SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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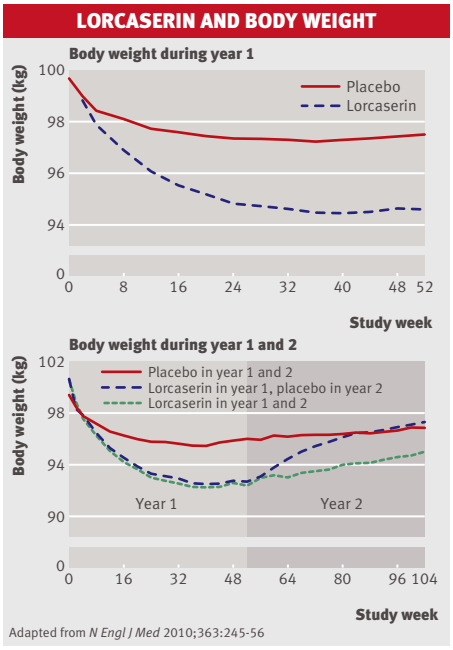
"It's often stated that before antiretroviral treatment, HIV infection was uniformly fatal, but that is not quite true. About one infected person in 200 failed to develop progressive disease while remaining untreated"

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

New weight loss drug clears its first hurdle



Lorcaserin, a selective serotonin receptor agonist, showed promise as a new weight loss drug in its first large trial. Overweight and obese adults taking the drug lost around 4 kg more in the first year than controls taking placebo (mean weight loss 5.8 kg *v* 2.2 kg, P<0.001). Both groups had regular counselling about diet and exercise.

Participants taking lorcaserin who lost ≥5% of their body weight in the first year were randomised again for the trial's second year. Those switching to placebo put weight back on. Those continuing with lorcaserin rebounded less and ended up around 2 kg lighter than controls, on average.

The modest weight loss was accompanied by equally modest but potentially more important improvements in markers of cardiovascular risk including blood pressure, serum lipids, and measures of glucose metabolism. These fringe benefits set the new drug apart from orlistat and sibutramine, says an editorial (pp 288-90). A better safety profile also sets lorcaserin apart from its notorious cousins fenfluramine and dexfluramine. Both were taken off the market when evidence of damage to heart valves emerged.

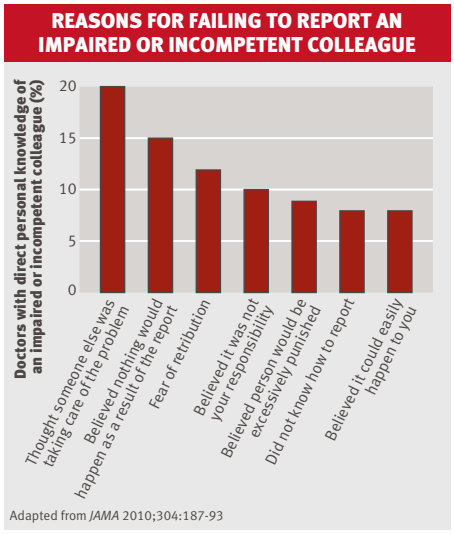
The manufacturer designed lorcaserin to avoid serotonin receptors on heart valves, and it caused no discernible damage in this trial. But doctors, patients, and regulators will need to be vigilant as evaluation progresses. This trial was big, but not big enough to rule out the possibility of valvular side effects later. Most drugs licensed for weight loss have eventually been scrapped after causing serious harm, says the editorial. Sibutramine, the latest to go, was removed from the European market in January this year. It is still available in the US.

N Engl J Med 2010;363:245-56

Many doctors unwilling to report incompetent colleagues

At least a third of US doctors don't believe they should report seriously impaired or incompetent colleagues to an appropriate authority, according to a survey. Nearly 2000 doctors in family practice, surgery, medicine, anaesthesia, cardiology, paediatrics, and psychiatry answered direct questions about their duty to report, and how prepared they were to deal with an impaired or incompetent colleague. Less than two thirds of those who answered the question completely agreed that doctors should report impairment and incompetence (1120, 64%). The same proportion felt prepared enough to take action. The survey had a response rate of 64% (1891/2938).

The current system of self regulation may not be good enough to ensure that incompetence gets referred, say the authors. Many doctors seem unwilling to regulate their colleagues, or feel unprepared in the face of a problem. Of the 309 doctors who said they had worked with an impaired or incompetent colleague, a third (105) did nothing, mainly because they believed someone else would deal with it or that nothing would happen after a report. Fear of retribution was also high on the list.



More should be done to help doctors understand their obligations and encourage reporting, says an editorial (pp 210-2). But peers monitoring each other isn't the only way to ensure quality and patient safety. The profession—ironically the word originates from the Latin meaning "to speak loudly and publicly"—is also regulated by performance measures, compulsory medical education, appraisal, recertification, and new ways of reporting critical incidents. All developed by doctors wanting to strengthen self regulation.

JAMA 2010;304:187-93

Earlier treatment of HIV saves lives

In Haiti the World Health Organization (WHO) recommends that people infected with HIV start antiretroviral treatment when their CD4 T cell count reaches or drops below 200×10^6/l. Starting treatment earlier would save more lives, however. In one trial, adults treated when cell counts were $200\text{-}350\times10^6$/l had a significantly lower mortality than those treated according to WHO recommendations over a mean follow-up of 21 months (23 deaths with standard treatment *v* 6 deaths with early treatment in each group of 408; hazard ratio 4.0 (95% CI 1.6 to 9.8)). Early treatment also reduced the risk of developing new tuberculosis (hazard ratio with standard treatment 2.0 (1.2 to 3.6)). The difference in survival was so convincing that a data monitoring board stopped the trial early and treated the remaining controls. The authors estimate that raising the threshold CD4 cell count for treatment from 200×10^6/l to 350×10^6/l would cost just $400 (£260; €310) per person, cut deaths by 75%, and cut incident tuberculosis by half.

Participants in this trial had a median age of 40 and a median CD4 cell count of 280×10^6/l at baseline. Controls waited an extra two years for treatment with zidovudine, lamivudine, and efavirenz. All participants were receiving prophylactic co-trimoxazole and a monthly food basket. Those with a positive tuberculin skin test also received prophylactic isoniazid. Controls were treated immediately if they developed AIDS or became pregnant.

N Engl J Med 2010;363:257-65

HAART as a control strategy?

Between 1996 and 2009, the number of people starting highly active antiretroviral therapy (HAART) increased more than fivefold in the Canadian province of British Columbia (from 837 to 5413, P=0.002). The average viral load of infected individuals fell dramatically during the same period, according to an analysis of surveillance data in the province, and new diagnoses of HIV infection fell by half (from 702 to 338 per year, P=0·001). The study's authors and an accompanying editorial (doi:10.1016/S0140-6736(10)61057-4) agree that the expansion of HAART probably reduced transmission of the virus and altered the course of the epidemic.

A close statistical correlation between increasing use of HAART, falling viral load in the community, and fewer cases of HIV infection over time is good circumstantial evidence of a causal link between more treatment and less new disease, says the editorial. The pattern was consistent during three distinct periods—an initial rapid fall in incidence of HIV during the first roll-out of HAART, then a period of relative stability for both treatment and new disease, and finally a further significant fall in new HIV diagnoses during a second period of HAART expansion between 2004 and 2009.

A closer look at the data suggests that injecting drug users benefited most during the study period, and drove the overall trends. More should be done to find, test, and treat other high risk individuals, says the editorial. Then international authorities can reasonably start to think of HAART as a control strategy for whole communities, not just a treatment.

Lancet 2010 doi:10.1016/S0140-6736(10)60936-1

Small excess mortality associated with early HIV infection

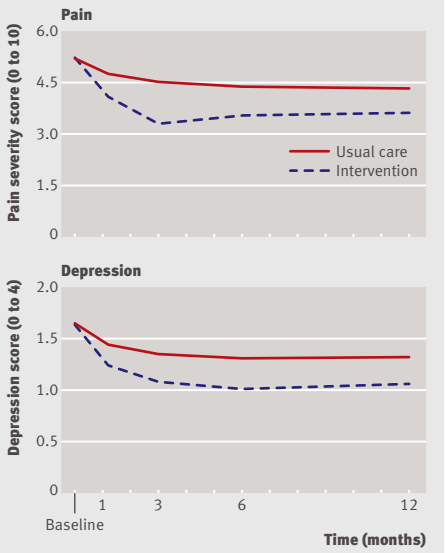
An analysis of data from 23 European and North American cohorts has confirmed that HIV is associated with an excess risk of death even in the early stages when CD4 cell counts remain high. Together, the cohorts included 40 830 adults with CD4 cell counts >350×10^6/l, the recommended threshold for treatment in many developed countries. Injecting drug users and heterosexual adults had the highest mortality relative to the general population (standardised mortality ratios 9.37 (95% CI 8.13 to 10.75) and 2·94 (2.28 to 3.73)). The excess risk was much more modest among men who have sex with men (1.30 (1.06 to 1.58)). For everyone, mortality rose as CD4 counts fell.

We still don't know what is behind the excess deaths, because people with high CD4 cell counts have a relatively intact immune system, says an editorial (doi:10.1016/S0140-6736(10)61033-1). Just 15% (61/419) of the deaths in this study were definitely caused by AIDS. Chronic inflammation, immune activation, or subclinical immunodeficiency may be contributing factors. At least part of the excess mortality is probably the result of confounding, however. The high risk in injecting drug users and heterosexuals may be more to do with social determinants of health such as income and education, behaviour, and coexisting chronic disease than with the HIV itself, says the editorial.

Lancet 2010 doi:10.1016/S0140-6736(10)60932-4

Telecare package helps alleviate pain and depression in adults with cancer

EFFECT OF TELECARE ON PAIN AND DEPRESSION



Adapted from *JAMA* 2010;304:163-71

Pain and depression are often under-recognised (and undertreated) in people with cancer. So researchers from the US designed and tested a programme to treat both problems in adults attending 16 oncology practices throughout Indiana. The intervention was delivered over the telephone by a nurse and a psychiatrist, who gave advice, assessed symptoms, and made treatment recommendations to each patient's oncologist. Scheduled calls were supplemented by extra calls when depression or pain got out of control. Patients reported their symptoms regularly via automated telephone or web based survey.

The telecare package worked better than usual care in 405 adults with diverse cancers, all of whom had inadequately treated pain, depression, or both at the start of the trial. All participants improved over 12 months, but those given the extra help improved significantly more. Pain scores, for example, fell from 5.2 to 3.6 in the intervention group and from 5.2 to 4.3 in the control group—a difference of 0.7 points on a 10 point scale (95% CI 0.02 to 1.39). Results for depression were of similar magnitude. The intervention had an inconsistent effect on quality of life. One of the two analyses found a significant improvement.

Telecare for cancer patients with poorly controlled pain or depression is clearly feasible, say the authors. But the overall effect looks modest. Future trials should try combining the package with telephone based psychotherapy in an attempt to improve symptoms still further, they suggest.

JAMA 2010;304:163-71

Time for mandatory regulation of imaging in the US

Yet more experts have called for tighter regulation of medical imaging in the US to try to control the population's growing exposure to radiation. Half of all radiation directed at US citizens now comes from medical imaging, they write. Quality assurance is patchy and largely voluntary, training for all types of staff is unregulated and often inadequate, and overuse of some imaging techniques, particularly computed tomography (CT), is out of control. An estimated 20-40% of the 80 million CT scans done each year in the US are clinically unnecessary.

Federal laws already govern quality assurance and training for mammography providers, even though mammography accounts for less than 1% of radiation from medical imaging. Policy makers should seriously consider similar federal legislation to regulate the rest, the authors write. Nationwide, mandatory standards would help guard against recent high profile incidents in which hundreds of patients received overdoses of radiation during CT scans.

Controlling overuse could be more difficult since the law can never replace clinical decision making. But it can sort out the perverse incentives that blight current systems for reimbursement, overhaul litigation laws that encourage defensive imaging, and perhaps even mandate the use of guidelines to justify scans.

Every year, US doctors order 10% more CT scans than they ordered the year before, say the experts. Flabby regulation is no longer a sustainable option.

JAMA 2010;304:208-9

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