

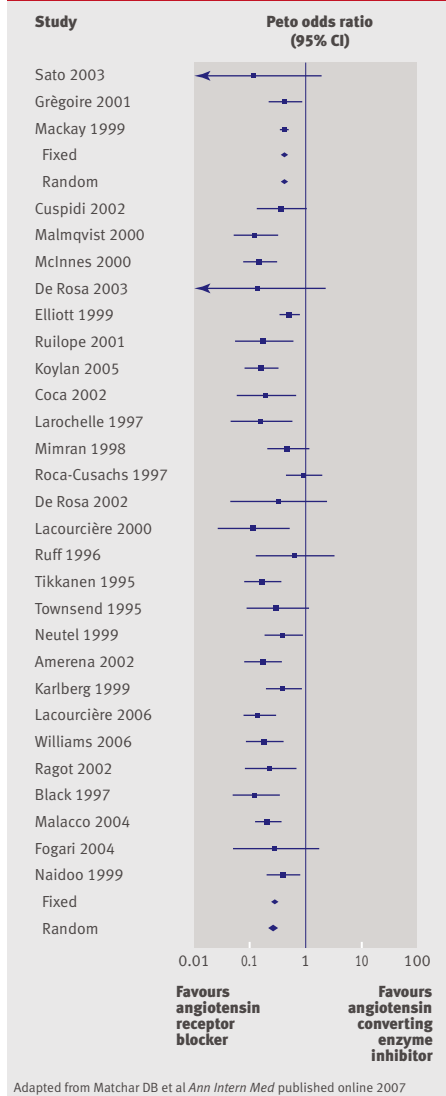
SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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ACE inhibitors and angiotensin II receptor blockers: little difference

EFFECT OF BOTH TREATMENTS ON COUGH



Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers are both popular and effective antihypertensive agents that work equally well for people with essential hypertension, according to a systematic review of 61 comparative studies. The evidence so far suggests the only difference between these drug classes is a higher risk of cough associated with angiotensin converting enzyme inhibitors (9.9% *v* 3.2% in a pooled analysis of 26 randomised trials). But as usual the evidence is full of holes.

Most studies lasted less than six months, and side effects were reported inconsistently, and data on outcomes that matter such as death, cardiovascular events, renal failure, and angio-oedema were too infrequent to be analysed reliably. The authors found no differences between the drug classes for any of these outcomes. But moderate differences may still exist, particularly for subgroups of patients—such as those with heart failure or diabetes—who were excluded from many studies. Only big expensive trials that go on for years not months will settle the matter either way.

Ann Intern Med 2007 www.annals.org/cgi/content/full/0000605-200801010-00191v1

Rosuvastatin doesn't work for older people with ischaemic heart failure

Statins prevent cardiovascular events, including deaths in patients with coronary artery disease. Intuitively, they should do the same for people with heart failure caused by the same disease. But rosuvastatin recently surprised researchers by failing to work in a large placebo controlled trial.

The 5011 participants were all over 60 with moderate or severe heart failure caused by ischaemia. Adding 10 mg a day of rosuvastatin to their already complex treatment regimens did not prolong survival or protect them from heart attacks or strokes. The only benefit, compared with placebo, was a small reduction in hospital admissions for cardiovascular causes (hazard ratio 0.92, 95% CI 0.85 to 0.99), mostly heart failure. Side effects were, if anything, more common in controls.

The researchers aren't sure why the statin didn't behave as expected. Perhaps the

disease was too advanced to benefit. Or perhaps patients' other drugs obscured any extra treatment effect from the statin. An editorial suggests that statins other than rosuvastatin may produce different results (doi: 10.1056/NEJMe0707221). We have been misled before by the widespread assumption that all statins are the same.

N Engl J Med 2007 doi: 10.1056/NEJMoa0706201

Immunity against some viruses would last for centuries

The immune system has a very long memory after live viral infections, say researchers who examined repeated blood samples from 45 volunteers working in a primate research centre in Oregon. The samples spanned up to 26 years of follow-up and showed that antibodies generated in response to natural viral infections have half lives ranging from an estimated 50 years for varicella zoster virus to more than 11 000 years for Epstein-Barr virus. Antibodies against mumps, measles, and rubella were also remarkably stable, implying lifelong immunity (estimated half lives 542 years, 3014 years, and 114 years).

Humoral immunity against tetanus and diphtheria, induced by vaccination with protein antigens, decayed much faster than that triggered by a natural viral infection. In vaccinated volunteers, tetanus specific antibodies had an estimated half life of just 11 years, and those directed against diphtheria had a half life of 19 years.

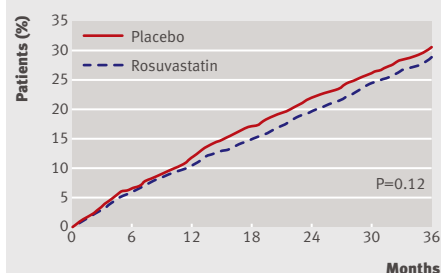
N Engl J Med 2007;357:1903-15

Mobilisation and paracetamol usually enough for simple acute back pain

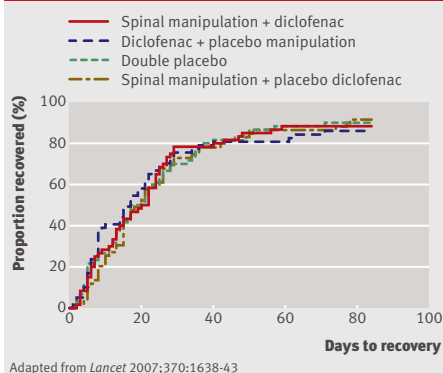
Most people who go to the doctor with acute back pain are advised to keep moving and take regular paracetamol. Adding diclofenac, spinal manipulation (physiotherapy), or both to this recommended first line strategy doesn't help them recover any faster, according to a randomised trial from Australia.

The 240 participants had their first pain free day in a median of about two weeks whether they had spinal manipulation alone, diclofenac alone, both extra treatments, or neither extra treatment. Time to more sustained recovery

EFFECT OF ROSUVASTATIN ON CARDIOVASCULAR DEATH, NON-FATAL HEART ATTACK, AND NON-FATAL STROKE



EFFECT OF INTERVENTIONS ON RECOVERY



was also comparable among the groups. Neither of the extra treatments had any effect on pain intensity or disability. The trial was carefully done, double blind, and fully controlled with placebo manipulation (detuned pulsed ultrasound) and placebo diclofenac. All treatments lasted up to four weeks and compliance was moderate to good.

General practitioners can now confidently reassure patients with uncomplicated acute back pain that they will probably recover within a few weeks if they avoid staying in bed, move around as much as possible, and take 1 g of paracetamol every four hours or so, say the authors. There is no need for the extra expense and risks of additional non-steroidal anti-inflammatory drugs or physiotherapy. A linked commentary says the same (p 1595). *Lancet* 2007;370:1638-43

Disability is worsening in obese Americans

Some evidence indicates that obese people are getting healthier. They have fewer cardiovascular risk factors than they used to, and mortality seems to be falling. Trends in disability are going in the opposite direction, however. Analysis of two routine national surveys from the US shows that disability in the over 60s is getting worse not better for people with a body mass index of at least 30. Between 1988 and 1994, 36.8% of this group reported difficulty with tasks such as walking a quarter of mile, lifting or carrying 10 lb, standing from an armless chair, or walking up 10 steps. That figure had increased to 42.2% by the second survey carried out between 1999 and 2004 ($P=0.03$). The gap between obese people and others widened between the surveys, even for more serious disabilities affecting activities of daily living.

Diabetes and arthritis may be partly to blame, says a linked editorial (p 2066). While public health efforts have helped reduce

cardiovascular risk factors such as smoking, high blood pressure, and abnormal serum lipids, strategies to prevent obesity related diabetes and arthritis have fallen behind.

JAMA 2007;298:2020-7

Excess risk of cervical cancer in pill users falls once pills are stopped

In 2005, the International Agency for Research on Cancer classified combined oral contraceptives as carcinogenic because of a significant association with cervical cancer. The report's authors challenged researchers to find out how long the risk lasted once women stopped taking their pills. A meta-analysis of about 85% of the known research on this topic finds that the excess risk decays relatively quickly, has disappeared completely within 10 years (relative risk of invasive cancer 1.65 for current users, falling to 1.05 after 10 years), and is confined to women who used combined oral contraceptives for at least five years.

Do hormonal contraceptives really cause cervical cancer? It is hard to say for certain, says a commentary (p 1591). Hormonal contraceptives may interact with human papillomaviruses to increase the likelihood that infection persists or to cause premalignant changes in the cervix. But it is also possible that these associations are simply the result of residual confounding. Women who use hormonal contraceptives have more sex than women who don't (although the researchers did their best to adjust for this), and they are less likely to use barrier methods—such as condoms—that protect against infection with human papillomaviruses. Women shouldn't let fear of cervical cancer stop them from taking effective hormonal contraceptives, the comment concludes.

Lancet 2007;370:1609-21

Mucosal treatment for ulcerative colitis passes preliminary trial

Patients with ulcerative colitis who don't respond to short term corticosteroids or immunosuppressants such as azathioprine or 6-mercaptopurine are left with few safe treatment options. So researchers have begun evaluating a new strategy designed to replace a missing chemical in patients' colonic mucus.

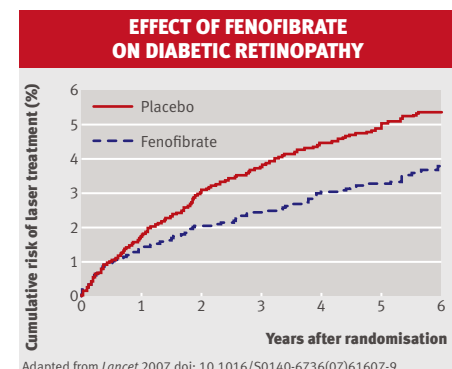
Phosphatidylcholine is essential for a properly functioning mucosal barrier and can be replaced with an oral capsule formulated to protect its contents from digestion. In a small preliminary trial, four capsules a day improved symptoms and helped patients with refractory

ulcerative colitis to withdraw corticosteroids. After 12 weeks of treatment, 12 of 30 patients who took the phosphatidylcholine were better and steroid free compared with only three of the 30 patients who took placebo capsules ($P=0.015$). Endoscopy findings were also improved, although mucosal healing was evident in only a handful of patients, perhaps because the study was so short. Bloating was the most common side effect—it was reported by 11 of 29 patients in the phosphatidylcholine group and six of the 30 controls.

The authors are encouraged by these early findings. Bigger and longer trials are likely to follow.

Ann Intern Med 2007;147:603-10

Fenofibrate may reduce the risk of diabetic retinopathy



The lipid lowering agent fenofibrate could be useful for treating diabetic retinopathy if findings from a recent clinical trial are confirmed. Nearly 10 000 patients with type 2 diabetes took fenofibrate or a placebo for five years in addition to their usual antidiabetic and cardiovascular drugs. Fenofibrate reduced the need for laser treatment of retinopathy by almost a third (3.4% v 4.9%, hazard ratio 0.69, 95% CI 0.56 to 0.84) and seemed to slow progression of disease in some patients.

These findings are a small slice of a large trial looking at all microvascular and macrovascular complications of diabetes so the results are still preliminary, says an editorial (doi: 10.1016/S0140-6736(07)61608-0). Most participants didn't have retinal photographs at the start of the trial because laser treatment for retinopathy was not the researcher's main focus. We still don't know for certain whether fenofibrate works best for patients with or without pre-existing retinopathy. In the 1012 patients who did have serial photographs, fenofibrate slowed the progression of existing retinopathy only—it did not help to preserve sight.

Lancet 2007 doi: 10.1016/S0140-6736(07)61607-9