

Short cuts

What's new in the other general journals

Effects of childhood cancers persist into adulthood

When researchers surveyed 11 481 children and adults who had survived at least five years after childhood cancer, nearly a fifth (19.6%) said they still had some sort of physical impairment. They were 4.7 times (95% CI 3.0 to 7.2) more likely than their healthy brothers and sisters to report problems taking care of themselves, and nearly 5.9 times (4.5 to 7.6) more likely to have trouble holding down a job or attending school.

Respondents who had had brain cancer or bone cancer were most likely to have long term problems—over a quarter of those who survived brain cancer and over a third of those who survived bone cancer reported some kind of physical restriction in their daily lives. Survivors of all cancers were more likely than their siblings to report endocrine, cardiac, pulmonary, or musculoskeletal problems, and 42.6% (4890/11481) had at least one neurological symptom such as pain, abnormal sensations, or weakness in their arms or legs.

As more children survive their initial cancers, health systems will have to get better at monitoring the prolonged aftermath and offering treatment and rehabilitation to the substantial number who need it, write the authors.

Ann Intern Med 2005;143:639-47

Undiagnosed organ donor infects eight people with hepatitis C

In summer 2002, a woman from Oregon developed acute hepatitis C six weeks after a patellar tendon graft with bone. The donor had no antibodies against hepatitis C in his blood at the time of his death two years before, and had subsequently donated

44 tissues and organs to a total of 40 people across 16 US states and two other countries.

A premortem blood sample from the donor contained RNA from hepatitis C virus, indicating that he had an undetected viraemia when he died. After a thorough search, investigators found eight recipients infected with the same virus genotype—all three of those who had received organs, all three of those who had received tendon grafts with bone, one out of the two people who had had a saphenous vein, and one out of the three people who had had a tendon graft without bone. Three of the eight had already had hepatitis C diagnosed, although the link with a tissue donor had been missed. One, a lung transplant recipient, died from the infection.

All organ donors are screened for antibodies against hepatitis C. This donor, however, was in the 8-10 week window between infection and the appearance of antibodies. Screening donor blood for viral RNA would pick up these rare cases, but it would be expensive—about \$2.3m for every infected donor taken out of circulation. The US Food and Drugs Administration is thinking about it.

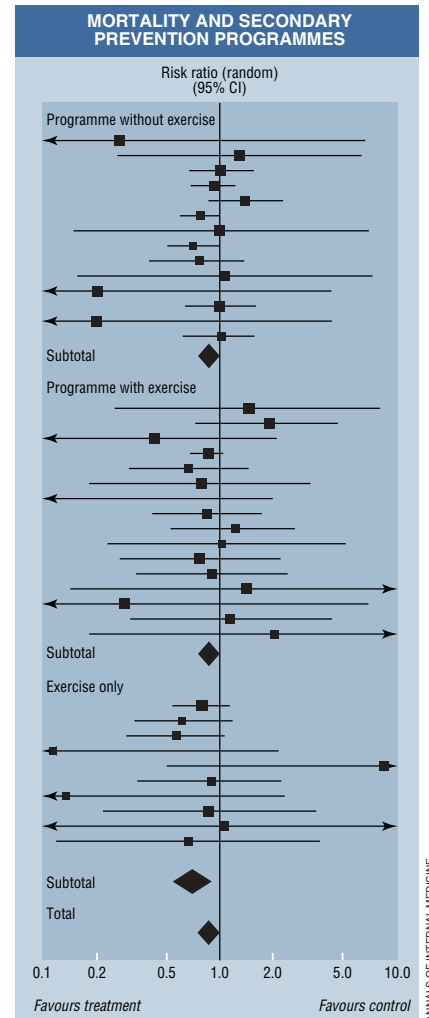
Ann Intern Med 2005;143:648-54

Cardiac rehabilitation seems to work—with or without exercise

In general, secondary prevention programmes for people with coronary heart disease seem to work. The components of individual programmes may vary, reports the latest meta-analysis, but taken together they improve coronary risk factors, reduce the risk of recurrent heart attacks (risk ratio 0.83, 95% CI 0.74 to 0.94), and even save lives—although it takes about two years for the mortality benefits to surface (risk ratio 0.53, 0.35 to 0.81 after two years).

Despite a great deal of research effort, however, it's still unclear which parts of a rehabilitation package work best. In this analysis of 63 randomised trials, there was little to choose between programmes of structured exercises, those combining exercise with counselling or education, and programmes with no exercise component at all.

The 63 randomised trials included 21 295 patients with established coronary heart disease. The trials were of average

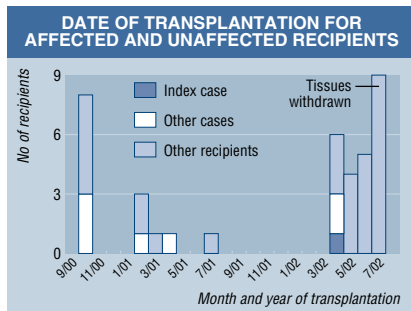


quality, and many had the kind of flaws that tend to make the intervention look better than it really is. Even so, the authors think the findings are clear—a wide variety of secondary prevention programmes offer benefits to people lucky enough to have access to one. Women, elderly people, and those in minority communities were under-represented in most trials.

Ann Intern Med 2005;143:659-72

Juvenile dermatomyositis probably not caused by parvovirus B19

Nobody knows what triggers juvenile dermatomyositis, but anecdotal reports have linked this and other autoimmune



diseases to parvovirus B19. A more scientific approach, however, failed to find any association between this common childhood infection and juvenile dermatomyositis.

In a case-control study, 62 children recently diagnosed with the condition were less likely to have IgG antibodies to parvovirus B19 in their blood than age and sex matched controls (25/62, 40% *v* 36/62, 58%, $P = 0.04$). Two children in each group tested positive for viral DNA in plasma, and the findings from a small sample of muscle biopsies were equally unconvincing.

The authors aren't sure why the controls in this study had a significantly higher prevalence of parvovirus infection, but the difference may be caused by geography. Cases were recruited from all over the United States, controls from a small area around a clinic in Washington DC.

JAMA 2005;294:2170-1

Stopping a clinical trial early can exaggerate the findings

More than one in a hundred clinical trials published in top general journals are stopped early because the intervention they are testing looks better than expected sooner than expected. Many of these trials are well publicised and test high profile treatments—usually new drugs for patients with cancer, heart disease, or HIV infection. An international team of researchers say doctors should treat the findings with scepticism after their study found that truncated trials were poorly reported, often funded by the drugs industry (64/143, 45%), and tended to exaggerate the benefits of treatment.

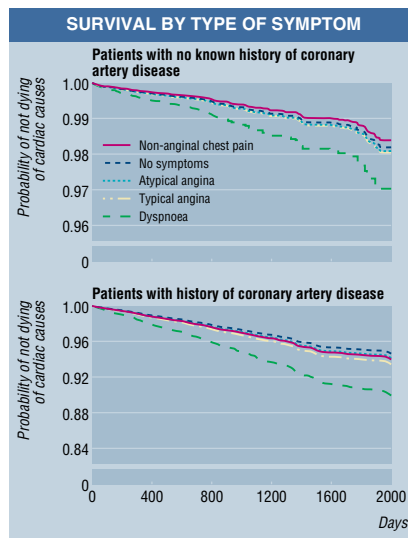
The 143 trials they found recruited 63% of their planned sample on average, and were stopped after a median of only 66 patients had reached the planned end point. Trials with fewer end points reported the biggest treatment effects.

Interpreting these trials can be a real problem, write the researchers. There's a danger that trials are stopped at a "random high," which would "regress to the truth" if the trial continued as planned. End points that are important to patients, such as side effects and overall survival, are often ignored.

Early termination of trials is significantly more common now than it was 30 years ago, and we need to be more cautious about fast tracking them into clinical practice. A clear and detailed statement, flagged up in the abstract, explaining the decision to stop a trial would help. Editors should also insist on proper statistical adjustment of implausibly good results.

JAMA 2005;294:2203-9.

Dyspnoea predicts high risk of death in patients with known or suspected coronary artery disease



In a cohort of 17 991 patients with known or suspected coronary artery disease, the 1091 that answered yes to the question "Do you experience shortness of breath?" were up to four times more likely to die of a cardiac cause during the next three years than patients who had other symptoms such as chest pain or no symptoms at all. Breathless patients were also significantly more likely than the rest to die from any cause.

The patients with dyspnoea had no other cardiac symptoms. Their breathlessness was an independent predictor of death whether or not they had known coronary artery disease.

The patients in this study had all been referred for cardiac stress testing using single photon emission computed tomography (SPECT). The test results did not explain why patients with dyspnoea were at such high risk of death, neither did tests of left ventricular function. But the author of a linked editorial (pp 1963-5) thinks myocardial ischaemia, left ventricular dysfunction, and obesity are all worth investigating further.

In the meantime, doctors should remember to ask about patients about breathlessness when they come for a functional evaluation of known or suspected coronary artery disease.

N Engl J Med 2005;353:1889-98

High concentration of inspired oxygen can reduce postoperative wound infections

Patients having open abdominal operations need high concentrations of inspired oxygen throughout the perioperative period, says one leading commentator (pp 2091-2), after a large randomised trial

found that extra oxygen during and after surgery reduced the risk of wound infections from 24% (35/143) to 15% (22/148). The idea is not new, but there's now enough evidence to justify putting it into practice. Extra inspired oxygen is cheap, and if it works as well in the real world as it did in this trial there would be 39% fewer surgical infections in the United States each year, saving a substantial amount of the \$1.8bn it currently costs to treat them.

The trial was double blind and included 300 Spanish adults having major colorectal surgery. Laparoscopic operations were excluded. Participants were given 30% or 80% inspired oxygen during surgery and for six hours afterwards. The researchers used standardised anaesthetic and antibiotic protocols, and diagnosed infections using criteria from the Centers for Disease Control and Prevention. The results are biologically plausible and consistent with *in vitro* work on wound infections, and with the only other high quality clinical trial. Extra oxygen during the perioperative period should now be part of general quality improvement measures, say the authors.

JAMA 2005;294:2035-42

High prevalence of diabetes in Cambodia could be a legacy left by the Khmer Rouge

Cambodia is still a relatively isolated and undeveloped country with a rural economy. Obesity is rare, and Cambodians eat a traditional diet including plenty of fruit, vegetables, and fish. Researchers were surprised, therefore, to find that a quarter of the adults in the suburban area of Kampong Cham had glucose intolerance. One in 10 had frank diabetes. One in four were hypertensive.

Their survey included 2246 randomly selected Cambodian adults living in two communities—one semi-urban, the other entirely rural. Rates of glucose intolerance and diabetes were slightly lower in the rural survey (10% and 5% respectively), but still much higher than expected and comparable with prevalence rates recently found in Hanoi (the capital of Vietnam) and Thailand.

Cambodians could have inherited their susceptibility to diabetes from an early history shared with the Indian subcontinent. But it's also possible that diabetes and hypertension are a legacy left by the Khmer Rouge, who starved and terrorised the Cambodian population in the late 1970s. Nutritional deprivation in the womb or in infancy has been linked repeatedly to impaired glucose tolerance later in life.

Lancet 2005;366:1633-9

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