Short cuts

What's new in the other general journals

Process measures are related to survival in elderly patients

The quality of medical care is best judged by patients' outcomes. But such data are often slow and difficult to collect. It's easier to measure process instead—the proportion of eligible patients who received a recommended treatment, for example. Where the recommended treatment is established as effective, this is fair enough. In many settings, however, particularly in the community, the relation between improved performance on measures of process of care and better health outcomes is little more than an assumption. The findings of a study of elderly people, in which this assumption was put to the test, are reassuring.

Using medical records of almost 400 elderly people living in the community, researchers assessed the quality of medical care received by using a broad set of process indicators. On average, these people had received about half the recommended care, but there was a large variation between individuals. These people were followed up for three years. After adjustment for sex, illnesses at baseline, and frequency of use of health services, no relation between quality and mortality was evident in the first 18 months of observation. After this, people with higher quality scores had lower mortality, and the difference increased as time went on.

Annals of Internal Medicine
2005;143:274-81

Varicella vaccination reduces use of health care

Before varicella vaccine was invented, almost everyone experienced chickenpox, usually in childhood. Routine vaccination started in the United States in 1995 and, by 2002, coverage in children aged 19 to 35 months was more than 80%. Not surprisingly, the incidence of chickenpox has declined considerably. Rather more importantly, medical complications related to varicella have also fallen substantially.

Using data from a national database of health insurance plans, investigators tracked trends in varicella related hospitalisations, visits to doctors, and medical costs between 1994 and 2002. Compared with the prevaccination period, hospitalisations fell by 88% and visits to doctors by 59%. The biggest effect was in

children less than a year old, although a decline was seen in all age groups—a striking example of the benefits of improved herd immunity.

The investigators estimate that in 1994 the direct costs of chickenpox in the US were nearly \$85m (£47m; €68m). By 2002, costs had fallen to \$22m. Savings in indirect costs are harder to measure, but they are likely to be considerably greater.

JAMA 2005;294:797-802

Homoeopathic remedies do not have specific effects

Many people believe that they have benefited from homoeopathic remedies, but it's hard to see how such preparations could work. As is often pointed out, by the time the serial dilutions have taken place, no molecules of the original homoeopathic cure remain. The explanation that succussion—vigorous shaking between dilutions—transfers to the solvent a memory that persists after the last molecule has gone cannot be squared with the principles of physical chemistry. So can it all be accounted for by a placebo effect? A meta-analysis comparing outcomes of placebo controlled trials of homoeopathy and conventional medicine shows that it can.

The investigators matched 110 randomised double blind trials of homoeopathy with 110 trials of conventional medicine for the disorder being treated and the type of outcome being measured. In both groups, smaller trials and those of lower methodological quality showed more beneficial treatment effects than larger and higher quality trials. Funnel plots showed evidence of publication bias in trials of both homoeopathy and conventional treatment. An analysis restricted to larger higher quality trials found no convincing evidence that homoeopathy was superior to placebo.

Meta-regression indicated that, as the standard error of the estimate of the treatment effect fell, the size of the treatment effect approached zero. The researchers concluded that the beneficial effects seen in trials of homoeopathy are unlikely to be specific and that they are compatible with placebo effects.

Lancet 2005;366:726-32

Anti-inflammatory treatment shows promise in COPD

The airflow obstruction in chronic obstructive pulmonary disease (COPD) is usually progressive and accompanied by chronic inflammation. Corticosteroids, however, have little long term effect: even high doses don't prevent deterioration. Phosphodiesterase 4 inhibitors, such as roflumilast, may be more effective. In animal models they suppress neutrophil activation and the production of cytokines and chemokines.

A multicentre randomised controlled trial involving 1400 patients with chronic obstructive pulmonary disease found that 24 weeks of treatment with roflumilast resulted in improvement in postbronchodilator measurements of FEV₁ and decreased frequency of exacerbations compared with placebo. The improvement in FEV₁ began within the first month of treatment and was maintained during the trial. Diarrhoea and nausea were the commonest adverse events, and dropout from the trial was more than 20% in the group treated with the higher dose of roflumilast.

Both placebo and treatment groups showed an improvement in health related quality of life scores over the duration of the trial, but the differences between groups weren't significant. The investigators believe that roflumilast is a promising candidate as an anti-inflammatory treatment for chronic obstructive pulmonary disease, but sceptics will want results from longer term studies to be sure that the improvements seen in spirometric measurements would indicate that patients feel better.

Lancet 2005;366:563-71

Two genetic polymorphisms increase susceptibility to bladder cancer

Many clinicians are weary of reading about associations between genetic polymorphisms and complex diseases. Because so many of these reports have

proved impossible to replicate, you may be forgiven for doubting whether the approach has anything useful to offer. A recent report implicating two genes in the pathogenesis of bladder cancer should be taken seriously for two reasons, however. Firstly, the study was large: it included more than 2000 cases and controls. Secondly, both genes are known to play a part in detoxifying potentially carcinogenic chemicals, such as aromatic amines.

Odds ratios for transitional cell carcinoma in people with deletions of one or both copies of the GSTM1 gene compared with people with both copies were 1.2 (95% CI 0.8 to 1.7) or 1.9 (1.4 to 2.7). The odds ratio was also greater for people with the NAT2 slow acetylator genotype compared with people with rapid or intermediate acetylator genotypes—particularly among cigarette smokers. In a meta-analysis of other studies, the investigators found similar summary estimates of the risk of bladder cancer associated with these genotypes, which they think (reasonably enough) makes their results all the more compelling. Although the increase in relative risk is fairly small—less than 2 in both cases—these polymorphisms are common and they may account for almost a third of cases.

Lancet 2005;366:649-59

Bone marrow micrometastasis is associated with poorer prognosis in breast cancer

Haematogenous dissemination of tumour cells has occurred in about a third of women with breast cancer by the time the disease has been diagnosed, but the clinical usefulness of such a finding has been in doubt. A pooled analysis of data from almost 5000 women with breast cancer whose bone marrow had been examined for metastatic cancer cells now clearly shows that it predicts a worse prognosis.

The investigators analysed individual patients' data from nine published or soon to be published studies. Bone marrow micrometastases were present in 1438 women. These women were more likely to have larger primary tumours, higher histological grade tumours, hormone

receptor negative tumours, and lymph node metastases. All of these features, of course, are associated with poorer prognosis themselves, but in a multivariate Cox regression model, the presence of bone marrow micrometastases remained an independent predictor of a poor outcome. The finding may be useful in the design of trials of systemic adjuvant therapy in which treatment stratification is based on the presence or absence of micrometastasis.

New England Journal of Medicine
2005;353:793-802

Erythropoietin stimulates development of proliferative diabetic retinopathy

Pathological growth of new retinal blood vessels can cause catastrophic loss of vision in people with diabetes. Vascular endothelial growth factor (VEGF), produced in response to ischaemia, is known to be involved, but, although inhibition of this growth factor reduces retinal neovascularisation, it does not stop it completely. New findings show that local production of erythropoietin is also a powerful stimulus for retinal angiogenesis.

The investigators measured concentrations of erythropoietin and vascular endothelial growth factor in the vitreous fluid of 73 patients with proliferative diabetic retinopathy and 71 non-diabetic patients with other eye diseases who were undergoing vitrectomy. Concentrations of both growth factors were much higher in patients with active proliferative diabetic retinopathy than in those with quiescent disease or non-diabetic controls. But the concentrations of the two factors were not closely correlated, and erythropoietin was more strongly associated with neovascularisation than was vascular endothelial growth factor. No correlation between vitreous and plasma concentrations of erythropoietin was found, indicating that the high concentrations found in the vitreous fluid are probably due to local production in the retina. Together with the fact that in animal studies erythropoietin blockade inhibited

retinal neovascularisation, these findings raise the possibility that erythropoietin or the signal transducers known to mediate erythropoietin responses could be potential therapeutic targets.

New England Journal of Medicine
2005;353:782-92

Long term aspirin reduces risk of colorectal cancer

Several randomised controlled trials have shown that regular use of aspirin reduces the risk of recurrence of colorectal adenoma or cancer. How effective it is in primary prevention is another question. Analysis of data from the large cohort of women enrolled in the US nurses' health study now indicates that both aspirin and non-steroidal anti-inflammatory drugs do reduce risk—but only after long term use.

The nurses' health study has been running since 1976. Data on the use of medication and the occurrence of disease are collected by using postal questionnaires sent out every two years. Use of aspirin has been recorded since 1980. Of more than 80 000 eligible women, 962 developed colorectal cancer. Overall, regular aspirin users had a significantly lower risk of the disease, after adjustment for known risk factors including age, smoking, alcohol use, body mass index, exercise, family history, and history of colonic polyp (relative risk 0.77, 95% CI 0.67 to 0.88). During the first five years of aspirin use, no risk reduction was apparent. After five years risk decreased progressively, although the change did not become statistically significant until aspirin had been used for 10 years. The apparent benefit was greater with increasing dose, reaching a maximum when tablets of 325 mg were taken 14 times a week. Regular use of non-steroidal anti-inflammatory drugs was associated with a comparable reduction in risk and a similar dose-response relation. It looks as if prevention of cancer needs substantially higher doses of aspirin than those recommended for the prevention of cardiovascular disease.

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