Short cuts

What's new in the other general journals

Trial challenges guidelines for patients with acute coronary syndrome

RISK OF COMBINED ENDPOINT BY SUBGROUP

The management of patients with an acute coronary syndrome has been edging towards a more invasive package, including drugs and early coronary angiography followed by revascularisation if appropriate. European and American guidelines recommend this approach, and many cardiologists accept it. But the evidence against routine aggressive treatment is mounting.

The latest randomised trial, which is large and well done, reports that patients treated early and invasively do no better, and may do worse, than similar patients who are managed with drugs then carefully selected for more invasive treatment later if they need it.

All 1200 Dutch patients had an acute coronary syndrome and a raised serum concentration of troponin T. They had the best available medical treatment, including aspirin, clopidogrel, enoxaparin, and statins. A total of 604 patients had early invasive treatment, starting with coronary angiography within 24 to 48 hours after admission. The rest were managed conservatively unless they remained unstable or failed an exercise test before discharge. A year later, 23% (137) of the patients treated aggressively, and 21% (126/596) of the patients treated more conservatively had died, had a heart attack, or come back in to hospital with angina. Overall mortality was low (2.5%) and was

the same in both groups. In this trial, as in others, early revascularisation was associated with a higher risk of heart attack, especially after the treatment (15% v 10%, $P=0.005$).

New England Journal of Medicine
2005;353:1095-104

Patients with most to gain are least likely to get drug treatments for heart failure

We already know that patients with heart failure don't always get the drug treatments they need. But a new study shows that the sickest patients are the most likely to miss out. In a cohort of 1418 hospital patients with heart failure, researchers found a paradoxical relation between risk of death and treatment with β blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers. All three classes of drug are known to prolong survival in patients with heart failure and are recommended in management guidelines from Canada and the United States.

In this Canadian study, discharge data from a national database showed that 81% of low risk patients and 60% of high risk patients were given ACE inhibitors on discharge from hospital; 86% and 65% were given either ACE inhibitors or angiotensin II receptor blockers; 40% and 24% were given β blockers. The inverse trend was significant for all three drug classes.

The mismatch between need and treatment persisted for at least 90 days, and was not explained by patients' age or sex, the presence of other serious diseases such as cancer, or contraindications to the drugs. All patients were younger than 80 and had a left ventricular ejection fraction of less than 40%.

The authors say that high risk patients have the most to gain from drug treatment, which is the cornerstone of management for heart failure. More should be done to find out why they don't get it.

JAMA 2005;294:1240-7

China develops a chronic disease burden to rival the US

As China develops a more Western culture, the causes of death are becoming more like those in the West. Cancer, heart disease, and stroke are now the three leading causes of death, accounting for two thirds of all deaths in Chinese people older than 40, a

cohort study shows. Cor pulmonale (right heart failure caused by chronic obstructive pulmonary disease) was the commonest cause of death from heart disease in this cohort. Lung cancer was the commonest cause of death from cancer. Unsurprisingly, an analysis of risk factors found that cigarette smoking was responsible for 8% of all deaths, an impact matched only by hypertension, which was responsible for 12% of all deaths.

These data come from a representative sample of 169 871 Chinese men and women who were interviewed and examined in 1991 and again eight years later. They show a clear transition in disease burden in China, which 50 years ago was dominated by pulmonary and infectious diseases, especially tuberculosis. Death rates from chronic diseases in China are now comparable with death rates from the same diseases in the US, and government health policy must evolve in parallel with these new threats. Strategies to control smoking and hypertension are two of the most important priorities, say the authors.

New England Journal of Medicine
2005;353:1124-34

Men with early prostate cancer may do better after higher dose radiotherapy

Most American men with prostate cancer are diagnosed early while their disease is still localised. Each year, more than 26 000 of them have external beam radiotherapy treatment. Improving technology means that their radiotherapy is more precisely targeted than ever before, so theoretically they can have a higher dose without any increase in collateral damage to the gut or urinary tract.

Researchers comparing the conventional 70.5 Gy with 79.2 Gy in a randomised trial found that men who received the higher dose were less likely than controls to have recurrent disease five years later. The higher dose didn't cause more serious side effects than the lower dose, but it did increase the risk of moderate side effects from the gut, such as rectal bleeding. Forty one per cent (81/196) of the men who had a lower dose and 57% (112/195) of those who had a higher dose reported gut side effects that scored 2 out of a possible 5 for severity ($P=0.004$).

Almost all the men survived until the end of the trial (97% *v* 96%), so the researchers used serum concentrations of prostate specific antigen (PSA) to track participants' disease. They defined recurrence as three successive increases in serum concentration of this marker. After a median follow up of 5.5 years, high dose radiotherapy reduced the risk of recurrence by almost half (38.6% *v* 19.6%, $P<0.001$), compared with a conventional dose. The reach of these results will be limited, however, until proton beam therapy—the modality used in this trial—is more widely available. Currently, only two centres in the US use it.

JAMA 2005;294:1233-9

American mortality study reports good news and bad news

Mortality data from the US show that Americans are living longer than ever before. The age standardised death rate from any cause has gone down by nearly a

third since 1970, and corresponding death rates for heart disease and stroke have more than halved. Death from unintentional injury, including road traffic crashes, is also substantially less likely now than in 1970; mortality dropped by 41% between 1970 and 2002.

A closer look at the data on death from stroke and unintentional injury shows some less encouraging trends, however. The decrease in death rates from unintentional injury seems to have slowed down since the early 1990s, possibly because the interstate speed limits were relaxed in 1987. The downward trend in stroke deaths has also bottomed out.

Mortality from cancer has fallen by a disappointing 2.7% since 1970, but the downward trend seems to be accelerating. Better tobacco control may be at least partly responsible, although it's had no impact at all on death rates from chronic obstructive pulmonary disease, which have doubled since 1970 and continue to increase.

One of the most worrying trends in these data is the predictable outcome of a Western fast food diet in an ageing population. Americans are now 45% more likely to die from diabetes than they were in 1987.

JAMA 2005;294:1255-9

Ciprofloxacin is an effective alternative to erythromycin for children with cholera

Children with cholera need rehydration first and foremost, then antibiotics to help stop the diarrhoea. The World Health Organization recommends a three day course of erythromycin, but a single dose of oral ciprofloxacin may be just as effective. A trial comparing the two treatments in

children from Bangladesh reports a cure rate of 60% (47/78) among those given ciprofloxacin and 55% (46/84) among those given erythromycin. Children were cured if their watery diarrhoea stopped two days or less after the start of treatment.

These findings look promising but are less convincing than they might be, according to a linked editorial (doi:10.1016/S0140-6736(05)67326-6). The trial was not blinded because the drug manufacturer, Bayer AG, failed to produce identical formulations of the study drugs. So it's possible that bias in favour of the new treatment crept in. It's also disappointing that the investigators chose to test a single dose of ciprofloxacin against a treatment requiring 12 doses over three days. These authors have already shown that a single dose of azithromycin works as well as erythromycin in children with cholera, so a trial comparing all three would have been nice. Finally, ciprofloxacin was slower than erythromycin at clearing *Vibrio cholerae* from children's stools. After three days, 58% (45/78) of the children given ciprofloxacin were still excreting *V. cholerae* compared with only 30% (25/84) of those given erythromycin.

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Suicide in male prisoners continues to increase

Between 1978 and 2003, 1312 men and boys committed suicide in prisons in England and Wales. This is more than five times higher than the rate of suicide in the general population, say a team of researchers from the United Kingdom. The study, which was based on an examination of all deaths in custody in 25 years, found that incarcerated boys between 15 and 17 years old were particularly vulnerable—suicides in this age group were 18 times more common inside prison than outside.

We have known for a long time that prisoners have a high risk of suicide, but this comprehensive study shows that the problem has been steadily worsening for decades and that the rate of suicide in male prisons is now at an all time high.

Why more and more men and boys are committing suicide in prison despite the best efforts of the criminal justice authorities, prison staff, and health professionals in England and Wales is unclear. A linked editorial (doi:10.1016/S0140-6736(05)67327-8) argues that the worsening epidemic simply mirrors the deteriorating mental health of prisoners, increasing numbers of whom are drifting into prisons only because psychiatric care in the community has failed them.

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