopped their treatment early (36.2% of the tiotropium group and 44.6% of controls). All 5993 participants were allowed inhaled corticosteroids, long acting and short acting  $\beta$  agonists, and theophyllines as well as their study drugs. As expected, tiotropium was an effective symptomatic treatment that improved health related quality of life and helped prevent exacerbations. Participants treated with tiotropium had 14% fewer exacerbations.

The hunt for disease modifying treatment may have run aground because COPD is such a heterogeneous disease, says an editorial (doi:10.1056/NEJMe0807387). New efforts to define the characteristics of various subgroups will help and should continue, starting with the large amount of data now available from this trial.

*N Engl J Med* 2008;358:1543; doi:10.1056/NEJMoA0805800

## Birth size may be a risk factor for breast cancer



A comprehensive review of 32 cohort and case-control studies has found a modest but significant link between larger size at birth and an increased risk of breast cancer later in life. Experts have long suspected that larger babies might be more likely to develop breast cancer, and this new work “all but confirms it,” says a linked commentary (doi:10.1371/journal.pmed.0050194).

In a pooled analysis of studies with reliable birth records, the risk of breast cancer went up between 6% (95% CI 3% to 10%) and 9% (0% to 19%) for each 2 cm increase in birth length and by 6% (2% to 9%) for each 500 g increase in birth weight. Birth length was the strongest and most independent predictor of risk after the authors adjusted for other factors associated with breast cancer, including age at menarche, parity, adult height and weight, and social class.

If the association is causal—a fairly big if—then birth size affects the risk of breast cancer about as much as drinking alcohol does, say the authors. They estimate that up to 5% of all cancers in developed countries could be attributable to large birth size, particularly length over 50 cm. One possible explanation is that the hormonal environment in utero programmes the infant breast to be more or less susceptible to cancer. Maternal hormones, including oestrogen, are known to influence birth size.

*PLoS Med* 2008;5:e193. doi:10.1371/journal.pmed.0050193

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