All you need to read in the other general medical journals

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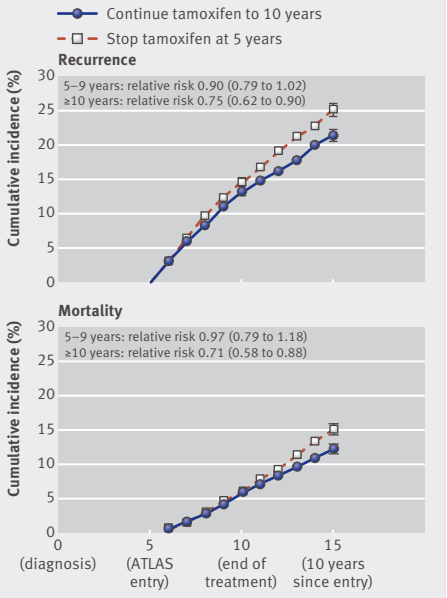
Ten years of tamoxifen works better than five

Risk of recurrence and mortality from breast cancer



Adapted from *Lancet* 2012; doi :10.1016/S0140-6736(12)61963-1

Tamoxifen helps prevent recurrences and prolongs life in eligible women with early breast cancer. Protection seems to accumulate over time, and in a recent long term trial 10 years of treatment worked significantly better than five. Eligible women who continued tamoxifen had lower mortality overall (639 deaths/3428 *v* 722/3418; event rate ratio 0.87, 95% CI 0.78 to 0.97), lower mortality from breast cancer, and fewer recurrences than women who stopped after five years. Tamoxifen has a well known carry over effect, and in this trial the mortality benefits became clear only after women had completed their 10 years of treatment.

Women who took tamoxifen for longer had more pulmonary emboli (rate ratio 1.87, 1.13 to 3.07) and more endometrial cancer (1.74, 1.30 to 2.34) than controls. But they had less ischaemic heart disease (0.76, 0.60 to 0.95). The authors and a linked comment (doi:10.1016/S0140-6736(12)62038-8) agree that the benefits of longer treatment outweigh the risks.

Women in these analyses had early breast cancers that expressed oestrogen receptors. Most were postmenopausal when they were recruited in 1996, after five years of treatment with tamoxifen. Newer antioestrogens are now available, and others will have to evaluate where agents such as aromatase inhibitors fit into the long term therapeutic picture, says the comment. But for women already taking tamoxifen, longer treatment is beginning to look substantially more protective than stopping at five years.

Lancet 2012; doi:10.1016/S0140-6736(12)61963-1

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Drugs and devices look more effective in studies sponsored by industry

A new meta-analysis has found, once again, that studies paid for by industry are more likely than studies paid for by independent sources to report results that favour the sponsor's product (risk ratio 1.24, 95% CI 1.14 to 1.35), conclusions that favour the sponsor's product (1.31, 1.20 to 1.44), and conclusions that don't match the results. The differences look slightly smaller than in previous reviews, but they were big enough to bias the evidence base, say the authors. Industry studies were also more likely than independent studies to report no significant harms.

Traditional sources of bias, such as lack of blinding or allocation concealment, didn't explain these differences, which remained significant in analyses controlling for sample size and other possible confounding factors. Industry sponsorship had no consistent impact on effect sizes. The authors pooled data from 48 studies that explored associations between industry sponsorship and published results.

Drugs and devices simply look better in studies sponsored by their manufacturers, they write. The tools we currently use to identify bias can't tell us why, although it may have something to do with sponsors' choice of comparator treatment, dose, or timing. Selective analysis, selective reporting, and spin have also been documented. Tools for scoring risk of bias in trials should probably include a separate domain on industry sponsorship.

Cochrane Database Syst Rev 2012;12:MR000033

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Cluster of rare fungal infections identified after tornado

In May 2011, a severe tornado killed 160 people in Missouri, USA, and injured 1000 others. Local doctors began reporting cases of severe injuries complicated by unusual fungal infections, and more active surveillance quickly identified 13 injured people with necrotising soft tissue infections caused by environmental fungi or mucormycoses. Five of them died within two weeks of diagnosis.

Penetrating trauma and a high number of injuries were the two factors most consistently associated with mucormycosis in a case-control study. The 13 cases had up to seven separate injuries, and a median of five each. They needed wide surgical excision of necrotic tissue, repeated an average of four times as infections progressed. DNA sequencing identified four different strains of *Apophysomyces trapeziformis* in infected wounds.

Nine people had been injured in houses in the path of the tornado, which touched down just west of the city of Joplin and moved east through the densely populated centre. Case patients and controls were caught off guard and unable to reach storm shelters or basements below ground.

Mucormycoses are rare but not unheard of after natural disasters, including the Indian Ocean tsunami in 2004, say the authors. Doctors treating injured people should consider the possibility when faced with infected necrotic wounds. Timely treatment with the right antifungal agent—in this case amphotericin B or posaconazole—might be life saving. Six of the patients in this series were treated initially with agents known to be inactive against mucormycoses. Three of them died.

N Engl J Med 2012;234:2214-25

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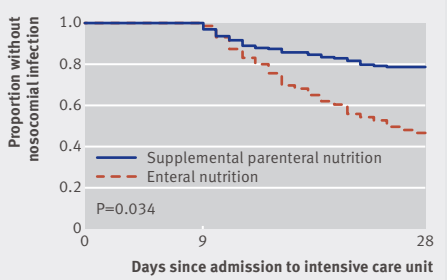
Give enteral nutrition a chance in critically ill adults

Nosocomial infections, by study group



Adapted from *Lancet* 2012; doi:10.1016/S0140-6736(12)61351-8

Intensive care specialists are still debating the best way to meet the complex nutritional needs of critically ill adults. International guidelines recommend enteral nutrition first but diverge on what to do when this is not enough. The latest

"This is the time of year when, as a GP who is still let loose on patients, I have to undergo my annual appraisal. I shall try to demonstrate that knowledge keeps entering my brain at a rate roughly sufficient to replace the increasing amount that leaks out" Richard Lehman's blog at www.bmj.com/blogs

trial tested top-up parenteral (intravenous) nutrition, starting on day 4 for five days. Adults given the top-up had fewer nosocomial infections than controls managed with enteral nutrition throughout (27% (41/153) *v* 38% (58/152); hazard ratio 0.65, 95% CI 0.43 to 0.97). They spent less time on antibiotics, but no less time in intensive care. Staff followed carefully crafted protocols for both types of feeding, including close metabolic monitoring. They used calorimetry to set targets for energy intake and avoid overfeeding. Adults given the extra parenteral nutrition received 103% of their target intake, compared with 77% for controls.

Although trials in this area don't always agree on the precise timing of parenteral nutrition, the evidence so far indicates that there is no particular hurry, says a linked comment (doi:10.1016/S0140-6736(12)61893-5). Day 4 is plenty soon enough, and most patients will come to little harm if they wait a few days longer. Parenteral nutrition should be considered only for patients who can't get what they need from the enteral route. All participants in the latest trial had energy deficits of 40% or more. They were expected to need intensive care for at least five days and to survive for at least a week. All had a functioning gastrointestinal tract. Thirteen per cent of adults given parenteral nutrition and 18% of controls died within 28 days, a non-significant difference.

Lancet 2012; doi:10.1016/S0140-6736(12)61351-8

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HIV treatment reduces transmission in serodiscordant heterosexual partners

The World Health Organization recommends antiretroviral drugs for all HIV infected adults in serodiscordant heterosexual relationships, whatever their immune status. The strategy helps prevent transmission in trials, but can it work on a bigger, messier scale in real populations? New analyses from China look encouraging, say researchers. Between 2003 and 2011, uninfected partners of treated people were significantly less likely to seroconvert than uninfected partners of untreated people (1.3 infections/100 person years (95% CI 1.2 to 1.3) *v* 2.6 (2.4 to 2.8)). After adjustments, treatment of infected partners was associated with a 26% reduction in risk of transmission to uninfected partners (hazard ratio 0.74, 0.65 to 0.84).

The analyses compared around 24 000 treated couples with nearly 15 000 untreated couples, all of whom were registered in China's national HIV epidemiology database. It is hard to say whether treatment was entirely responsible for reducing transmission, because people who were treated were older, sicker, and may have had less sex, or less risky sex, than those who were not yet treated, says a linked comment (doi:10.1016/S0140-6736(12)62005-4). But the findings hint at a direct effect. Treated couples looked better protected, despite the relatively low CD4 counts (and presumably higher viral loads) necessary for treatment in China.

Treatment was associated with lower transmission when HIV had been acquired from a transfusion of blood products (50% of the treated couples) or heterosexual sex, but not when it had been acquired from injecting drugs.

Lancet 2012; doi:10.1016/S0140-6736(12)61898-4

Cite this as: *BMJ* 2012;345:e8390

Worsening eyesight among US adults

The prevalence of poor eyesight that can't be corrected with glasses or contact lenses has gone up in the US. The regular national survey conducted between 1999 and 2002 reported a prevalence of 1.4% (95% CI 1.2% to 1.6%) in adults over 20 years old. By the 2005-08 survey, prevalence had risen to 1.7% (1.5% to 2.0%), a significant difference that extrapolates to an extra 700 000 US adults with visual acuity worse than 20/40 in the best performing eye.

Age, poverty, and longstanding diabetes were all associated with non-refractive visual impairment in these surveys. Because poverty did not increase between the surveys, and age groups were analysed separately, the authors suspect diabetes is at least partly to blame for the nation's worsening eyesight. The proportion of adults reporting diabetes for at least 10 years rose from 2.8% to 3.6% between the surveys. The biggest relative increase occurred in people under 40 years (0.3% to 0.7%; P=0.03), who also reported one of the biggest increases in non-refractive visual impairment (0.6% to 1.0%; P=0.09).

The authors couldn't identify the causes of visual impairment in survey respondents, so they weren't able to explore the contribution made by retinopathy, cataract, glaucoma, and macular degeneration.

JAMA 2012;308:2361-8

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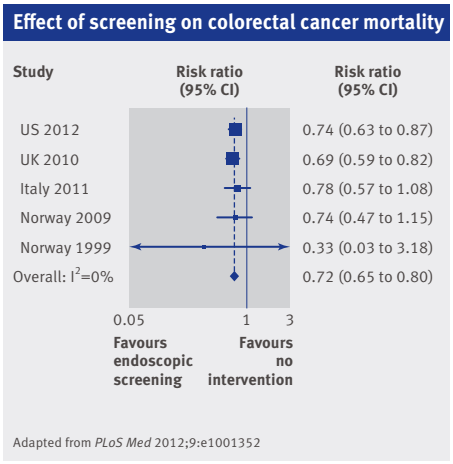
Screening with flexible sigmoidoscopy helps prevent cancers and deaths



Screening 1000 middle aged adults with flexible sigmoidoscopy would prevent just under three colorectal cancers (2.8, 95% CI 1.4 to 4.0) and just over one death from colorectal cancer (1.2, 0.8 to 1.5), according to a meta-analysis of five large trials from Europe, Scandinavia, and the US. In pooled analyses, screening cut the incidence of colorectal cancer by 18% (relative risk 0.82, 95% CI 0.73 to 0.91) and mortality from colorectal cancer by 28% (0.72, 0.65 to 0.80), when compared with no screening or usual care.

The five included trials tested slightly different screening protocols, but most started with flexible sigmoidoscopy (usually once only) then moved on to full colonoscopy for adults with high risk findings, such as large or multiple polyps. In two trials, small polyps were removed at the initial screen. In others, all patients with disease were referred on for treatment. As expected, screening based on flexible sigmoidoscopy was best at preventing left sided cancers (3.0 (2.2 to 3.7) avoided cases per 1000 screened).

Pooled analyses add power and precision to estimates of benefit from individual trials, and the authors are now confident that this kind of screening can help prevent cancers and save lives (or at least prevent deaths from colorectal cancer). It is much less clear how screening with flexible sigmoidoscopy compares with primary use of colonoscopy, or faecal occult blood tests. Colonoscopy is already more popular in the US, say the authors. The meta-analysis did not report on possible harm from screening.

PLoS Med 2012;9:e1001352

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