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**David Kermac Macmeikan Thomas**  
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Cervical intraepithelial neoplasia and higher long term risk of cancer

Women treated for CIN3 should have long term regular screening, even if they are beyond the normal age limit.

In some countries, such as the United Kingdom, women have long term intensive surveillance after conservative treatment for high grade cervical intraepithelial neoplasia, whereas in others, such as the Netherlands and Finland, they return to regular screening after a few years. The second choice is based on the consistent observation that most recurrences of cervical intraepithelial neoplasia occur in the first two to three years after treatment.3

In this week's BMJ, Strander and colleagues provide strong evidence that women treated for cervical intraepithelial neoplasia grade 3 have a long lasting excess risk of invasive cervical cancer.7 Among more than 130,000 women with this condition, the age adjusted incidence was more than double that of the general population up to 20-25 years after diagnosis. The excess incidence was greater in women treated at older age and in recent years.

How do these findings translate into clinical recommendations? The important question is how different follow-up schedules compare in terms of effectiveness and cost in preventing the excess risk of cancer. Unfortunately, we have no direct evidence to answer this question, as no large study of the risk of cancer has also reported women’s individual follow-up history.3 4

Long term surveillance with intensive cytology might be an option. However, the relative protection afforded by different frequencies of testing in the general population2 cannot be assumed to be the same for women treated for high grade cervical lesions. Indeed, without data on individual follow-up the long term excess risk of cancer may be explained by cytology becoming less accurate in the long term in treated women or by women not attending long term intensive follow-up or even regular screening.1 It would take a long time for prospective studies of women with different follow-up regimens to identify the most effective regimen. Case-control studies comparing the follow-up of women who developed cancer with those who did not might provide crucial information in the short term.

The interval since the last normal cytology result is the key variable, and studying the risk of cancer according to this interval and time since treatment might identify the best regimen.

Testing for human papillomavirus DNA has consistently been shown to be more sensitive than cytology for detecting short term occurrence of cervical intraepithelial neoplasia in treated women.6 Long term schedules need to be defined. Repeated testing for human papillomavirus may be needed to control the long term risk of cancer, because residual infection might be difficult to detect and new infection needs to be identified. Increased risk of cancer could be the result of a new or persistent infection rather than treatment failure. Women who were previously infected could still have the same risk factors such as behaviour or susceptibility to infection. The high negative predictive value of human papillomavirus means that women could be tested less often compared with cytology. The scarce data available on follow-up by colposcopy do not show a substantial advantage over cytology.7

One clear indication is that women treated for cervical intraepithelial neoplasia stage 3 should continue surveillance beyond the age limit of regular screening. Such age limits have been adopted for the general population as cancer risk drops to negligible values in previously regularly screened women, but Strander’s study2 shows that this is not the case in women who had cervical intraepithelial neoplasia stage 3.

According to Strander’s data,2 any follow-up policy that can confer the same cancer risk as that seen in the general population would avoid 21.5 cancers per 100,000 person-years (including an unknown but possibly large proportion of microinvasive carcinomas) in these high risk women. Related disadvantages are not only financial but include stress related to long term intensive surveillance and the risk of having to be retreated unnecessarily as a result of false positive histology. Increased frequency of testing will lead to an increased number of biopsies and, in the general population, about 15% of diagnoses of cervical intraepithelial neoplasia grades 2-3 are not confirmed at review.8

The higher incidence of recurrence of cervical neoplasia in women treated in recent years correlates with the use of more conservative treatments. As for all ecological correlations, alternative explanations are difficult to exclude. For example, the higher prevalence of human papillomavirus in recent years might have made persistent hazardous sexual behaviour increasingly risky. Again, comparing by calendar period the type and characteristics of treatment (for example, if excision margins were free of dysplasia) in women who did and did not
develop cancer would provide precious information.

In the meantime, returning to the widespread use of hysterectomy for cervical intraepithelial neoplasia is clearly unacceptable, especially as only some high grade cervical lesions progress to cancer and the incidence of false positive histological diagnosis is relatively high. Regarding excision, no significant difference in obstetric outcomes has been shown between cold knife conisation and other excisional techniques, although short term complications were more frequent with cold knife conisation.

Current evidence calls for high quality conservative treatment—this might be more achievable in centres with a high workload volume. In addition, more attention should be paid to the completeness of excision, especially in older women who have a higher risk of cancer.


Defining a high performance healthcare organisation

Composite measures of performance are insufficient on their own

Why are high performing healthcare organisations so hard to find? In this week’s BMJ, Wilson and colleagues report a study that evaluates 69 facilities in 30 US states that receive categorical funding for HIV services.1 The authors assessed performance using a bundle of eight clinical measures considered by a panel of experts to represent high quality of care for HIV. They found that few organisations scored highly across more than a handful of measures.

Interpreting the results at face value suggests that these facilities are not performing well, and that their organisations do not support strong systems of care for people living with HIV. We would expect all clinics to provide comprehensive elements of care that have been shown to improve patients’ outcomes. However, closer scrutiny of the study raises methodological and theoretical questions about the selection and measurement of the indicators and, importantly, the association between overall performance and designation as a high performing healthcare organisation.

Composite measures are commonly used to monitor performance in healthcare systems. An overall score is computed by aggregating each component into a bundle of related measures. Bundled measures, however, are not all alike. Selecting measures appropriate to the system under review and defining those measures consistently is crucial to generating meaningful performance data.2 As Nolan and Berwick3 point out, some groups of measures are linked because they constitute a sequence of essential steps.

leading to one desired outcome, such as an infection control procedure, and omission of one measure compromises the outcome. Other bundles are related to disease; these bundles include appropriate monitoring, treatment, and preventive screening indicators that may need a broad range of strategies to implement within one system of care.

Although the bundle used in Wilson and colleagues’ study comprised measures of comprehensive ambulatory care for HIV, they reflect a different type of complexity. Four measures—prescription of highly active antiretroviral therapy (HAART), prophylaxis against *Pneumocystis carinii*, screening for hepatitis C, and flu vaccination—require a provider to follow recommended guidelines. Three other measures—screening for cervical cancer, screening for tuberculosis, and suppression of viral load—are partly dependent on the patients’ behaviour and might not yield a reliable picture of organisational quality.

Suppression of viral load is a particularly difficult outcome to interpret as several variables determine the likelihood of response. In some people, suppression never occurs because of resistance to antiretroviral agents; others recently started on HAART might not yet show suppression despite responding to treatment. More importantly, some people do not show suppression because they do not adhere to their regimen.

Although these measures form an ideal package, they are affected not only by the behaviour of the provider, but also by delivery of services, the structure of the organisation, and the behaviour of patients. Ideally, high quality care provided by a model system would consistently perform the activities associated with all these measures; in truth, this rarely occurs. Even if all measures are satisfied during one time period they are not likely to be sustained over time.

High performing organisations are characterised by sustainable performance over time. As complex and dynamic units, organisations face staff turnover, changing leadership, and the effects of external factors. They have unique cultures that influence the quality and sustainability of performance.

Studies of high performing organisations find that a good infrastructure is crucial for sustained high performance. Infrastructure unifies important organisational elements, including meaningful strategy and inspired vision implemented by a consistent leadership, a commitment to meeting the expectations of consumers, a dedicated structure for quality, and constant feedback to staff. Moreover, attaining the highest levels of performance is not an overnight effort. Time is needed for whole system transformation that includes changing culture, redesigning processes, and crafting solid information systems that support useful and robust measurement, while keeping the vision of quality in sight at all times. Once this transformation is complete, appropriate measures of performance should consistently reflect improved outcomes.

A comprehensive package is necessary to measure system-wide performance, but a one time measurement is clearly not sufficient. Performance must be measured over time to identify whether quality, once achieved, is sustained. In addition, models of organisational clinical performance and frameworks for quality assessment must be united to help us understand the attributes of healthcare organisations that perform well. Frameworks such as the Malcolm Baldridge quality award criteria and the European Foundation quality management excellence model offer a starting point to link organisational variables to clinical outcomes. We have much to learn about how these models intersect, and we need a better understanding of the relation between structural elements and clinical performance. The paradigms of effectiveness research, the psychology of planned social change, organisational theory, and social anthropology may contribute to our understanding of dynamic and complex organisations. Identifying essential attributes of high performing organisations and disseminating strategies for improvement will help us to achieve consistent performance of the highest quality to benefit the general population.

What then is a high performing organisation? Even without looking at performance data, high performance is often apparent when visiting an organisation—performance data are openly displayed on the walls, staff are familiar with their performance, and they openly share ideas for improvement. Evidence of patient input and a commitment to meeting consumer expectations confirm that an organisation is performing well. When the organisational elements supporting sustainable high performance are in place, measurement across appropriate elements is bound to reflect improvement; while performance rates may not all be in the top quarter, they may well be when measured the next time.

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7 Staines AS. From quality improvement programs to improved results for patients. 18th Annual Forum on Quality Improvement in Health Care, 10 Dec 2006, Orlando, Florida, USA; session L21.
Rate control in permanent atrial fibrillation
Guidelines on the use of digoxin are inconsistent with evidence from randomised trials

Atrial fibrillation is the most common cardiac arrhythmia and it causes substantial morbidity, especially in elderly people. In June 2006, the UK National Institute for Health and Clinical Excellence (NICE) published new guidelines for control of heart rate in people with chronic atrial fibrillation. The guidelines depart from historical practice by recommending that instead of digoxin, β adrenoceptor blockers or rate limiting calcium antagonists should be the preferred initial monotherapy, except in predominantly sedentary people. Similarly, the revised 2006 joint American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) guidelines recommend the use of β blockers or calcium antagonists alone to control heart rate. We have reviewed the evidence to support this fundamental change in practice and challenge its safety.

No single definition of ideal control of heart rate in chronic atrial fibrillation exists. Rate control drugs aim to reduce heart rate at rest and during exercise, without causing excessive nocturnal bradycardia. The ultimate aim of treatment is to improve symptoms and exercise tolerance, and to prevent cardiomyopathy induced by tachycardia. To reduce morbidity, the benefits of treatment need to be weighed against the harms. A substudy of the atrial fibrillation follow-up investigation of rhythm management (AFFIRM) study found no association between achieved ventricular rate and overall survival or quality of life.

Epidemiological studies in the United Kingdom and the United States have reported an overall decline in the use of digoxin, perhaps as a result of recent recommendations. People with atrial fibrillation sometimes take β blockers or calcium antagonists for indications other than arrhythmia. In a descriptive study of the management of rate control in 2027 people, the AFFIRM investigators reported no significant difference in adequate control of heart rate at rest and exercise in people treated with β blockers alone or digoxin alone, which suggests that digoxin is still one of the first line drugs for the management of heart rate.

Of previously published systematic reviews, one highlighted the lack of evidence on optimal control of heart rate in people with atrial fibrillation and the importance of symptom control. In the other, the comparisons of β blockers and calcium antagonists with placebo were confounded by most patients on either treatment arm also being on digoxin. Clearly, larger randomised trials are needed to inform prescribing decisions. However, the current evidence on which recommendations have been made is summarised below.

We searched the literature using the Medline, PubMed, and Cochrane databases for studies published in English. By reviewing bibliographies of relevant articles we identified additional studies. We reviewed 57 studies, including 25 randomised double blind controlled trials, assessing digoxin, β blockers, calcium antagonists, and combinations for rate control in chronic atrial fibrillation. The smallest trial recruited six participants and the largest included 136. Differences in methodology and outcomes make direct comparisons difficult. Only a minority of studies reported symptom scores and patient preferences.

Digoxin has long been used for control of heart rate in chronic atrial fibrillation. It acts primarily by exerting a vagomimetic influence on the atrioventricular node and has a positive inotropic effect. It has few side effects but has a flat dose-response curve and a narrow therapeutic index, so that subtherapeutic doses are often used. It is less effective at controlling heart rate during exercise and in states of increased sympathetic activation.

In people with atrial fibrillation, β adrenoceptor blockers have heterogeneous effects on heart rate, depending on their specificity for the β receptor and how much concomitant β agonist activity they possess. Ten studies evaluated β blockers alone. The β blocker was better than digoxin in controlling heart rate at rest in only one study, although it improved heart rate during exercise in four studies. Xamoterol (discontinued in the United Kingdom in 2000) was the only β blocker to improve exercise tolerance compared with digoxin, but at the expense of worsening control of heart rate. In six other studies, exercise capacity did not improve when β blockers were used alone. In comparison, several studies have shown that better heart rate control at rest and during exercise is achieved with combined digoxin and a β blocker than with digoxin alone. However, the effect of this combination on exercise tolerance is not consistent—some studies reported deterioration in exercise capacity, some reported improvement, and others reported no change. Other side effects were reported with the use of β blockers in the above studies and, importantly, two studies reported worsening symptoms of heart failure on withdrawal of digoxin in people with heart failure.

The calcium channel blocker diltiazem has been evaluated in five studies. They found that diltiazem was better than digoxin at controlling heart rate during exercise, but not during rest, and no improvement was seen in exercise capacity. Eleven studies assessed the combination of diltiazem and digoxin; most of these reported improved heart rate control at rest and exercise when compared with digoxin alone. Two also found improved exercise tolerance with the combination. One person developed worsening heart failure...
After discontinuation of digoxin while receiving diltiazem 360 mg daily,^{30} in another study, two people with previous episodes of heart failure deteriorated when digoxin was discontinued.^{30}

Results were similar when monotherapy with verapamil was compared with digoxin. Verapamil improved heart rate during exercise compared with digoxin in three studies.^{31} Exercise tolerance with verapamil alone improved in two of the three studies that tested it.^{32} The combination of digoxin with verapamil provided better heart rate control at rest and during exercise than digoxin alone.^{20} Bradycardic episodes or pauses were sometimes seen with the combination. Exercise tolerance was not consistently improved despite better heart rate control, with some studies reporting improvement in heart rate variability, with others no change.^{18} Concomitant use of both drugs increases digoxin concentrations.

Limitations to the use of verapamil and diltiazem include their negative inotropic effects and considerable dose related side effects.

In patients with chronic atrial fibrillation, digoxin has been the mainstay of treatment for many years, so new recommendations relegating digoxin should be evidence based and safe. We believe that little evidence exists that monotherapy with β blockers or calcium channel blockers improves exercise tolerance compared with digoxin. On the contrary, there is clear evidence that when β blockers are used alone, exercise capacity may worsen, especially in people with a history of heart failure.

Similarly, little evidence exists that monotherapy with these drugs improves heart rate control at rest and during exercise compared with digoxin alone. Beneficial effects on heart rate variability, together with improved exercise tolerance, have only been shown with the combination of digoxin and a β blocker or calcium channel blocker. We believe that the combination of digoxin and a β blocker or calcium antagonist should be recommended as first line management. We emphasise that it is safest to start treatment with digoxin first.

All references are in the version on bmj.com

**Meningitis after cochlear implantation**

The risk is low, and preventive measures can reduce this further

Since the 1980s, more than 80 000 people have received cochlear implants worldwide.^{1} These implants are designed to enable people who are severely or profoundly deaf to experience sound and speech. Since 1990, implantation has become standard treatment for people who cannot communicate effectively despite well fitted hearing aids.^{2} Children who are deaf when they are born can perceive sound and learn to speak if they receive cochlear implants at a young age (ideally under 18 months).^{3} The use of cochlear implants has been thought to be safe.^{4} But since 2002 the number of patients with meningitis related to cochlear implantation has increased worldwide.^{5} Mortality and neurological complications after meningitis are high. We need to investigate the reasons for this and look at measures to reduce them.

*S. pneumoniae* is the most common organism involved.^{6} The incidence of pneumococcal meningitis was found to be more than that of an age matched cohort in the general population.^{7} Risk factors include: a particular design of implant (withdrawn from the market in 2002); inner ear malformations; leakage of cerebral spinal fluid after implantation; presence of a ventriculoperitoneal shunt; and a history of otitis media.^{6}^{8}

An animal model of implant related pneumococcal meningitis has been developed.^{9} This model has been used to quantify the bacterial threshold for pneumococcal meningitis and to study the pathogenesis of the disease and interventional strategies for reducing risk.^{10} A laboratory study showed that the presence of a cochlear implant in healthy animals reduced the number of bacteria needed to induce pneumococcal meningitis and therefore increased the risk of meningitis.^{11} Moreover, the surgical insertion of the implant, which involves fracturing the bony structures of the inner ear, was also an independent factor for subsequent risk of pneumococcal meningitis.^{12}

Patients and their carers need to be informed of the risk of developing meningitis after implantation. This is especially true for patients with pre-existing risk factors. Patients should be told that although a cochlear implant increases the relative risk of pneumococcal meningitis compared with the age matched population, the absolute risk of meningitis is still low and the benefits of the implant outweigh this low risk.^{6}^{7}^{13}

What can be done to reduce the risk of meningitis? The risk of developing meningitis after cochlear implantation can be lowered by implementing several strategies.^{7} All implant recipients should be given vaccines that cover *S. pneumoniae* as recommended by the US Centers for Disease Control and Prevention.^{14} Patients who develop symptoms of acute otitis media or bacteraemia should be assessed and treated urgently.^{7} This is particularly important for recipients of cochlear implants who have other pre-existing risk factors. Oral antibiotics may be adequate for most episodes of complicated acute otitis media in implant recipients. Intravenous antibiotics should be combined with mastoid drainage to prevent meningitis in recipients with mastoiditis.^{7} We recommend the insertion of tympanostomy tubes and the use of prophylactic antibiotics in implanted children prone to otitis media until they grow out of their susceptibility to otitis media.

All references are in the version on bmj.com
encourages a view of unselected acute older patients as a loss leader. Experienced nurses who should act as mentors, educators, and role models are being financially rewarded for leaving the bedside and taking on management roles. Once they have taken the corporate shilling, they are no longer an independent advocate for patient care. While there is no excuse for the total lack of care or professionalism described by the author, system reform could prevent a repetition of this tale. If the same performance pressures were applied to basic care and communication as for outpatient access times or financial balance then perhaps directors of nursing and trust boards would take more interest.

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What’s wrong with the NHS?

Well, if you are old and frail . . .

The personal view describing deficient care of the author’s ageing mother with mental health problems was harrowing. Although many service users do not experience such poor care, there is much objective evidence of “undignified and indifferent care” and “deep rooted and persistent attitudes by hospitals and staff to older people.” The old and mentally ill suffer discriminatory attitudes considered unacceptable in other groups.

Some of the problems described are down to lack of professionalism. Ageist attitudes in society infect clinical professionals. Patients with legitimate medical illnesses are labelled as “social admissions” or “bed blockers,” rather than being diagnosed and treated. Even though much hospital and primary care work involves older frailer patients, most medical and nursing students don’t want to work with older people. Specialist training for care of the elderly and mental health is inadequate for future needs. A 2001 national service framework recommended education and training for all professionals caring for older people, but no funds were earmarked and it hasn’t happened. The Healthcare Commission’s plan to use inspection and performance management to improve these aspects of care provides some hope. But we still have a system with a clear hierarchy of performance targets, and the “basic care” clearly lacking in this case is well down the list.

The recent report on the Maidstone and Tunbridge Wells scandal showed how external targets distort priorities. The whole performance framework for the NHS conditions are risk factors for pre-eclampsia, then inflammation may be important in the pathophysiology of pre-eclampsia.

Evidence suggests pre-eclampsia may be an inflammatory disorder. Serum CRP concentrations were significantly higher in all groups of women whose hypertension developed during pregnancy than in controls and those with chronic hypertension.

Other workers have investigated haemostatic function after pre-eclampsia to determine future risk of coronary heart disease. Patients with a history of pre-eclampsia had higher plasma concentrations than controls of von Willebrand factor and fibrinogen, which correlated with blood pressure increases but not proteinuria during the index pregnancy. The authors concluded that persistent endothelial dysfunction, continuing haemostatic alterations, and dyslipoproteinaemia after pre-eclampsia may be associated with future coronary heart disease.

Another study measured plasma thrombomodulin values in primigravids at risk of pre-eclampsia. Increases in plasma thrombomodulin were not seen until week 32 in uneventful pregnancies, but were present by week 24 in women who later developed hypertensive complications.

Thus, in addition to considering pre-eclampsia as a risk factor for future vascular events in women, it should be considered an inflammatory disease to help identify factors that can predict its severity and develop new therapeutic strategies.

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Competing interests: None declared.

Pre-eclampsia

Pre-eclampsia is an inflammatory disorder

Two recent articles highlight the link between pre-eclampsia and cardiovascular diseases including ischaemic heart disease, hypertension, and stroke. The common factor in these conditions is endothelial dysfunction. What triggers this endothelial damage is not clear. Interestingly, atherosclerosis—an initiating factor for most of these diseases—has been increasingly recognised as an inflammatory disorder. Inflammatory markers, such as C reactive protein (CRP), increase in atherosclerosis and are risk factors for ischaemic heart disease, diabetes mellitus, and cerebrovascular disease. If these different conditions are risk factors for pre-eclampsia, then inflammation may be important in the pathophysiology of pre-eclampsia.

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Competing interests: None declared.
REDDING CARBON FOOTPRINTS

How telemedicine helps

Last year Stott and Godlee asked what we as health professionals can do about climate change.1

Three examples show how doctors can reduce their carbon footprint using telemedicine. A telepaediatric service in Queensland, Australia, provides a broad range of specialist services to children living remotely.2 Telemedicine is used to manage 17% of paediatric outpatients with burns. Over six years, 1000 videoconference consultations eliminated about 1.4 million km of patient travel,3 which reduced CO₂ emissions by 39 tonnes each year. If the analysis included all telepaediatric activity (around 1300 consultations a year), the benefits would be even greater.

In the United Kingdom a neurologist now carries out half of his rural clinics via videoconferencing.4 This eliminates 2560 km of travel each year, and reduces greenhouse gas emissions by 705 kg. Even a 20% reduction in travel of all UK specialists would eliminate tonnes of greenhouse gas emissions annually.

A recent study estimated that about 36% of the 32 241 092 annual home nurse visits across Canada could be performed virtually. This would eliminate 120710648 km of travel each year and reduce greenhouse gas emissions by 33220 tonnes each year.

Despite the feasibility and value of virtual health techniques in many clinical situations, uptake remains slow. Our examples show the environmental benefit of telemedicine, which accrues each year. This should encourage doctors and professional bodies to become more socially and environmentally responsible by asking whether they could perform some of their current practice virtually.

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Competing interests: None declared.


SHOULD DRUGS BE DECRIMINALISED?

Prohibition is an ideologically driven failure

Califano’s objections to legal regulation of illicit drugs are based on misrepresentation of the reform position bolstered by irrelevant, cherry picked, or misleading facts.1 A similar piece appeared in the Financial Times4 and was systematically critiqued in the paper’s economists’ forum.3 While Califano’s rhetoric has since been moderated, and facts fine tuned, the conceptual flaws remain.

The example of Zurich’s “needle park” misrepresents legalisation as heroin was never legally supplied. As an experimental tolerance zone it was a failure. Yet, Califano fails to mention that the government responded by legalising heroin. It set up clinics for long term users, where legally prescribed heroin was used under supervision. The success of this approach on key social, health, and criminal justice indicators led to its replication by many countries including Canada, Australia, and much of mainland Europe. The UK is piloting a similar scheme.

Califano relates Italy’s high heroin addiction rate to its de facto decriminalisation for possession, but other countries with similar approaches have lower levels of addiction (Netherlands, Portugal), while the UK has a punitive approach yet higher addiction. Califano’s grotesque conflation of Italy’s decriminalisation policy with the spread of AIDS ignores the reality that supervised use of prescribed heroin with clean needles results in zero HIV transmission. Califano defies a policy that caused the tragic outcomes he identifies, while attacking advocates of responses that eliminate the problem.

Cheap illicit drugs are freely available under prohibition. Despite Califano’s assertions, once an illicit market is established (and criminal profiteers will see to that) levels of use are mostly culturally determined and demand led. Problematic drug use is not driven by changes in availability or price.3 Califano doesn’t understand that the huge profits offered by prohibition attract the violent gangsters now in control, while it is precisely because drugs are dangerous that they need to be regulated and controlled.

They are too dangerous to be left in the hands of criminals.

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Competing interests: None declared.


Debate the balance of harm

Any resolution of the debate should focus on the balance of harm.2 But neither side has defined what evidence could or should be brought to bear on this.

Clearly, being addicted to a drug is harmful, but would it be more harmful if the person could access constant strength pure drugs? I have never seen figures on mortality of long term users of pure heroin, and liberalisers need to use this evidence to make a clear case.

If drugs are decriminalised, the number of users could possibly increase. The balance of harm to society here depends on two factors—the increase in harm to addicts and the reduction of crime associated with addiction. Because a large proportion of crime is drug related, harm should be reduced. In Switzerland, medicalisation of the problem seems to have reduced the number of new addicts.3 Why did neither side quote this experiment?

The debate could be improved by prohibitionists spelling out their assumptions and evidence about how much harm would be caused by increased use, and explaining why that would be worse than the current situation where prisons and crime are dominated by the side effects of prohibition. The liberalisers should explain what sort of liberalisation is proposed and what the balance of harms is; they should admit that some things could get worse with some policy options.

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Sweden’s story in responses

Echoing Califano’s citation of Sweden’s drug policy in his contribution to the head to head debate,1 H Craabé writes:

“Around three decades ago, Sweden adopted the goal to create a ‘drug-free society.’ The result is impressive with essentially the lowest rates of drug abuse in Europe, lower than, for example, the Netherlands and much lower than the UK.”

But, replies Andrew Byrne, “Sweden’s goal of a drug-free society has been a cruel hoax on its people. Read the official EMC [European Monitoring Centre] figures from Lisbon: high rates of hepatitis C, enormous alcohol problems, amphetamines at higher rates than many other European countries. Its approach has been repressive, expensive, and largely ineffective. Along with the USA, Sweden is one of the last western countries without a needle services for drug users. This leads to HIV, bacterial infections, and other preventable and costly burdens on the Swedes.”

Stephen A Rolles concludes that there is no correlation between the harshness of prohibition’s enforcement and the use or misuse of drugs. "Some countries with harsh enforcement policies (including, prominently the UK and US) have very high levels of use while other countries with very different policies, such as Greece, or more famously, the Netherlands, have low levels of use comparable to Sweden.”

Sharon Davies letters editor, BMJ, London WC1H 9JR

1 Califano JA, Jr. Should drugs be decriminalised? No. BMJ 2007;335:967. (10 November.)

Try a little compassion

The idea that the availability of drugs creates addicts is rubbish and backs up the panoply of sanctions that support the present law.1 2

Most people accept that government is responsible for preventing the actions of some people harming others. Thus, we can harm ourselves by smoking, drinking, and overeating, but unless these habits damage others the law is indifferent, and rightly so. Laws arbitrarily criminalising the ingestion of some substances are illogical and discriminatory. Another government responsibility is to ensure that all available drugs are clean, relatively safe, licensed, and strictly controlled. Illegal drugs absolve government from this responsibility. Thus, the effects of the illegal filthy brown heroin and the sharing of “gear” in prisons (where there is still no needle exchange) is nobody’s responsibility.

Our heroin addicts are a pretty docile lot, who cause little mayhem compared with alcohol users, but the harm caused to them—HIV, hepatitis B, hepatitis C, cellulitis, and death by overdose—is caused by the illogical, uncaring ass of a law and is totally disproportionate to their “crime.”

I am surprised at the lack of compassion for drug addicts in your articles. For the past 18 months, we have asked addicts to tell us their life stories (not asking them direct questions, just listening) and have recorded and coded important events. Nearly all our addicts have had terrible, nay, horrific, childhood experiences, and I now believe there is a strong association between this and their addiction. We also noticed that many had a “dual diagnosis” of mental illness, much of which predated drug taking.

It seems to me the huge amounts of money spent in the UK to maintain the illegal drugs status quo should be used to set just laws and rescue addicts from the consequences of legalised societal neglect dressed up in a sanctimonious, self righteous law. We should also check and prevent the conditions that “create” the next generation of addicts by helping families to love and care for (not just abuse) their children and only separate children from their parents as a last resort.

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Competing interests: None declared.

1 Chan K. Should drugs be decriminalised? Yes. BMJ 2007;335:966. (10 November.)

2 Califano JA, Jr. Should drugs be decriminalised? No. BMJ 2007;335:967. (10 November.)

Look beyond legalisation

Many issues go beyond the medical arguments for the decriminalisation of drugs.1 The use of illegal drugs has increased in the past few decades. In 1970, there were around 5000 problematic drug users in the UK, and now there are between 280000 and 500000.2 The National Treatment Agency recently released figures showing that spending on drug services had increased over the past few years, although the number of people who became addiction free had hardly changed in three years (5739 drug free three years ago and 5829 in 2006).3 Thus, we are not succeeding in treating addiction.

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Competing interests: None declared.

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PROBIT cohort to assess important health outcomes at older ages that observational studies had associated with infant feeding. Cluster randomised allocation of the breastfeeding promotion intervention yielded two groups that differed greatly in the duration and exclusivity of breast feeding. This created a unique opportunity to study longer term child health outcomes, including growth, adiposity, neurocognitive development, behaviour, and dental caries, as well as asthma and allergy. 1,2

In our recent BMJ paper reporting on the last two outcomes, my colleagues and I did not compare any breast feeding with no breast feeding. 3 All PROBIT infants were breast fed at birth; the difference between the two randomised groups was limited to the duration and exclusivity of breast feeding. Our inference was thus not that “breast feeding has no effect,” but that prolonged and exclusive breast feeding did not protect against asthma and allergy. That inference is justified by the randomised design, intention to treat analysis, and observed results.

Finally, the wide confidence intervals noted by Silvers et al around the cluster adjusted odds ratios for the skin prick test results have nothing to do with “important confounding and predictor variables.” 4 As shown in table 1, and as expected from the randomised allocation, the two groups had similar baseline characteristics. 4 The wide confidence intervals are a function of the high degree of clustering for the skin prick test results (table 5). Clustering was far less evident for the allergic symptoms and diagnoses (table 4) and for the sensitivity analysis for the skin prick tests (table 6), with considerably narrower confidence intervals.

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Competing interests: None declared.

1 Silvers KM, Epton MJ, Frampton CM. Study was not designed to test the hypothesis. BMJ 2007;335:899. (3 November.) doi:10.1136/bmj.91981.395197.BE

POVERTY ON THE DOORSTEP

Summary of responses
Why do people ignore poverty on their doorstep? 2 They don’t, says Peter West. “Many people help, for example, through reading schemes in schools and by working in many different community groups. In addition, many British people give money to charities to help improve the social conditions of poor people.” 3

It is not surprising that rich Britons concentrate their charitable efforts on poverty in the developing world, adds Rachel Walpole. “It is not a matter of whether or not our fellow Britons are poor through their own choices; it is just that in worldwide terms, they are rich.”

Our choices define and divide us, says Alison Munns, who lists as her competing interests “inner ‘new town’ GP, socialist, mother, observer of the genetic inheritance of incapacity benefit (families where no adult has worked in two generations), sponsor of an African child, and supporter of local charities.” She describes waiting for her son to finish karate training in “a community hall full of children who are courteous, respectful, and working hard. In sharp contrast outside are children of the same age trampling on the flower beds and hurling stones and abuse at the shop windows. It is not cash, connections, or class that separate them. Someone made a choice.”

“You did,” responds L S Lewis. And it is indeed cash, connections, or class that separate them.

But Munns responds “I know that some in the club have very little in terms of material possessions. I know that some of the children outside have more in the way of material possessions than my child. They or their families made the choice to spend that which they have (time and money) in the way that they do. We will get nowhere in understanding or changing our world by saying that those families who choose to let their children damage property and insult adults have no choice when other families (who objectively have less resource) do not behave in that way.”

Choice requires insight, points out Richard Bartley, quoting Ruskin: “Education is not that one knows more, but that one behaves differently.”

Indeed, so the state must act as a catalyst that allows people to drag themselves out of poverty by making better choices, says Ben Dean. Munns concludes: “I know why I make the choices I do. Other people know why they make the choices that they do. But we shy away from asking about them. Much easier to say they have no choice or that they do not have the capacity to make a true choice as they lack insight. I don’t think as a society we want to hear the answers that we would get if we did ask. But if we don’t the elephant stays in the room.”

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Competing interests: None declared.

1 Cohen D. Why do people ignore poverty on their own doorstep? BMJ 2007;335:888. (27 October.)
2 Electronic responses. Why do people ignore poverty on their own doorstep? bmj.com 2007;335 www.bmj.com/cgi/eletters/335/7625/888

GMC AND THE MMC COLLAPSE

Role of the PLAB test
The summary of responses published under the banner “GMC and the MMC collapse” contains several inaccurate statements about the role of the General Medical Council and that of the Professional and Linguistic Assessments Board (PLAB) test. 1 As the medical regulator, the GMC sets the standards of practice in the UK. It has no role in workforce planning, including recruitment and retention of doctors to work in the NHS. The GMC has never conducted a recruitment drive for medical staff either within the UK or overseas.

The PLAB test is one way that international medical graduates (IMGs) can show their medical skills and knowledge in order to join the UK medical register. It is not a tool for controlling the number of doctors entering the UK or for determining who should get jobs. If, after considering the relevant information, IMGs wish to take the PLAB test, we do not think they should be compelled to come to the UK to sit part 1 of the test. To withdraw or ration the PLAB test would deny IMGs the opportunity to demonstrate their knowledge and skills and to compete for jobs. That would be unfair.

For the past 10 years we have warned prospective candidates for the PLAB test to check the job situation before applying for the test. The GMC website clearly states that the job situation has been increasingly difficult for IMGs for several years.

Finally, the GMC makes no profit from the PLAB test. The fees pay only for the costs of running the test.

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Competing interests: None declared.

1 Davies S. Summary of responses. BMJ 2007;335:842. (27 October.)
Report says consultant contract has not increased productivity despite 27% pay rise

Adrian O'Dowd LONDON

Consultants in England are now being paid on average 27% more than they were three years ago but are working fewer hours and are less productive, says a highly critical report published by MPs.

Doctors’ leaders, however, have rejected much of what the report says, claiming that criticism of consultants and their pay is “unfair and relentless.”

The parliamentary Committee of Public Accounts’ report into the new consultants’ contract, published this week, says that it has been a costly failure so far and that its introduction in 2003 has cost £150m (€210m; $310m) more than the government estimated. It says that most of the contract’s aims had failed to materialise.

The Department of Health agreed a new national contract for NHS consultants in England in October 2003 after three years of negotiations with staff and managers’ representatives. It was the first major revision of the consultant contract for more than 50 years.

However, say the MPs, implementation of the contract was rushed, and many of the intended benefits have not materialised.

The report says that although consultants’ pay has, on average, increased from £86746 to £109974—a 27% rise rather than the 15% the government predicted—and the number of hours they work has fallen, as yet no measurable improvements in productivity have been achieved.

Jonathan Fielden, chairman of the BMA’s Central Consultants and Specialists Committee, reacted angrily, saying: “The chairman of the Committee of Public Accounts … ignores the vast efforts that consultants have made to reduce waiting times and improve patient care and fails to appreciate the enormous pressure that hospital trusts have been under to meet government targets. Our most senior doctors are worth every penny.”


Practice based commissioning is delivering only “modest” results

Zosia Kmietowicz LONDON

Practice based commissioning is failing to deliver the benefit for patients envisaged by the government because of a lack of incentives to get GPs on board, says the public spending watchdog.

The policy to devolve responsibility for commissioning services from primary care trusts to general practices at the local level was introduced in 2005-6 and is a main plank of the NHS reform programme.

But the Audit Commission says it is suffering from poor support from primary care trusts for GPs to develop projects—including accurate information on budgets, what savings have been made, and how these savings could be used to develop other services.

“Unless you get the financial infrastructure right it [practice based commissioning] won’t work,” said Andy McKeon, managing director for health at the Audit Commission. For its new report the commission interviewed staff at 16 primary care trusts and three general practices and conducted a survey of 623 general practices, to which 122 GPs and practice managers (20%) replied.

“The scale of service redesign achieved through PBC [practice based commissioning] has been modest so far,” says the report. Most practices reported that they had neither the resources nor the time to implement commissioning; only 18% of practices responded positively to both questions.

Nearly three quarters of survey respondents said that their primary care trust was not supporting them in building capacity to implement commissioning.

Putting Commissioning into Practice is available at www.audit-commission.gov.uk.
**IN BRIEF**

**Use of osteoarthritis drug is suspended in UK:** The UK Medicines and Healthcare Products Regulatory Agency has suspended sales of the osteoarthritis drug lumiracoxib (Prexige), pending a Europe-wide review next month. The latest global safety data have shown an increase in the risk of serious liver problems with the licensed dose of 100 mg after treatment of less than a month. Around 5000 UK patients have received the drug since it became available in 2005, and 8.5 million prescriptions have been written worldwide. (See [www.mhra.gov.uk](http://www.mhra.gov.uk))

**Additional box warning for rosiglitazone:** GlaxoSmithKline has agreed to upgrade the information in its warning box on rosiglitazone (Avandia), a drug approved in 1999 for the treatment of type 2 diabetes. The warning refers to a meta-analysis of 62 clinical studies involving 14 327 patients that showed an increased risk of ischaemic heart attacks and angina, but it states that the available data on the risks are inconclusive. (See [www.fda.gov](http://www.fda.gov))

**HIV prevention in China gets cash boost:** The Bill & Melinda Gates Foundation has pledged $50m (£24m; €34m) to help the Chinese government and aid organisations increase access to HIV prevention among people in high risk groups, such as injecting drug users, sex workers, and men who have sex with men. The money will also be used to combat discrimination against HIV positive people.

**Ireland has rise in emergency admissions for pancreatitis:** The number of emergency admissions for acute pancreatitis in Ireland has grown by 54% in eight years, from 622 in 1997 to 959 in 2004, shows research (Journal of Public Health 2007;29:398-404). The number admitted with accompanying alcohol misuse has also risen, from almost 14% of admissions for acute pancreatitis to just over 23%, reflecting a rise in per capita alcohol consumption, say the authors.

**Dutch group calls for cash incentives for organ donation:** Financial incentives to promote organ donation from living donors is worth considering morally and practically, says the Netherlands’ Centre for Ethics and Health ([www.ceg](http://www.ceg)). It has advised the Dutch government that the best option would be to offer lifelong exemption from health insurance, estimated to be worth around €60 000 ( £29 000; $59 000) per person.

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**Ministers veto equal access for children of non-Israeli citizens**

**Judy Siegel-Itzkovich** JERUSALEM

A bill that would have entitled children who live in Israel but lack citizenship to access health services in the same way as their Israeli peers has been vetoed by the ministerial committee on legislation.

The finance ministry opposed it on the grounds that it would “encourage illegal immigration” to the country, and the health ministry said that existing arrangements met the health needs of all children residing in Israel who are not citizens.

The bill was tabled by Physicians for Human Rights-Israel as an amendment to the National Health Insurance Law of 1994 and presented by the left wing member of the Knesset (the Israeli parliament) Dov Hanin. An appeal seems unlikely, but he will now try to persuade a cabinet minister to bring it before the committee again.

In February 2001 an arrangement was made to provide health services to children who are Israeli residents but not citizens. These included children of foreign workers, new immigrants whose parents’ citizenship status had not yet been recognised, refugees, and children of “mixed” parentage.

The Meuhedet health maintenance organisation, the country’s third largest, was contracted to provide these children with health services. But Physicians for Human Rights-Israel says that in practice many of these children are not getting the care they need and that their lives are already difficult.

The examples they cite include children having to wait six months before becoming eligible for health services and others being excluded from treatment for certain conditions that they had before they arrived in Israel.

Children who are not citizens cannot receive some services if their parents don’t register and pay a user’s fee—unlike Israeli citizens, who are automatically entitled to these services. There is also no mechanism to exempt certain families from having to pay fees, says the organisation.

If a child’s father is an Israeli citizen but the mother is a foreigner the couple must undergo expensive and lengthy genetic testing to prove that they are the parents before they can register their child with Meuhedet. If one (or both) of the parents is Palestinian they cannot receive services from Meuhedet under the 2001 arrangement. And children living alone in Israel and unable to register are left without any health care, says the human rights organisation.

Ran Cohen, director for migrants and residents without official status at Physicians for Human Rights-Israel, said that the organisation would continue to fight for the right to health services for all children living in Israel.

“This is governmental refusal to recognise the suffering of thousands of children, and [it] also violates international agreements to which Israel has committed itself,” he said.

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**Swiss hospitals admit to allowing assisted suicide on their wards under guidelines**

**Annette Tuffs** HEIDELBERG

The University Hospital in Bern, Switzerland, admitted last week that an assisted suicide of a terminally ill patient took place on its premises in April 2007. The hospital’s management and its ethics committee sanctioned the assisted suicide of a patient with cancer who was too ill to be transported anywhere else, a hospital spokesperson said.

The patient was helped by a member of the Swiss organisation Exit, which provides assistance to patients living in Switzerland who wish to commit suicide. Helping terminally ill patients to commit suicide is not illegal in Switzerland.

After the Bern hospital’s announcement the university hospitals of Lausanne and Geneva also admitted that assisted suicides had taken place on their premises. The Swiss Academy of Medical and Natural Sciences ([www.samw.ch](http://www.samw.ch)) ruled in 2007 that hospitals could decide for themselves whether or not to allow assisted suicide.

Most hospitals in Switzerland have established guidelines on assisted suicide that require a patient’s mental capacity to be assessed and that assisted suicide can take place in hospital only if it is impossible for the patient to be taken home or to other private settings. Each case must be individually approved by a special hospital committee.

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Threat to break patents saves Brazil $1bn in cost of HIV treatment, study shows

Michael Day LONDON
Brazil’s policy of bargaining with drug companies over the cost of antiretrovirals—and flouting some international patents—saved the country $1bn (£0.5bn; €0.7bn) between 2001 and 2005, a study has found.

The researchers, from the Harvard School of Public Health, decided to carry out a detailed analysis of the cost of drugs for HIV in Brazil because they thought that little was known about the long term costs associated with providing highly active antiretrovirals to HIV patients in developing countries (PLoS Medicine 2007;4(11):e305).

Brazil has free and universal access to antiretrovirals and is considered a model for other countries trying to boost their public treatment programmes.

US companies are fined for payments to surgeons

Janice Hopkins Tanne NEW YORK
Five US manufacturers of hip and knee replacements have settled with the federal government after being accused of paying orthopaedic surgeons to use their products. Four of the companies will pay $311m (£150m; €212m) in fines to the federal government.

The companies have admitted paying many orthopaedic surgeons “consulting fees” to use their devices.

The settlement was announced on 27 September by Christopher Christie, US Department of Justice attorney for northern New Jersey. When the Department of Justice was asked whether any action would be taken against the surgeons who accepted the payments, a spokesman would say only that the investigation was ongoing.

Criminal complaints were filed against four of the companies, charging them with conspiring to violate federal laws against kickbacks (unlawful payments by companies to individuals to use the companies’ products). The four companies are Zimmer, DePuy Orthopaedics, Biomet, and Smith & Nephew. A fifth company, Stryker Orthopaedics, cooperated with the US attorney’s office and will not pay a fine.

The amount of the fines reflects the companies’ market share, the justice department said. Zimmer will pay $170m, DePuy $85m, Smith & Nephew $29m, and Biomet $27m.

The four companies were accused in the criminal complaint of “using consulting agreements with orthopaedic surgeons as inducements to use a particular company’s artificial hip and knee reconstruction and replacement products.”

The complaint said, “The investigation revealed that this was a common practice by the companies from at least 2002 through 2006.”

Surgeons who had agreements were paid “tens to hundreds of thousands of dollars per year for consulting contracts and were often lavished with trips and other expensive perquisites,” the justice department’s press release says.

As part of the settlement the companies agreed to change their practices in dealing with doctors, educate their sales staff, and follow rules on compliance, to avoid further prosecution.
Return to the true path?

Nicholas Timmins considers whether the government’s decision to cut back its planned use of the private sector in the NHS is pragmatic or ideological

Nicholas Timmins FINANCIAL TIMES
Happy trade unions, a fuming private sector, bewildered taxpayers, patients who are still waiting, and—almost certainly—an inquiry by the National Audit Office.

That was the outcome of health secretary Alan Johnson’s announcement last week that only three more schemes are definitely going ahead from the second wave of contracts for diagnostic services and new independent sector treatment centres in England.

Mr Johnson’s written statement dealt merely with the 16 contracts still extant from a negotiation that has been going on for three years now. Six other schemes were cancelled. Seven remain under procurement—although the health department says that there is “no guarantee” they will go ahead, despite giving private assurances to the companies that they will.

But behind Mr Johnson’s studiedly low key statement was a bigger picture. What, under Tony Blair’s government, was originally meant to be about £6bn (€8.4bn; $12.3bn) worth of business for the private sector over five years has now shrunk in stages to no more than around £2.5bn worth. Even this figure assumes that all the remaining schemes go ahead. If they don’t the final total may be nearer £2bn.

In other words a programme launched with two key objectives—providing some extra capacity for the NHS but at the same time deliberately injecting some private competition into the supply of care—has been cut by around two thirds.

It is that second objective of extra competition that the Brown government “no longer seems quite to believe in or be willing to pay for,” says Julian Le Grand, the London School of Economics professor who was Tony Blair’s Downing Street health adviser.

Mr Johnson insisted that slashing the size of the programme “does not represent a change in policy.” The independent sector retains “an important and increasing role in the NHS,” he said. But Karen Jennings, head of health at the public sector trade union Unison, welcomed what she called “a change of emphasis.” Jonathan Fielden, chairman of the BMA’s Central Consultants and Specialists Committee, said it was “a welcome turnaround.”

The health department admitted that it has already spent almost £93m on the procurement, with more to come as it pays out millions in private sector costs (potentially tens of millions) for cancelling contracts at the last minute. Mr Fielden said it was “a crying shame” that so much taxpayers’ money has been wasted. Conservative MPs take an even stronger view, and the National Audit Office hinted that it would probably accede to their demands for an inquiry.

Mr Johnson cited improved performance and productivity by the NHS itself as the reason for cancelling the deals. He insisted that his position was “pragmatic not ideological” and was to do with value for money. Primary care trusts can still—and will—contract locally with the independent sector, he said.

Better performance in the NHS was also the reason Mr Johnson gave for cancelling an already running contract for diagnostics with Care UK in the West Midlands. Less than 5% of the contract’s

Government warns of tough competition for posts next year

Lynn Eaton LONDON
The Appeal Court’s ruling against the Department of Health’s plan to restrict the number of medical graduates from outside the European Union who can apply for UK training posts will mean an average of three doctors applying for each post in 2008, government officials say.

The health department plans to appeal against the judges’ ruling on the case, which was brought by the British Association for Physicians of Indian Origin (BAPIO) (BMJ 2007;335:1009, 17 Nov). But this could take several months. Meanwhile the status quo will prevail—and department officials say that this will be the case until the 2009 intake at the earliest.

The Appeal Court’s ruling means that medical graduates who gained their degree overseas and who are already working in Britain will be able to apply in the next recruitment round, which starts in January. Additionally, an unknown number of non-EU medical graduates who are not currently in the UK could also apply for training posts.

Doctors protest at the application chaos

The Modernising Medical Careers team announced in October that recruitment in 2008 would be carried out locally by individual deaneries and that more than one recruitment round would take place next year. The first round begins in January.

A health department official could not confirm reports that as many as 2000 additional training posts will be created for the January round.

It is understood that the department is working with the Home Office to see how the current immigration rules might be amended from 2009 to ensure that trainee doctors from the UK face less competition in future.

Donaldson defends decision not to resign over training chaos

Adrian O’Dowd LONDON
England’s chief medical officer, Liam Donaldson, has told MPs that he was right not to resign over the chaotic recruitment system for junior doctors.

Professor Donaldson, giving evidence to the parliamentary health select committee, said he would not take personal and sole responsibility for the problems faced by junior doctors this year when they applied for posts under the new Modernising Medical Careers (MMC) programme.

The committee, in the first evidence session of its inquiry into the MMC programme, asked why Professor Donaldson had not felt it appropriate to leave his job, considering the scale of the problems. Thousands of junior doctors failed to find training places through the programme, and many complained that the new system failed to take proper account of their achievements.

Professor Donaldson told the committee: “The experience for the junior doctors con-
Hospitals without expertise should not offer trauma care

Zosia Kmietowicz LONDON

Less than half of people who sustain serious injuries receive good care before they arrive in an emergency department, a new report says. And it says that such failings in care continue once the patients have arrived at hospital.

A team approach is needed to deliver effective care for trauma patients in the same way that cancer services teams have worked across healthcare disciplines to improve outcomes, said Simon Carter, one of the report’s authors.

“We need to see significant improvements made now to pre-hospital and hospital trauma care in order to prevent the unnecessary death of young patients, with its tragic consequences for families, not to mention the economic cost to the nation,” he added.

The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) looked at 795 patients who had a severe injury between February and April 2006 and who were treated in hospitals in England, Wales, Northern Ireland, and the offshore islands. Most of the injuries were the result of road traffic incidents or falls from a height.

The report found that 20% of hospitals did not have a dedicated trauma team and that more than half of patients who needed neurological services were taken to a hospital without such facilities. Some hospitals should consider opting out of providing trauma care because they do not have the expertise to provide the required level of care, said George Finlay, a clinical coordinator at NCEPOD and one of the authors of the study.

“We need to look at how we can organise trauma care on a regional basis. For example, we need protocols for ambulance crews to bypass the nearest hospital if this is not the most appropriate hospital,” he said.

Trauma is the leading cause of death in the first 40 years of life and is also a large socioeconomic burden: for every death from trauma there are two survivors with a serious or permanent disability. Hospitals that deal with more than 20 severe trauma cases a week have a better quality of care, he explained.

The report found other failings once patients have reached hospital. Medical staff often did not appreciate the severity of the injuries, displayed little urgency in caring for them, and made incorrect clinical decisions.

The report calls for all hospital trusts to have 24 hour trauma teams with a consultant in charge of managing the care of severely injured patients. Trauma services may need to be reconfigured in some regions and should consider putting a doctor in with the ambulance crew in cases of trauma. The report also recommends that patients with severe head injuries should undergo computed tomography within one hour of admission to hospital.

Another of the study’s authors, Ian Martin, lead clinical coordinator at NCEPOD, said, “Patients with severe head injury require immediate airway control and early arrival at a centre with on-site neurosurgical services.”

Trauma: Who Cares? can be seen at www.ncepod.org.uk
Papworth Hospital can resume performing heart transplantsations, says Healthcare Commission

Caroline White LONDON

England’s health services watchdog, the Healthcare Commission, has said that surgeons can resume heart transplant surgery at Papworth Hospital near Cambridge.

Earlier this month the commission had suspended operations pending an investigation into the higher than expected mortality found among 20 people who received heart transplants at the hospital this year (BMJ 2007;335:955, 10 Nov).

The commission’s two week review, which looked at the clinical care provided to eight patients who died and the trust’s response to the deaths, concluded that there were no common factors to explain the deaths, which could not have been prevented. And there was no evidence that care had been inadequate, it said.

The selection of patients deemed suitable for surgery was “extremely rigorous,” and the decision to transplant had been appropriate in all cases, said the commission.

The trust had also acted responsibly by promptly alerting the chief medical officer to the higher than expected death rate and by seeking external expertise, the commission said.

The commission found that the periods that transplanted hearts were without a blood supply (ischaemic time) were longer in those patients who died than in other patients; but these were, on average, lower than in previous years at the trust and in line with the national average.

It says too that some patients had a combination of factors that increased their risk of transplant failure—such as being older, a long ischaemic time, and a mismatch in size.

UK says that the rights of

Susan Mayor LONDON

The UK government is to review human rights legislation to ensure that the rights of all elderly people in care are protected. Its decision came in response to a report that highlighted particular problems affecting this age group.

The proposal should close a loophole that has meant that elderly people living in privately owned care homes were not covered by the Human Rights Act and could therefore be evicted.

In its response to the report on the rights of older people in care from the parliamentary joint select committee on human rights, published in July (BMJ 2007;335:367), the government has agreed that legislation needs to adequately protect the rights of such people.

It said that it will consider extending legislation on the duty of the public sector in its proposed Equality Bill, which should be introduced in this parliamentary session, to cover

Cancer incidence among young is higher in the south

Roger Dobson ABERGAVENNY

In England the South East had the highest incidence of cancer among teenagers and young adults, a new study shows, while the North East had the lowest. And there was a trend for cancer incidence in this age group to be lower in local wards with greater deprivation, it found.

The study, which involved more than 35000 people aged 13 to 24, gives details of the incidence of specific cancers in the nine Government Office Regions in England and according to levels of deprivation in the census ward of residence of patients at the time of diagnosis (British Journal of Cancer 2007;96:1760-6 2007).

It shows that cancers in this age group were more common in less deprived areas (P for trend <0.001).

“These cancer incidence patterns differ from those seen in both children and older adults and have implications for aetiology and prevention,” the authors write.

They say that although previous studies have looked at variability in the incidence of cancer at different ages in Britain, the fact that cancer is more likely to occur in middle aged and elderly people (more than 75% of cancers are in people aged over 60) has masked patterns of disease among young people.

The study used data from all nine regional cancer registries in England from 1979 to 2001 to look at variability in the incidence of cancer by region and deprivation score of census ward (as measured by the Townsend deprivation index) among people aged 13 to 24.

The results showed that 35291 cases of cancer occurred in 186 million person years at risk, giving an overall incidence of 188 cases per million person years at risk. The incidence varied from 173 in the North East to 208 in the South East and South West.

Although there was a significant trend towards a lower incidence with increasing deprivation, the patterns of incidence varied by diagnostic group.

The incidence of leukaemia, particularly that of chronic myeloid leukaemia, was highest in the most deprived areas, but no significant trends were shown in the incidence of acute lymphoblastic leukaemia or myeloid leukaemia.
Controversial embryo bill receives second reading in Lords

Lynn Eaton LONDON

The government’s human embryology and fertilisation bill had its second reading in the House of Lords this week, amid concerns that it would enable lesbian couples to have fertility treatment more easily. Some groups have also objected to the fact that it allows the creation of “interspecies embryos” for research purposes.

The bill drops the requirement that fertility specialists, when considering whether a woman is suitable for fertility treatment, have to account of the need of the child for a father. This has not prevented lesbians from accessing in vitro fertilisation in the past, but its removal will deal with government concerns that the clause could amount to discrimination in the provision of goods and services.

The bill also recognises same sex couples as legal parents, in keeping with changes in the law allowing civil partnerships.

Introducing the bill on Tuesday in the House of Lords, the health minister Ara Darzi explained that the government wanted to ensure that the law remained effective and fit for purpose in the 21st century. The bill would help maintain the UK’s position as a world leader in groundbreaking research into the treatment of serious diseases, he said, including through embryonic stem cell research.

Lord Darzi said, “Technology has moved on, and so have attitudes. There are, for example, novel ways of creating embryos for research.”

The bill would ensure that all embryos, whether inside or outside the body, were covered by regulation. The existing law covers only human fertilisation and does not adequately cover emerging processes for creating embryos, he said.

The House of Lords discussed proposals to clone embryos from women who have mitochondrial diseases with donated mitochondria from another woman and sperm from the first woman’s partner, thus ensuring that the diseases were not passed on to the child.

Incidence of certain types of cancer (cases per million person years at risk) among people aged 13-24 years in England

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Government office region</th>
<th>All regions</th>
<th>P value for variability</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>North East</td>
<td>North West</td>
<td>Yorkshire &amp; Humbersides</td>
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<tr>
<td>Germ cell tumours</td>
<td>21.5</td>
<td>24.7</td>
<td>24.1</td>
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<tr>
<td>Leukaemia</td>
<td>21.1</td>
<td>20.7</td>
<td>19.6</td>
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<tr>
<td>Lymphoma</td>
<td>39.9</td>
<td>42.2</td>
<td>42.3</td>
</tr>
<tr>
<td>Melanoma</td>
<td>13.3</td>
<td>15</td>
<td>15.6</td>
</tr>
<tr>
<td>All cancers</td>
<td>173.1</td>
<td>185</td>
<td>185.4</td>
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</tbody>
</table>

Source: British Journal of Cancer

“There is consistent evidence of a role for infections in leukaemia in young children, but other factors such as traffic density and benzene exposure should be explored [in this age group], especially in densely populated areas with high leukaemia incidence, such as London and the South East,” says the report.

The incidence of lymphoma fell as deprivation increased.

Nigel Ellis, head of investigations at the commission, said that the safeguards and checks the commission had requested of the trust would ensure that “everything possible is being done to protect heart transplant patients,” and he added that the watchdog would keep a close eye on death rates at the trust over the next few months.

The trust has fully accepted all the review’s recommendations.

Steven Tsui, clinical director for transplant services at the trust, said, “We believe the process we have gone through in this review has been rigorous and proper and will help to continue to provide the best possible outcomes for our patients.”

Intervention at Papworth Hospital NHS Foundation Trust is at www.healthcarecommission.org.uk.

But none of the cases reviewed was at such a high risk that the transplantation should not have gone ahead, the report says.

The commission has recommended that the trust take all possible steps to minimise the time that any organ is without a blood supply, particularly in cases where more than one organ is being retrieved from the same donor.

It recommends that consideration also be given to the feasibility of introducing a national standard on information that trusts should be given about retrieved organs.

The Department of Health should also set a mortality threshold for the trust, breaches of which should prompt a wider review of procedures, it said.

all elderly people must be protected

age and that it will look at whether there is a case for prohibiting age discrimination in the provision of goods and services.

The law lords ruled this summer that the Human Rights Act did not cover elderly people being cared for in private nursing homes.

It made its ruling in relation to an 84 year old woman from Birmingham who had been threatened with eviction after a disagreement between her family and the company running the private nursing home where she was living. The legal argument centred on whether the care home was providing a public function and was therefore bound by the Human Rights Act. The law lords ruled that it was not.

At the time the charity Help the Aged said that the ruling left vulnerable elderly people open to “neglect, abuse, and eviction, without redress through the Human Rights Act.”

In its report the joint committee said that the human rights of care home residents should be more explicitly spelt out in care home standards, “to avoid the unfortunate impression that the human rights of people in care homes are less important and less enforceable than the human rights of patients in hospitals.”


Technology has superseded old ways to create embryos

Controversial embryo bill receives second reading in Lords

Lynn Eaton LONDON

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Antiobesity drug rimonabant linked to anxiety and depression

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<thead>
<tr>
<th>EFFECT OF RIMONABANT ON DEPRESSION AND ANXIETY</th>
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<tbody>
<tr>
<td>Depression</td>
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<tr>
<td>RIO Europe</td>
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<td>RIO Lipids</td>
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<td>RIO North America</td>
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<td>RIO Diabetes</td>
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<td>RIO Overall</td>
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Adapted from Lancet 2007;370:1706-13

Soldiers’ mental health deteriorates for months after returning from Iraq

The US Department of Defense uses a brief questionnaire and interview to screen all soldiers returning from Iraq for evidence of mental health problems. The programme began as a single screen soon after coming home, but soldiers are now screened a second time, three to six months later. An analysis of the first 88235 soldiers to have both screens shows that their mental health worsens during the six months or so between screens. The proportion of soldiers vulnerable to post-traumatic stress disorder increased from 11.8% to 16.7% for regular soldiers and from 12.7% to 24.5% for reserves. The proportion screening positive for depression, interpersonal aggression, and overall mental health risk also increased. So did use of mental health services.

Both screening rounds together found that 20% of regular soldiers and more than 40% of reserves returning from Iraq had some kind of mental health problem.

Overall, reserves seemed to suffer more than regular soldiers, despite reporting similar rates of traumatic combat experiences. The stresses of returning to civilian life could be to blame, say the authors. But reserves may be in more of a hurry than regulars to report health problems, because their standard military health insurance runs out after six months.

JAMA 2007;298:2141-8

Vaccine preventable diseases fall to all time low in the US

The incidence of many infectious diseases has fallen to an all time low in the US thanks to vaccination programmes for infants and children, say researchers from the Centers for Disease Control and Prevention in Atlanta. A systematic examination of national data from before and after the introduction of 12 childhood vaccines shows dramatic declines of 99-100% in the number of cases of diphtheria, measles, mumps, polio, and rubella. Cases of mumps, tetanus, and pertussis have fallen by 92-96% since vaccination was introduced in 1980. In 2006 no deaths from diphtheria, measles, mumps, polio, or rubella were reported.

More recently, vaccination against Haemophilus influenzae type b (Hib) has been associated with a 99.5% reduction in deaths from invasive disease. Deaths from hepatitis A, hepatitis B, and varicella have fallen by more than 80% since vaccines were introduced. Deaths from invasive pneumococcal disease have fallen by a more modest 25.4%.

The researchers estimate that routine childhood vaccinations save about 33000 lives in every birth cohort and save society about $43bn (£21bn; €29bn) in direct costs, disability, and lost productivity from vaccine preventable diseases.

JAMA 2007;298:2155-63

Disagreement over intellectual property delays health strategy for poor countries

The controversial matter of intellectual property is holding up the development of an important multinational strategy to tackle diseases that afflict mainly poor countries.

An editorial describes how strategic talks between 140 member states of the World Health Organization were suspended earlier this month when delegates failed to reach agreement after six days of negotiations. They won’t be resumed until spring next year.

The whole process has been plagued by disagreements over protection of intellectual property, and in a linked correspondence published in the Lancet, health officials from Thailand, the Maldives, India, and Sri Lanka accuse the drug industry of hijacking a web-based public hearing in an attempt to influence the strategy’s final content (doi: 10.1016/S0140-6736(07)61689-4). Forty three of the 68 contributions to the hearing supported robust measures to protect intellectual property, including 14 contributions from patient advocacy groups, and three from professional organisations. Eleven of the 14 patient groups and all three professional organisations had taken money directly or indirectly from drug companies.

Contributors to public hearings should be required to declare competing interests, say the officials.

Lancet 2007;370:1666
Cituximab buys more time for some people with advanced colorectal cancer

Traditional cytotoxic treatments for cancer preferentially kill rapidly dividing cells. More recently, researchers have turned their attention to the growth factors expressed by some cancers, targeting them with specifically designed monoclonal antibodies. Cituximab is one such antibody, directed against the epidermal growth factor receptor, which is often expressed in colorectal cancers.

In one trial, infusions of the antibody prolonged survival by about six weeks for patients with advanced colorectal cancer who had failed to respond to the recommended chemotherapy. All 572 participants had cancers expressing the receptor and all had the best available supportive care. Controls who had no other treatment survived a median of only 4.6 months.

Most people who had weekly cituximab infusions developed a characteristic rash (88.6% v 16.1%, P<0.001), and about one in five had an infusion reaction. Serious adverse events including pain were more common in the cituximab group. But patients given the drug still reported a better quality of life than controls at eight weeks.

Cituximab had a measurable effect on less than half the patients who received it. So a marker for those most likely to benefit would be useful, say the authors. In this trial, patients who had a severe drug rash survived the longest (median 8.4 months).

Teriparatide better than alendronate for steroid induced osteoporosis

Three experts have called on the federal government to come up with a national strategy to find the necessary “surge capacity” and to make sure it is properly funded. The private health sector is unlikely to provide the extra beds and personnel on its own, particularly in a perverse system that makes it more financially attractive to close emergency departments than to keep them open.

Local hospitals can help by sharing information about capacity and staffing, and by looking locally for extra space in schools, churches, and other community buildings, say the experts. In the meantime, they urge the federal government to do something urgently about the estimated 116,000 shortfall in available nurses. In 2006, nearly 43,000 qualified applicants were turned away from nursing colleges because of shortages of teachers and classrooms. Being prepared means extra professionals as well as buildings and equipment. Nursing shortages leave a big hole in current disaster plans.

People walk further wearing pedometers

Pedometers are a cheap, easy, popular, and apparently effective way to motivate people to take more exercise. Pooled results from eight randomised controlled trials and 18 observational studies suggest that people who use a pedometer take about 2000 more steps a day than they otherwise would, walking about one extra mile. In this systematic review, use of a pedometer was associated with a 27% increase in physical activity, a decrease in body mass index of 0.38 (P=0.03), and a 3.8 mm Hg reduction in systolic blood pressure (P<0.001). Pedometers worked best for people given a target number of steps—say 10,000—to aim for each day.

Most of the participants in these studies were women under 60. Pedometers may not be associated with these kinds of health benefits in men or in older adults of either sex, say the researchers. The studies they reviewed were reasonably good quality, but still fairly small, brief, and heterogeneous. A programme of larger trials that include men and women, old and young, could help to disentangle the effects of pedometers from the effects of the exercise counselling, step diaries, and healthier eating that often come with them.
Should all medical students be graduates first?

**YES**

Ed Peile

professor of medical education, Institute of Clinical Education, Medical School, University of Warwick, Coventry

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We must stop the headlong rush of pupils going straight from school into five year long medical courses. Bright teenagers are encouraged by teachers and parents to maximise their potential by aiming for the kudos and earning power of medicine. As consultants in their 20s, they will have little more breadth to their life experience than when they were studying during the week and spending their weekends meeting the unwritten requirements for school leavers to get into medical school—by working in care homes, hiking for the Duke of Edinburgh Gold Awards, and practising for grade VIII cello.

If we do what we have always done, we will always get a niche medical workforce. Diversity of the medical workforce has been hampered for too long by the “rhubarb forcing” techniques of secondary schools. Better grades at A Levels are a predictor for medical student success, but our failure to nurture talent in deprived schools, coupled with the coaching power of private schools, has ensured that by restricting entry to medical school to those with better grades at A levels we are further disadvantaging some school leavers.1

**Graduate entry medicine can widen diversity**

Graduate entry medicine in the United Kingdom was predicated on faster production of doctors and on broadening the field from which they are recruited.2 Such courses should make efficient use of existing educational and healthcare capacity to produce more medical graduates and increase flexibility to respond to changing demand.2 Graduate medical schools can be especially well placed to draw out the broader range of skills needed by future doctors.3 Students who were underdeveloped at school can get another chance to read medicine after achieving good grades in a first degree.4 American doctors progress from high school through university to medical school. Australian graduate entry education was directed towards achieving diversity and moving away from “a narrow secondary education with a bias towards quantitative subjects.”5 In countries where the graduate entry degree is entirely self funded, medicine enables students to do a self fulfilling first degree in arts or sciences and then a vocational degree with sufficient earning potential to pay back debt after graduation. But graduate entry degrees can only deliver workforce diversity if selection strategies support this aim.6

Around 10% of UK medical school places are on graduate entry courses. Such courses can undoubtedly deliver the education in four years and enable intelligent graduates to move from science or arts learning at university to the level of competence needed for foundation year work in medicine.

Attributes associated with such courses include maturity,6 which is related to ability to handle responsibility,7 and benefits accruing from curriculum design—graduate entry medicine has been an incubator for curriculum development.10 Other attributes relate to previous university studies.11 Graduates should be at an advantage, as experience helps learners to deal with abstraction. Graduate schemes can concentrate on developing professional study skills rather than acquiring tertiary study skills.7

Peter McCrorie, a pioneer of graduate entry teaching, pointed out that for graduate entry medicine to make a difference, courses must “build upon their strengths, motivation, and prior learning.” A student explained, “Graduates have already learnt how to study and how to ration the other temptations of student life in order to keep up with their studies. This makes them better able to handle a self-directed learning approach.”12

**Cost benefits in meeting NHS workforce needs**

Cost comparisons are difficult because of the present system of bursaries and charges for second degrees, and such factors as the need to repeat a year on a fast track course or the inclusion of intercalated degrees in conventional courses. A study from South Africa compared data on conventional course costs with projections for a graduate entry course and found similar total years of study, student costs, and costs to society for a four year graduate entry course and a six year undergraduate programme.13 The problem of fast track students who end up needing extra time is contentious, and should be determined on the basis of academic progress.

There are not sufficient published data on attrition rates across medical courses to complete the cost comparison, but graduates are probably more likely to complete the course. The age range of entrants to St George’s Medical School was 21–44 years in 2003. Age at entry is one factor relevant to length of career service in the National Health Service. The prediction that graduates would make a more informed career choice14 because of their wider personal experience at university and elsewhere remains unproved. US data indicate that older graduates practice more readily in underserved areas and are more likely to work in primary care. Data from Australia also suggest that graduate entry schemes better prepare doctors for the workplace in some important aspects of patient care and team working, as well as in self directed learning.14

Although there is little support among UK medical education policymakers for the two cycle Bologna model for medical programmes,15 a system of graduate only programmes would enable the reclassification of such programmes at masters level.

A change to a single system of graduate entry medical schools in the UK should attract mature learners with high levels of motivation, independence of outlook, and orientation towards hard work. Graduate entrants have the additional maturity and strengthened interpersonal skills necessary to provide the diverse multi-skilled workforce needed for the future.

Competing interests: None declared. EP is responsible for the graduate entry fast track course at Warwick Medical School.

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1 Forth and Pantazis.4

2 Forth and Pantazis.4

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15 Forth and Pantazis.4
Most people in the UK enter medical college straight from school. Ed Peile argues that changing to a single system of graduate entry medical schools would provide the diverse multiskilled workforce needed for the future, but Charles George thinks that there is insufficient evidence to make this a criterion of entry.

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NO Traditionally, admission to a UK medical school has been directly after leaving school or one year later. In a survey carried out for the Council of Heads of Medical Schools (CHMS) in 1998, only 15.6% were mature (21 and over), and the proportion of these 2955 students who were graduates was not given. Since the late 1990s, the numbers of students entering existing medical schools have expanded and four more schools have been created in England. The demography of people applying for a place has changed, and in the period 2003-2005 22.4% of entrants were mature.

We do not need to modify the current system by restricting entry to graduates. It would be discriminatory to school leavers and to mature non-graduates to limit medical training to people who already have a degree in the absence of any convincing evidence of benefit. It would also cost more to the taxpayer for students to do both a first degree and a postgraduate medical degree.

Mature students and graduates
My experience of mature medical students and graduates at entry derives from more than 25 years as a clinical academic at the University of Southampton. There, from the first entry of students in 1971, we encouraged applications from “mature” people, taking up to 15%. Without exception, they were committed to becoming doctors, and had to be in view of the financial and other sacrifices they had to make. Their “wastage rates” were low, with almost all completing the course. In addition, they brought the diversity sought by Professor Peile and the medical schools to the student body—one of the guiding principles advanced by CHMS. But it was chiefly their experience of “life in the real world” that benefited the university and subsequently their patients. Importantly, these attributes applied equally to graduate entrants and those without degrees. Consequently, in my view, it would be wrong to discriminate between these two categories of mature students and to do so would limit the diversity sought by CHMS.

After publication of the first edition of Tomorrow’s Doctors, the education committee of the General Medical Council made informal visits to medical schools in the late 1990s. The visitors talked with and listened to several hundred medical students and preregistration house officers (foundation year one doctors). These articulate young people pointed out that it is illegal to discriminate on the grounds of age and that by 18 they could buy alcohol, smoke, drive a car, enlist in the armed services, and vote. They thought that graduate only entry schemes would discriminate against school leavers and non-graduate mature students in the absence of convincing evidence for such schemes.

School leavers are intelligent, multitalented, committed, and come with excellent study skills and there is no evidence that graduate entrants make better doctors. The evidence here derives mainly from cohort studies performed at individual medical schools. Examples include Nottingham, United Kingdom, where James and Chilvers followed the students entering between 1970 and 1995. Graduate entrants were more successful in the first three years of the course, with more obtaining a first class Bachelor of Medical Science degree. However, graduate entrants in the period 1986-1990 were less successful in the final BMBS (Bachelor of Medicine, Bachelor of Surgery) examinations. These results suggest that the graduate entrants were less competent as clinicians than their school leaver counterparts. Although the numbers are not large, these findings are consistent with a study of interns in New South Wales. However, a study from New South Wales found no significant differences between school leavers and graduate entrants in terms of academic performance (measured by the award of honours) or in career positions obtained after qualifying.

Academic medicine
Worldwide, there are concerns about recruitment into academic medicine, and intuitively recruiting science graduates into medicine ought to be beneficial. However, the Newcastle experience failed to produce evidence in favour of this idea. It contrasts with the well documented benefits of an intercalated BSc which was extremely important to my career as a clinical academic. Each year, about 30 of the most able students can proceed to an MB PhD programme, which contrasts with more than 1000 in the United States, where such programmes have been running successfully for several decades.

While selection for a career in medicine is problematic, CHMS (now the Medical Schools Council) and the universities have tried hard to make entrants more representative of all sections of society. Although the selection of school leavers relies heavily on academic performance at A level, follow-up of those entering the former Westminster Medical School between 1975 and 1982 showed that A level grades had long term predictive validity for both undergraduate and postgraduate careers.

In conclusion, although graduate entrants increase the diversity of our future doctors, there is insufficient evidence to make this a universal criterion for entry. Finally, we should not forget that graduate and mature entrants are subject to additional stresses, such as balancing commitments and lack of leisure time. They also face extra financial pressures when in 2006 the median debt of all people qualifying in medicine was £22,500 (£33,000; £46,000).

Competing interests: None declared.

All references are in the version on bmj.com

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Mixed messages over breast milk and brainy babies

Was the media understandably confused over the link between breast feeding and IQ, asks Margaret McCartney

Breast feeding “is best for a brainy baby,” “unlocks IQ,” and “links to higher IQ,” said the headlines earlier this month. The Daily Mail (6 November) explained, “Breast feeding really does make babies brainier, a major study suggests. British researchers have found that mother’s milk in the first few months of life can boost children’s IQ by seven points. This applies in nine cases out of 10, where the younger inherits a common but newly identified ‘brain boosting’ gene.”

The research purporting to show that breast means brains was published by the US journal Proceedings of the National Academy of Sciences (PNAS 2007; 0:0704292104v1-0). The researchers, from King’s College London, Duke and Yale universities in the US, and the University of Otago, New Zealand, were interested in finding a genetic variable which mediated the effects of breast feeding. In two birth cohorts, they found an “association between breast feeding and IQ . . . moderated by a genetic variant in FADS2, a gene involved in the genetic control of fatty acid pathways.” If babies had this variant—and 90% did—then breastfeeding produced a small increase in measured IQ.

The problem is that many news reports on health research appear with front page prestige, only to be flatly contradicted a little later. “Just when you thought scientists had made their minds up on a topic—from life on Mars to the health dangers of bacon butties—another study comes along to upset the consensus,” said the Independent in response, quite understandably.

Breast feeding owns a generous portion of controversies. In 2006, the media reported a study, published in the BMJ, that concluded that breast feeding made no difference to the intelligence of the babies (BMJ 2006;333:945).

According to last week’s reports, the reverse was now true. “The finding adds to the mounting evidence that breast fed babies are happier, healthier, and brighter than those raised on formula milk,” said the Daily Mail. But does it? What was not clear from most press reports was that some of the data—from the New Zealand Dunedin cohort—included in the Proceedings of the National Academy of Sciences study had already been examined, except with rather different results. The Dunedin cohort was included as part of a meta-analysis on the effect of breast feeding and intelligence—yes, the same study published in the BMJ in 2006, which found no effect. This study, which also included a prospective sibling pairs study, showed that crucially, once other factors including maternal intelligence had been adjusted for, there was no increased intelligence found in breast fed children. Multiple environmental influences affected child intelligence, explained the authors. The positive association of breast feeding with intelligence previously shown could be explained, not by the breast feeding itself, but by multiple confounding factors, mainly maternal intelligence, but also including maternal education, and the child’s social environment.

The abstract for the new Proceedings of the National Academy of Sciences study did not mention the previous meta-analysis. Instead it started with the assumption that “Breast fed children attain higher IQ scores than children not fed breast milk” without making it clear that this was (and is) unproven. Newspaper reports tended towards reporting the paper as certain evidence that breast feeding produced cleverer kids.

Was this fair? While the authors did adjust for maternal intelligence, they did not show how much of the breast feeding effect this explained. Nor did they adjust their results for all known potential confounding factors. Last year’s BMJ editorial, accompanying the meta-analysis concluded that the “results may help doctors when giving advice on breast feeding to mothers with particular problems—for example, women who take drugs to prevent seizures or depression . . . These data indicate that one consideration—an adverse long term effect on cognitive function—need not be of concern.” Should this new study change practical advice to patients?

Advice about breast feeding is a common GP request. After reading the latest headlines, I went online to read the original Proceedings report. Only the abstract was available free, and paying the requisite $10 allowed viewing of this complex paper for two days only. This hardly allows for a wide dissemination of knowledge for discussion and critique.

Later I was given a “factsheet,” produced by the authors, which was seemingly given to some journalists covering the story. It ends with a cautionary note that “This study must be repeated by other research teams in other countries. Although we were able to test the finding in two countries, scientific findings only gain trustworthiness after they are repeated by different teams. Genetic findings have been particularly difficult to repeat.” This seems sensible. But it is not one that has been repeated by the press. The public get a daily onslaught of mixed messages from “researchers” whose minds seem to be in a state of flux. Who could blame lay people for being or becoming cynical, uninterested, or even angry with the apparent constant volte-faces of research findings?

We should be thinking of better ways to engage with and explain to the public the meanings, shortcomings, and uncertainties of research. We should be thinking of better ways to engage with and explain to the public the meanings, shortcomings, and uncertainties of research rather than to constantly defend it. It would have made sense to me, for example, to put at least the abstract (and preferably the full paper) of this latest work on the web (some organisations like the Medical Research Council do make their research freely available) with a critique of what this research means, and what it does not. A statement that, in light of new research, we now need a further meta-analysis into the effects of breast feeding on intelligence, would have been most useful. This would be both an admission of uncertainty and a compass for how to reduce it.

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Measuring performance and missing the point?

Targets do not necessarily translate into improvements for service users. Iona Heath, Julia Hippisley-Cox, and Liam Smeeth argue that performance measurement in the UK is shifting focus from what each patient needs and those who need it most.

Since April 2004, the performance of general practitioners has been measured and remunerated against a limited, although increasing, number of easily measurable clinical activities. This initiative is unique worldwide and is attracting considerable international interest. It therefore behoves us to think critically about what we are doing.

General practitioners have responded by systematically recording the listed activities, apparently performing well above expectation, and the whole exercise has been hailed as a success for quality of care. Despite evidence that these sorts of incentives improve the quality of documentation while having a much more limited effect on underlying standards of care, there have undoubtedly been useful achievements. Of these, probably the most substantial are improvements in diabetic control and innovations in computer prompting systems. However, the system is in danger of missing the point of both quality and general practice.

**Treatment by numbers**

The clinical activities that are measured and rewarded by the quality and outcomes framework are largely evidence-based. Nevertheless, almost all interventions cause some harm, and even when effective treatments are applied to a series of patients in clinical practice some will be harmed (although more will benefit). The risks of harm tend to increase with age, as does the potential for benefit. The stakes therefore become higher as the evidence becomes more tenuous because of these, probably the most substantial are improvements in diabetic control and innovations in computer prompting systems. However, the system is in danger of missing the point of both quality and general practice.

Evidence based care was never meant to be a substitute for clinical judgment but, combined with the inducements of the quality and outcomes framework, it becomes so. Mechanistic blanket management strategies, embedded into computer software, become fixed and static with the danger that innovation will be stifled. Interventions become routine, and practitioners are no longer required to grapple with the innate uncertainty of each different clinical situation. Most randomised trials systematically exclude patients’ symptoms, functional status, comorbidity, severity of illness, ideas, and preferences. Yet these are the factors which should fundamentally affect decisions about appropriate treatment.

Within large study populations, there will be smaller populations sharing different characteristics whose response to a given treatment will differ from that of the larger group. Such groups could be systematically harmed by the intervention, and there are currently no robust systems in place to measure or monitor this.

The quality and outcomes framework diminishes the responsibility of doctors to think, to the potential detriment of patients, and encourages a focus on points scored, threshold met, and income generated. To give just one example, the failure to make any allowance for age means that doctors are encouraged to overtreat hypertension in old people with the danger of causing fainting, falls, and fractures.

The whole initiative is based on reductive linear reasoning that views the body as a machine and assumes that a standardised treatment will produce an equally standard unit of beneficial outcome. However, any practising clinician knows that the same treatment applied to two people with the same diagnosis can produce very different outcomes. Complexity theory suggests that the body is more usefully regarded as a complex adaptive system, characterised by rich interactions between multiple components that produce unpredictable outcomes. This analogy makes much more sense of clinical experience. Psychological states and social contexts exert measurable effects on the functioning of the body. Standardised treatments ignore all of this.

**Best way to reach goals?**

The quality and outcomes framework necessarily concentrates on clinical activities that are easily measured. Clearly, one of the easiest is the issuing of prescriptions. This leads to a situation where epidemiological research, with its tendency to extrapolate from short term studies over the whole of the remaining life span, combined with computer driven surveillance of whole populations, is driving hugely increased prescribing of some drugs. Almost all of this is designed to prevent future events rather than alleviate present suffering. Prevention has its merits, but was this an intention of the framework.
and what are the opportunity costs for other healthcare interventions?

One of the aims of the framework is to tackle health inequalities, but it has the potential to work in the opposite direction. Most fundamentally, it encourages the illusion that health inequalities can be solved by the health service and allows policy makers to ignore the extent to which health inequalities are a symptom of socioeconomic inequalities that continue to widen. The framework situates health inequalities at the level of the individual and ignores the political, social, and cultural context within which people find themselves. It is based on the astonishing assumption that everyone wants to live as long as possible whereas, in reality, some people seek to end their lives prematurely. Others adopt more chronically self-harming behaviours in the full awareness that they are likely to shorten their lives, clearly prioritising coping in the immediate future above the uncertainties of the long term.

As there is a socioeconomic gradient for the prevalence of almost every disease, the poor are much more likely to experience comorbidity. The most marginalised people, who have a combination of physical and mental illnesses often compounded by drug or alcohol dependence, are difficult to engage in health care and even more difficult to coerce into the framework’s unitary care pathways. Patients living in adverse social circumstances are also more likely to be taking maximal tolerated therapy in these areas have to work harder to achieve the same remuneration. 3 The increased payments for higher disease prevalence do not take severity and complexity into account. Working in poorer areas becomes less desirable, further reducing quality of care or even making care difficult to find (figure). Furthermore, there is evidence that payment for performance systems reward already high achievers and penalise low achievers and so exacerbate inequalities.4

What’s not measured

Three quarters of the population do not have any of the diseases included in the quality and outcomes framework,5 and ever since its introduction, special interest groups have been lining up to have their particular priority included among the targets. However, worthy attempts to include depression have only made matters worse as the imposition of standardised questionnaires and scoring systems serves simply to reify and medicalise distress and unhappiness. Authentic dialogue between doctor and patient is disrupted and many doctors feel fundamentally compromised.6

None of the framework measures estimate clinically important outcomes. What they assess is treatment processes that are supposed to lead to improved outcomes. A marked discrepancy exists between the likely effect on health and the level of monetary reward, and there seems to have been no attempt to align the two.7 Until the undoubted and now well documented increase in process is translated into tangible outcomes such as diabetes complication rates, renal failure in hypertension, or incidence of myocardial infarction or smoking related deaths, the benefits and cost effectiveness of the exercise cannot be estimated. Outcomes are much more difficult to measure than processes, especially at the level of individual practices, but the heightened emphasis on process brought about by the framework should not be allowed to distract from the fundamental aims of medical care.

Competing interests: All the authors work as NHS general practitioners and are therefore subject to the quality and outcomes framework. J H-C has been commissioned by the Department of Health, National Audit Office, and Disability Rights Commission and the Information Centre to do analysis to inform the development of the quality and outcomes framework. This article reflects her views rather than the views of the commissioning bodies. Contributors and sources: LS is supported by a Wellcome Trust senior fellowship in clinical science. The core ideas in this article arose from discussions between all three authors. IH wrote the first draft and all authors contributed to serial drafts and agreed the final submission. IH is guarantor.

Provenance and peer review: Commissioned; externally peer reviewed.

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Long term risk of invasive cancer after treatment for cervical intraepithelial neoplasia grade 3: population based cohort study

Björn Strander, senior consultant,1 Agneta Andersson-Ellström, senior consultant,1 Ian Milsom, professor,1 Pär Sparén, professor of medical epidemiology2

ABSTRACT

Objective To study the long term risk of invasive cancer of the cervix or vagina after treatment for cervical intraepithelial neoplasia grade 3.

Design Prospective cohort study.

Setting Swedish cancer registry.

Participants All women in Sweden with severe dysplasia or cervical carcinoma in situ (equivalent to cervical intraepithelial neoplasia grade 3) treated during 1958-2002 (n=132493) contributing 2315724 woman years.

Main outcome measures Standardised incidence ratios with risk of cancer in the Swedish general female population as reference, and relative risks in multivariable log-linear regression model, with internal references.

Results Women with previous cervical intraepithelial neoplasia grade 3 had an increased risk of invasive cervical cancer compared with the general female population (standardised incidence ratio 2.34, 95% confidence interval 2.18 to 2.50). The increased risk showed a decreasing trend with time since diagnosis for women treated later than 1970 but the risk was still increased after 25 years. An effect of age was found, with an accentuated increase in risk for women aged more than 50. The excess risk for cervical cancer associated with previous cervical intraepithelial neoplasia grade 3 has steadily increased since 1958. For vaginal cancer the standardised incidence ratio was 6.82 (5.61 to 8.21) but this decreased to 2.65 after 25 years. Adjustments in the multivariable log-linear regression model did not substantially alter these results.

Conclusions Women previously treated for cervical intraepithelial neoplasia grade 3 are at an increased risk of developing invasive cervical cancer and vaginal cancer. This risk has increased since the 1960s and is accentuated in women aged more than 50. The risk is still increased 25 years after treatment.

INTRODUCTION

The principle behind population based screening for cervical cancer is the detection and treatment of precancerous lesions to prevent the development of cervical cancer. Many countries and settings also offer follow-up programmes to find and treat residual or recurrent disease. Although most women treated for high grade dysplasias are protected from invasive cervical cancer, reports have shown an increased risk for high grade dysplasia and for cervical cancer among treated women.1-5 Knowledge about the risk of invasive cancer after treatment is important as a basis for follow-up programmes. Even with vaccination of young females against certain high risk types of human papillomaviruses, surveillance after treatment of high grade cervical lesions will still be required for the foreseeable future.

It is possible to analyse the efficacy and potential weaknesses of screening programmes using data from the national Swedish cancer register, which was established in 1958, eight years before the first regional screening programme was introduced. Since the foundation of the cancer register it has been mandatory to report all cancers as well as some precancerous lesions, such as cervical carcinoma in situ. The reporting is double—both pathologists and clinicians report the cases—and regional cancer registers follow up all discrepancies and unclear cases. The coverage and quality of the data are high.6-7

We investigated whether Swedish women treated for severe dysplasia or cervical carcinoma in situ have an excess risk of cervical and vaginal cancers.

METHODS

In November 2005 we retrieved all histopathology reports of cervical carcinoma in situ, or severe dysplasia bordering on cervical carcinoma in situ, from the Swedish cancer register for 1958-2002. These diagnoses are equivalent to cervical intraepithelial neoplasia grade 3, and the register stipulates obligatory reporting of them. The register includes dates of death and emigration through linkages to the national Swedish causes of death register and national Swedish population register, respectively. We used the patients’ unique registration number to link their details to the cancer register; 881 women had a diagnosis of invasive cervical cancer and 111 women had a diagnosis of vaginal cancer. Lesions of both the external part of the cervix (portio) and the vagina are classified as cervical and lesions of both the vulva and vagina are classified as vulval.
Statistical analysis
For women with an initial diagnosis of cervical intraepithelial neoplasia grade 3 we determined person time at risk and the number of observed and expected cervical cancers according to the yearly incidence, by five year age groups, from the general female population, using Epicure version 2.1 (Hirosoft, Seattle, Washington). We calculated standardised incidence ratios with 95% confidence intervals using SAS version 9. To account for prevalent cancers in the cohort we excluded the first year of follow-up from the analyses. We calculated the absolute risk changes, presented as difference in incidence, as the incidence − (incidence/standardised incidence ratio).

These analyses were also done separately for the number of observed and expected squamous cell cancers, adenocarcinomas or adenosquamous cancers of the cervix, and vaginal cancer. For multivariable regression analyses we assumed that the observed number of cases followed a Poisson distribution, and we weighted the number of observed cases by the log of the number of expected cases. These analyses were carried out using SAS version 9.

RESULTS
Overall, 132 493 women had a diagnosis of cervical carcinoma in situ or severe dysplasia (equivalent to cervical intraepithelial neoplasia grade 3) recorded in the Swedish cancer register during 1958-2000, contributing 2 315 724 woman years. Of these women, 881 had a diagnosis of invasive cervical cancer more than one year after treatment for cervical intraepithelial neoplasia grade 3. The overall standardised incidence ratio for women with previous cervical intraepithelial neoplasia grade 3 to develop invasive cervical cancer was 2.30 (95% confidence interval 2.15 to 2.46) compared with the general female population (table 1). The risk was significantly increased in all age groups, birth cohorts, and periods of diagnosis. The risk was highest among women diagnosed with CIN 3 at an older age and during the years 1958-70. The risk was also highest for women with a longer time since diagnosis and for those whose diagnosis was recorded in the first period of diagnosis.

Table 1 | Risk of invasive cervical cancer and vaginal cancer among women with previous cervical intraepithelial neoplasia grade 3 (CIN 3)

<table>
<thead>
<tr>
<th>Variables</th>
<th>No of cases</th>
<th>Expected No</th>
<th>Woman years</th>
<th>SIR (95% CI)</th>
<th>Change in incidence/100 000</th>
<th>SIR (95% CI)</th>
<th>Change in incidence/100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>881</td>
<td>382</td>
<td>2 315 724</td>
<td>2.30 (2.15 to 2.46)</td>
<td>21.5</td>
<td>111</td>
<td>16.28 (2.32 to 24.18)</td>
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<tr>
<td>Birth cohort:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;1915</td>
<td>94</td>
<td>13</td>
<td>52 583</td>
<td>6.99 (5.65 to 8.55)</td>
<td>153.2</td>
<td>25</td>
<td>1.39 (0.43 to 2.35)</td>
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<tr>
<td>1915-29</td>
<td>225</td>
<td>84</td>
<td>376 018</td>
<td>2.66 (2.33 to 3.03)</td>
<td>37.3</td>
<td>44</td>
<td>6.45 (4.26 to 9.64)</td>
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<tr>
<td>1930-9</td>
<td>166</td>
<td>75</td>
<td>476 699</td>
<td>2.21 (1.89 to 2.57)</td>
<td>19.1</td>
<td>18</td>
<td>3.60 (2.46 to 5.01)</td>
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<tr>
<td>1940-9</td>
<td>191</td>
<td>113</td>
<td>761 352</td>
<td>1.69 (1.46 to 1.94)</td>
<td>10.2</td>
<td>16</td>
<td>3.45 (2.65 to 4.83)</td>
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<td>1950-9</td>
<td>157</td>
<td>73</td>
<td>462 532</td>
<td>2.13 (1.81 to 2.49)</td>
<td>18.0</td>
<td>7</td>
<td>1.16 (0.51 to 2.02)</td>
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<tr>
<td>1960-9</td>
<td>47</td>
<td>20</td>
<td>163 772</td>
<td>2.28 (1.67 to 3.03)</td>
<td>13.8</td>
<td>1</td>
<td>0.23 (0.01 to 0.45)</td>
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<td>≥1970</td>
<td>1</td>
<td>1</td>
<td>22 768</td>
<td>0.58 (0.01 to 3.22)</td>
<td></td>
<td></td>
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</tbody>
</table>

Age at diagnosis of CIN 3 (years):

<table>
<thead>
<tr>
<th>Period of diagnosis:</th>
<th>No of cases</th>
<th>Expected No</th>
<th>Woman years</th>
<th>SIR (95% CI)</th>
<th>Change in incidence/100 000</th>
<th>SIR (95% CI)</th>
<th>Change in incidence/100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958-70</td>
<td>241</td>
<td>127</td>
<td>647 924</td>
<td>1.89 (1.66 to 2.14)</td>
<td>17.5</td>
<td>7</td>
<td>0.71 (0.24 to 1.18)</td>
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<td>1971-80</td>
<td>313</td>
<td>145</td>
<td>925 035</td>
<td>2.15 (1.92 to 2.40)</td>
<td>18.1</td>
<td>14</td>
<td>0.23 (0.07 to 0.39)</td>
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<td>1981-90</td>
<td>244</td>
<td>85</td>
<td>569 220</td>
<td>2.86 (2.52 to 3.25)</td>
<td>27.9</td>
<td>27</td>
<td>2.59 (2.08 to 3.10)</td>
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<td>1991-2002</td>
<td>83</td>
<td>23</td>
<td>173 545</td>
<td>3.52 (2.80 to 4.36)</td>
<td>34.2</td>
<td>8</td>
<td>0.71 (0.24 to 1.18)</td>
</tr>
</tbody>
</table>

Time since diagnosis (years):

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>No of cases</th>
<th>Expected No</th>
<th>Woman years</th>
<th>SIR (95% CI)</th>
<th>Change in incidence/100 000</th>
<th>SIR (95% CI)</th>
<th>Change in incidence/100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cancer</td>
<td>881</td>
<td>382</td>
<td>2 315 724</td>
<td>2.30 (2.15 to 2.46)</td>
<td>21.5</td>
<td>111</td>
<td>16.28 (2.32 to 24.18)</td>
</tr>
<tr>
<td>Vaginal cancer</td>
<td>2</td>
<td>0</td>
<td>868</td>
<td>16.1 (1.95 to 58.16)</td>
<td>216.2</td>
<td>2</td>
<td>0.04 (0.00 to 0.86)</td>
</tr>
</tbody>
</table>

SIR=standardised incidence ratio. SIR and change in absolute risk expressed as change in incidence per 100 000 woman years for whole population and stratified for birth cohort, age at diagnosis of CIN 3, period of diagnosis, and time (years) since diagnosis and the detection of invasive cancer.
birth cohorts, except for the latest (women born after 1969), for whom the risk did not differ from unity. The most noticeable increase was in the earliest cohort (women born before 1915). The risk was increased in all ages when treated aged more than 20, with an accelerated increase after age 50. For each decade since the 1960s the time trend was of increasing risk, with a standardised incidence ratio of developing invasive cancer after treatment for cervical intraepithelial neoplasia grade 3 almost twice as high if treatment was undertaken during 1991-2000 compared with 1958-70.

Overall, 746 of the 881 women with cervical epithelial cancer had squamous epithelial cancer (85%), 131 had adenocarcinoma or adenosquamous carcinoma (15%), and four had other diagnoses. The standardised incidence ratio for developing invasive squamous cell cervical cancer was slightly higher (2.49, 2.32 to 2.68) than that for all cervical cancers, but the pattern in different periods, age at diagnosis of and treatment for cervical intraepithelial neoplasia grade 3, and time since diagnosis did not differ from the overall data for all invasive cervical cancer (data not shown).

The risk of developing adenocarcinoma or adenosquamous carcinoma also increased (standardised incidence ratio 1.62, 95% confidence interval 1.36 to 1.93). The risk seemed to be inflated particularly for women treated for cervical intraepithelial neoplasia grade 3 in the 1990s, and time since diagnosis had no effect (data not shown).

When controlling for period of diagnosis and time since diagnosis in the multivariable regression model, a trend (P<0.001) was found of increasing risk of cervical cancer with increasing age at diagnosis, with a noticeable acceleration after age 50 (table 2). The time trend of increased risk for each decade since the 1960s also remained in the multivariable regression model (P<0.001), with the risk of developing invasive cancer almost twice as high if treatment for cervical intraepithelial neoplasia grade 3 was undertaken during 1991-2000 compared with 1958-70. A slight decrease in relative risk was found by time since diagnosis (P=0.04), although none of the risk estimates significantly deviated from unity. Further analysis showed a significant interaction between period of diagnosis and time since diagnosis (P<0.001). Stratifying for time period showed an increased risk of acquiring cervical cancer with time after treatment during 1958-70, whereas the risk decreased with time after period of diagnosis after 1970 (table 3): standardised incidence ratio 2.16 (1.51 to 2.59) up to 15 years after treatment and 1.50 (1.07 to 2.10) up to 25 years after treatment.

In the multivariable regression model the risk for adenocarcinoma or adenosquamous carcinoma also increased with age at diagnosis of cervical intraepithelial neoplasia grade 3 as well as if the period of diagnosis was after 1970 (data not shown).

### Vaginal cancer

The risk of developing vaginal cancer, a rare disease, after treatment for cervical intraepithelial neoplasia grade 3 was small in absolute terms—111 cases, with 95% being squamous epithelial cancer: incidence 5/100 000 woman years. The observed number was, however, almost seven times higher than expected. The standardised incidence ratios showed an increased risk with age and with period of diagnosis but a decreased risk with time since diagnosis (table 1). In the multivariable regression analysis, however, a decreasing risk was found with period of treatment (table 2). The decreased risk with time since diagnosis persisted and after 25 years it was one fifth of the risk in the reference follow-up period (2-4 years). No evidence was found of an interaction between period of diagnosis and time since diagnosis (P=0.45).

To account for possible misclassification of cervical cancers as vaginal cancers the data for cervical and vaginal cancers were pooled. Two women had both diagnoses and were censored at the time of the first diagnosis. In total, 990 cases were found (incidence rate 43/100 000 woman years) and the risk of cervical or vaginal cancer after treatment for cervical intraepithelial neoplasia grade 3 was increased 2.5 times compared with the general female population (standardised incidence ratio 2.48, 2.33 to 2.64).

### Table 2 | Relative risks compared with internal references of invasive cervical cancer and vaginal cancer among women with previous cervical intraepithelial neoplasia grade 3 (CIN 3)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Relative risk (95% CI) of cervical cancer</th>
<th>Relative risk (95% CI) of vaginal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis of CIN 3:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤20</td>
<td>0.49 (0.16 to 1.53)</td>
<td>*</td>
</tr>
<tr>
<td>20-29</td>
<td>0.67 (0.55 to 0.81)</td>
<td>2.25 (1.04 to 4.87)</td>
</tr>
<tr>
<td>30-39†</td>
<td>1.00 (1.00 to 1.00)</td>
<td>1.00 (1.00 to 1.00)</td>
</tr>
<tr>
<td>40-49</td>
<td>1.23 (1.03 to 1.48)</td>
<td>2.41 (1.31 to 4.45)</td>
</tr>
<tr>
<td>50-59</td>
<td>2.67 (2.16 to 3.29)</td>
<td>2.90 (1.47 to 5.73)</td>
</tr>
<tr>
<td>60-69</td>
<td>4.75 (3.63 to 6.21)</td>
<td>3.81 (1.77 to 8.19)</td>
</tr>
<tr>
<td>70-79</td>
<td>6.00 (3.88 to 9.28)</td>
<td>6.44 (2.71 to 15.33)</td>
</tr>
<tr>
<td>≥80</td>
<td>6.38 (1.58 to 25.70)</td>
<td>9.72 (2.15 to 44.04)</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Period of diagnosis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1958-70†</td>
<td>1.00 (1.00 to 1.00)</td>
<td>1.00 (1.00 to 1.00)</td>
</tr>
<tr>
<td>1971-80</td>
<td>1.37 (1.27 to 1.07)</td>
<td>0.54 (0.33 to 0.87)</td>
</tr>
<tr>
<td>1981-90</td>
<td>1.76 (1.63 to 1.35)</td>
<td>0.78 (0.46 to 1.31)</td>
</tr>
<tr>
<td>1991-2000</td>
<td>1.80 (1.65 to 1.27)</td>
<td>0.46 (0.20 to 1.04)</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>0.007</td>
</tr>
<tr>
<td>Time since diagnosis (years):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2</td>
<td>1.16 (0.88 to 1.54)</td>
<td>2.09 (0.94 to 4.65)</td>
</tr>
<tr>
<td>2-4‡</td>
<td>1.00 (1.00 to 1.00)</td>
<td>1.00 (1.00 to 1.00)</td>
</tr>
<tr>
<td>5-9</td>
<td>1.03 (0.85 to 1.26)</td>
<td>0.95 (0.50 to 1.80)</td>
</tr>
<tr>
<td>10-14</td>
<td>0.94 (0.76 to 1.18)</td>
<td>0.66 (0.33 to 1.31)</td>
</tr>
<tr>
<td>15-19</td>
<td>0.84 (0.65 to 1.08)</td>
<td>0.45 (0.21 to 0.95)</td>
</tr>
<tr>
<td>20-24</td>
<td>0.86 (0.64 to 1.15)</td>
<td>0.44 (0.20 to 0.96)</td>
</tr>
<tr>
<td>≥25</td>
<td>0.91 (0.67 to 1.23)</td>
<td>0.21 (0.09 to 0.47)</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Interaction category.
†Referent category.
‡This category was collapsed with 20-29 years owing to lack of cases.
*Reference category.
†Result of multivariable log-linear regression, with adjustment for age at diagnosis of CIN 3, period of diagnosis, and time (years) since diagnosis and the detection of invasive cancer.

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DISCUSSION
Women have a high excess risk of developing invasive cervical cancer after treatment for cervical carcinoma in situ or severe dysplasia bordering on cervical carcinoma in situ (equivalent to cervical intraepithelial neoplasia grade 3). The risk has increased since the 1960s and is almost twice as high for women treated in the 1990s compared with those treated during 1958-70.

One possible explanation is differences in treatment modalities. The Swedish cancer register does not, however, include data on treatment. Over the period studied (1958-2000), however, a strong consensus throughout Sweden has been to treat women with a diagnosis of cervical intraepithelial neoplasia grade 3 and to offer intensified follow-up with cytology for at least five years. We are confident therefore that most of the cohort with a diagnosis of cervical intraepithelial neoplasia grade 3 had been treated. In the 1960s high grade cervical dysplasia was treated by hysterectomy, and cold knife conisation was considered a conservative treatment. During the 1980s more conservative modes of treatment such as cryotherapy, cautery, and laser vaporisation or conisation became popular. Cold knife conisation was fairly uncommon in Sweden in 1990, when large loop excision of the transformational zone was introduced. Large loop excision of the transformational zone is now the dominant method of treatment for dysplasia in Sweden as in the rest of Europe. This development has been favourable for preservation of fertility and for minimising postoperative morbidity but leaves more tissue at risk of recurrent dysplasia and possibly also undetected residual dysplasia. Women of fertile age have been treated more conservatively since the 1960s, and they have a considerably lower risk of cancer than older women. Despite this the changed patterns in therapy can help explain the trend over time, as the trend remained after adjustment for age in the multivariable regression model. One study looked at the influence of treatment modalities but did not find any significant difference in recurrence of cervical intraepithelial neoplasia or incidence of cancer between women who had undergone hysterectomy and those who were treated by conservative methods. One weakness of the study, however, was the small number of women who had had a hysterectomy.

A possible shift in diagnostic criteria over time must also be considered. The incidence of cervical intraepithelial neoplasia grade 3 has been stable since 1968, however, with a 10% drop after the early 1980s, corresponding to treatment extended to women with milder grades of dysplasia. We can also speculate that the increased prevalence of human papillomavirus infection over the years has had a greater impact on women treated for cervical intraepithelial neoplasia grade 3 compared with the general population. Cervical intraepithelial neoplasia grade 3 is to a large extent caused by persistent infection with human papillomavirus. Thus this cohort has a proved susceptibility to high risk infection, which remains as a risk factor and might make these women more vulnerable to increased exposure to the virus. The classic lifestyle risk factors for human papillomavirus infection as well as cervical cancer, such as number of partners, number of partners’ partners, and cigarette smoking, may also remain throughout life in women treated for cervical intraepithelial neoplasia grade 3 and therefore constitute an increased risk despite treatment.

The increased risk of cervical cancer in the entire cohort did not decline substantially in the 25-30 years after treatment, but a stratified analysis showed opposite trends with period of diagnosis (table 3). In women treated after 1970 the trend is of decreasing standardised incidence ratios, but their risk of cervical cancer is still increased compared with that of the general population. After 10 years of follow-up the standardised incidence ratios for women with cervical intraepithelial neoplasia grade 3 treated before or after 1970 are similar.

Swedish women with no history of diagnosis of high grade dysplasia have a low risk of developing dysplasia and cancer after the age of 50. In most organised screening programmes this has justified less frequent screening or stopping screening in women around age 60. Those women treated for cervical intraepithelial neoplasia grade 3 are, however, still at risk. The clinical implication of our findings is that women treated for cervical intraepithelial neoplasia need special programmes for long term follow-up, with cytology and possibly testing for human papillomavirus. Stopping such a programme in women aged 60 is not justified if they were aged more than 35-40 when treated.

We have no clinical data on the women after treatment for cervical intraepithelial neoplasia grade 3, but according to Swedish guidelines such women are offered frequent appointments for screening after treatment and their motivation for attending has generally been high. It is not unreasonable to assume that these women have been more closely followed up with cytology than the general population. The noticeable increase in incidence of cervical cancer for women aged more than 50 at the time of treatment could partly be due to lack of follow-up but it could also lead to questioning the follow-up programme of cytology alone, which has been customary in Sweden as elsewhere. Testing for human papillomavirus DNA has shown to be of some benefit in identifying women in

### Table 3 | Standardised incidence ratios (SIR) for cervical cancer by time since diagnosis of cervical intraepithelial neoplasia grade 3 (CIN 3), stratified by period of diagnosis

<table>
<thead>
<tr>
<th>Time since diagnosis of CIN 3 (years)</th>
<th>SIR (95% CI) for diagnosis during 1958-70</th>
<th>SIR (95% CI) for diagnosis during 1971-2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>0.62 (0.23 to 1.64)</td>
<td>4.42 (3.48 to 5.61)</td>
</tr>
<tr>
<td>2-4</td>
<td>1.17 (0.76 to 1.80)</td>
<td>3.32 (2.83 to 3.90)</td>
</tr>
<tr>
<td>5-9</td>
<td>1.99 (1.50 to 2.63)</td>
<td>2.84 (2.46 to 3.27)</td>
</tr>
<tr>
<td>10-14</td>
<td>2.40 (1.81 to 3.17)</td>
<td>2.16 (1.81 to 2.59)</td>
</tr>
<tr>
<td>15-19</td>
<td>2.29 (1.67 to 3.14)</td>
<td>1.65 (1.29 to 2.10)</td>
</tr>
<tr>
<td>20-24</td>
<td>2.06 (1.46 to 2.92)</td>
<td>1.50 (1.07 to 2.10)</td>
</tr>
<tr>
<td>≥25</td>
<td>1.82 (1.37 to 2.43)</td>
<td>1.45 (0.88 to 2.41)</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.005</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
The risk of invasive cervical cancer is more than double that of the general population at least 10 years after treatment for cervical intraepithelial neoplasia grade 3.

Long term incidence of vaginal cancer after treatment for cervical intraepithelial neoplasia grade 3 is poorly documented.

**WHAT THIS STUDY ADDS**

Women are at an increased risk of invasive cervical cancer more than 25 years after treatment for cervical intraepithelial neoplasia grade 3.

The risk of invasive disease is noticeably increased in women aged more than 50 when treated.

The risk of vaginal cancer is increased in women treated for cervical intraepithelial neoplasia grade 3.

The relative risk in women treated for cervical intraepithelial neoplasia grade 3 to develop vaginal cancer compared with the general age matched population seems to be even higher than for invasive cervical cancer. The 111 cases in this study contributed 8% of all the 1358 cases of primary vaginal cancer in Sweden diagnosed during 1958-2002. Our study confirms observations in smaller studies that cervical intraepithelial neoplasia grade 3 is related to vaginal cancer. These two cancers can be connected for at least two reasons. Firstly, about 60% of cases of vaginal cancer are related to high risk human papillomavirus infection and share this risk factor with cervical carcinoma observed in several studies.

The strength of this study is the size of the study cohort, comprising almost 2.5 million woman years after diagnosis of cervical intraepithelial neoplasia grade 3. This is more than four times the combined data in a recently published meta-analysis. Furthermore, the completeness of records in the Swedish cancer registry is high, and linkage to comprehensive records covering the entire Swedish population makes it possible to keep track of migration and deaths.

The weaknesses of this study are that we could not link the data to mode of treatment or to hysterectomies and we lacked information on how the women have been followed up. We can only speculate therefore about the influence of these modalities.

**Conclusion**

Women treated for cervical intraepithelial neoplasia grade 3 are at increased risk of developing invasive cancer in the remaining cervix or vagina. This risk has increased with changes in treatment modalities since the 1990s compared with treatment in the 1960s, is higher for women who are older (≥50 years) at treatment, and remains increased 20 or more years after treatment compared with the general population. The question on how follow-up should be carried out is not resolved but this study implies that it has been insufficient and that prospective studies for strategies of long term follow-up after treatment of high grade cervical lesions are needed. Until we have learnt more we should at least offer women who have been treated for cervical intraepithelial neoplasia grade 3 cytological smears at regular intervals, preferably for at least 25 years, independent of age.
Contributors: BS and IM conceived the study. BS, AAE, and PS designed the study. BS and PS analysed the data. All authors drafted and revised the manuscript. PS is guarantor.

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Competing interests: None declared.

Ethical approval: Data retrieval was approved by the ethics committee of the Karolinska University Hospital (No 02-556).


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ABSTRACT

Objectives To examine associations between child wellbeing and material living standards (average income), the scale of differentiation in social status (income inequality), and social exclusion (children in relative poverty) in rich developed societies.

Design Ecological, cross sectional studies.

Setting Cross national comparisons of 23 rich countries; cross state comparisons within the United States.

Population Children and young people.

Main outcome measures The Unicef index of child wellbeing and its components for rich countries; eight comparable measures for the US states and District of Columbia (teenage births, juvenile homicides, infant mortality, low birth weight, educational performance, dropping out of high school, overweight, mental health problems).

Results The overall index of child wellbeing was negatively correlated with income inequality ($r=-0.64$, $P=0.001$) and percentage of children in relative poverty ($r=-0.67$, $P=0.001$) but not with average income ($r=0.15$, $P=0.50$). Many more indicators of child wellbeing were associated with income inequality or children in relative poverty, or both, than with average incomes. Among the US states and District of Columbia all indicators were significantly worse in more unequal states. Only teenage birth rates and the proportion of children dropping out of high school were lower in richer states.

Conclusions Improvements in child wellbeing in rich societies may depend more on reductions in inequality than on further economic growth.

INTRODUCTION

The wellbeing and behaviour of young people have recently attracted increasing attention from the media, policy, and law, with concern expressed over violence, drunkenness, antisocial behaviour, obesity, self harm, and pregnancy. A recent Unicef report, which assembled 40 indicators of child wellbeing in rich countries, concluded that children in Britain and the United States fared less well than in any of the other 21 countries included in its analysis.1

If, as Marmot has suggested,6 social gradients in health in rich countries reflect social position, and more unequal societies have worse health, then perhaps differences in social status are exacerbated in societies with wider differences in income.

The indicators of child wellbeing used in the Unicef report are ecological measures for whole countries. As the report does not attempt to explain the national differences in child wellbeing it described, we decided to see how they were related to three macro-economic measures: material living standards (average income, as measured by gross national income per capita), the scale of differentiation in social status (as measured by income inequality), and social exclusion among families with children (as measured by the proportion of children living in relative poverty). Although additional measures of material standards, differentiation in social status, and social exclusion might be desirable, none are so widely available as—or necessarily better than—gross national income per capita (converted according to local prices), income inequality, and percentage of children in relative poverty.

Having looked at the associations between these three macro-economic variables and the Unicef indicators internationally, we extended our analysis to indicators of child wellbeing among the 50 states of the US to see if the pattern of international associations was confirmed in an independent setting.

METHODS

International comparisons

In 2007 Unicef published an overview of child wellbeing in rich countries.3 Data sources included sample surveys, such as the OECD (Organisation for Economic Cooperation and Development) programme for international student assessment and the World Health Organization’s study of health behaviour in school age children, and routinely collected data, such as the OECD health database, the WHO mortality database, and the World Bank world development indicators.7 Reporting dates differ for different components of the index, ranging from 1998-2005.

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doi:10.1136/bmj.39377.580162.55
The Unicef index was originally constructed in three tiers (table 1). Forty items were grouped into 18 subdimensions. These were then taken, three at a time, to form the six main dimensions (material wellbeing, health and safety, educational wellbeing, family and peer relationships, behaviours and risks, subjective wellbeing). Components were combined as averages of their z scores. Full descriptions of both the index and the underlying methods have been previously reported.17

The Unicef index contains measures both of child wellbeing and of factors conducive to wellbeing. As we wanted to see how wellbeing might be determined by the proportion of children living in relative poverty, it was necessary to remove the relative poverty item, leaving 39 items, and recalculate the index. Where necessary, we have reverse scored indicators so that low scores consistently indicate worse outcomes.

Selection of countries
Unicef published an overall ranking for child wellbeing for 21 OECD countries. Incomplete data were also reported for some other countries excluded from the overall ranking. We included only countries that had income inequality data and were among the richest 50 in the world and excluded those with populations of less than two million to avoid possible tax havens. This meant adding Australia (21 indicators), Japan (19 indicators), Israel (39 indicators), New Zealand (20 indicators), and Slovenia (25 indicators) to the Unicef set, and excluding the Czech Republic, Hungary, and Poland. The 23 countries included were Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, the Netherlands, New Zealand, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland, the United Kingdom, and the US.

Income inequality data came from the United Nations development programme human development indicators, 2003-6. As survey dates vary for different countries (from 1992 to 2001), and as the lag time for effects will vary for different components of the index, we took the average income inequality across the reporting years 2003-6.4 Income inequality was measured as the ratio of the total annual household income received by the richest 20% of the population to that received by the poorest 20%. This ratio ranged from 3.4 in Japan, the most equal country, to 8.55 in the US, the most unequal.

Child relative poverty was measured as the percentage of children aged 0-17 years in households with an income equivalent to less than 50% of the national median. This shows the impact of income inequality specifically on children. Data within the period 1999-2001 came from the OECD.7 As expected, income inequality and child relative poverty were positively correlated for our 23 countries ($r=0.72, P=0.0002$), indicating that they share about half (52%) of their variance.

Average income was measured as gross national income per capita at 2003 purchasing power parities in US dollars and obtained from the World Bank world development indicators database.5

Statistical methods
We estimated Pearson’s correlations to see how the index of child wellbeing and its six dimensions and 39 indicators were related to income inequality, children in relative poverty, and average income.

US comparisons
To provide independent tests of the international pattern of associations we tabulated associations among the 50 US states (and the District of Columbia) of eight indicators of child wellbeing. We examined previously published associations with teenage births, juvenile homicides, educational performance, and rates of high school drop out.4 10-12 We also conducted four new analyses: firstly, we replicated previous findings for infant mortality and low birth weight so that we could present them in a form consistent with the other outcomes, and then we analysed the proportion of children who are overweight and rates of child mental health problems.

As a measure of income inequality for the US, we use the Gini coefficient of the inequality of household incomes in 1999 provided by the US Census Bureau13 (the Gini coefficient varies between 1, indicating maximum inequality, and 0, indicating perfect equality). Average income, measured as per capita income in 1999, was also obtained from the US Census Bureau.14 Data on children in relative poverty are not available for all states, so our US comparisons are restricted to income inequality and average income.

Data on infant mortality15 and low birth weight16 for 2002 came from the US National Centre for Health Statistics. Data on the proportion of overweight children and the proportion of children with moderate or severe difficulties in the area of emotions, concentration, behaviour, or getting along with others were obtained from the 2003 US National Survey of Children’s Health.17

RESULTS
The overall index of child wellbeing was closely and negatively correlated with income inequality ($r=−0.64, P=0.001$) (figure) and children in relative poverty ($r=−0.67, P=0.001$) but not with average income ($r=0.15, P=0.50$). Adjustment for income inequality or children in relative poverty did not change the lack of association between child wellbeing and average income in rich countries.

Table 1 shows the correlations between income inequality, children in relative poverty, and average income on one hand and the six dimensions and 39 items of the Unicef index on the other.

Associations with income inequality
Among the main dimensions of child wellbeing, health and safety and behaviours and risks were significantly
Table 1  Structure of the Unicef index of child wellbeing and correlations of six main dimensions and 39 items with income inequality, child relative poverty, and average income*

<table>
<thead>
<tr>
<th>Structure of the Unicef index of child wellbeing and correlations of six main dimensions and 39 items with income inequality, child relative poverty, and average income*</th>
<th>Income inequality</th>
<th>Child relative poverty</th>
<th>Average income</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P value</td>
<td>r</td>
</tr>
<tr>
<td>Overall Unicef index</td>
<td>−0.64</td>
<td>0.001</td>
<td>−0.67</td>
</tr>
<tr>
<td><strong>Material wellbeing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>−0.36</td>
<td>0.10</td>
<td>−0.37</td>
</tr>
<tr>
<td>Deprivation:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low affluence (child’s own report)</td>
<td>−0.41</td>
<td>0.08</td>
<td>−0.40</td>
</tr>
<tr>
<td>Few educational possessions (desk, computer, textbooks etc)</td>
<td>0.00</td>
<td>0.99</td>
<td>−0.26</td>
</tr>
<tr>
<td>Few books</td>
<td>−0.37</td>
<td>0.08</td>
<td>−0.34</td>
</tr>
<tr>
<td>Work:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No employed parent</td>
<td>−0.23</td>
<td>0.29</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Health and safety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>−0.53</td>
<td>&lt;0.01</td>
<td>−0.71</td>
</tr>
<tr>
<td>Infant mortality</td>
<td>−0.76</td>
<td>&lt;0.001</td>
<td>−0.66</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>−0.42</td>
<td>0.048</td>
<td>−0.62</td>
</tr>
<tr>
<td>Immunisations:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>−0.11</td>
<td>0.60</td>
<td>−0.06</td>
</tr>
<tr>
<td>Diphtheria-pertussis-tetanus (DPT)</td>
<td>−0.04</td>
<td>0.86</td>
<td>−0.32</td>
</tr>
<tr>
<td>Polio</td>
<td>−0.05</td>
<td>0.82</td>
<td>−0.49</td>
</tr>
<tr>
<td>Child mortality:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accident/injury mortality</td>
<td>−0.27</td>
<td>0.21</td>
<td>−0.40</td>
</tr>
<tr>
<td><strong>Educational wellbeing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>−0.41</td>
<td>0.06</td>
<td>−0.55</td>
</tr>
<tr>
<td>Achievement:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maths scores</td>
<td>−0.50</td>
<td>0.03</td>
<td>−0.41</td>
</tr>
<tr>
<td>Reading scores</td>
<td>−0.25</td>
<td>0.28</td>
<td>−0.29</td>
</tr>
<tr>
<td>Science scores</td>
<td>−0.36</td>
<td>0.11</td>
<td>−0.13</td>
</tr>
<tr>
<td>Participation:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Further education</td>
<td>−0.67</td>
<td>&lt;0.001</td>
<td>−0.66</td>
</tr>
<tr>
<td>Aspirations:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspiring to low skilled work</td>
<td>0.46</td>
<td>0.04</td>
<td>0.19</td>
</tr>
<tr>
<td>Not in education, employment, or training</td>
<td>0.32</td>
<td>0.18</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>Peer and family relationships</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>−0.37</td>
<td>0.08</td>
<td>−0.26</td>
</tr>
<tr>
<td>Family structure:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single parent households</td>
<td>0.01</td>
<td>0.96</td>
<td>0.10</td>
</tr>
<tr>
<td>Step-parent households</td>
<td>0.08</td>
<td>0.73</td>
<td>0.23</td>
</tr>
<tr>
<td>Family relations:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eat together regularly</td>
<td>−0.22</td>
<td>0.32</td>
<td>−0.22</td>
</tr>
<tr>
<td>Child talks to parents</td>
<td>0.10</td>
<td>0.68</td>
<td>0.00</td>
</tr>
<tr>
<td>Peer relations:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Peers are kind&quot;</td>
<td>−0.50</td>
<td>0.02</td>
<td>−0.54</td>
</tr>
<tr>
<td><strong>Behaviours and risk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>−0.58</td>
<td>0.004</td>
<td>−0.33</td>
</tr>
<tr>
<td>Risk behaviour:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoke cigarettes at least once a week</td>
<td>0.11</td>
<td>0.64</td>
<td>−0.10</td>
</tr>
<tr>
<td>Been drunk twice or more</td>
<td>0.23</td>
<td>0.33</td>
<td>0.17</td>
</tr>
<tr>
<td>Cannabis in past year</td>
<td>−0.29</td>
<td>0.22</td>
<td>−0.36</td>
</tr>
<tr>
<td>Teenage birth rate</td>
<td>−0.74</td>
<td>&lt;0.001</td>
<td>−0.65</td>
</tr>
<tr>
<td>Had sex by age 15 years</td>
<td>−0.04</td>
<td>0.88</td>
<td>0.06</td>
</tr>
<tr>
<td>Condoms used during last sexual intercourse</td>
<td>0.33</td>
<td>0.23</td>
<td>0.45</td>
</tr>
<tr>
<td>Experiences of violence:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involved in fighting</td>
<td>−0.20</td>
<td>0.39</td>
<td>−0.32</td>
</tr>
<tr>
<td>Victim of bullying</td>
<td>−0.47</td>
<td>0.04</td>
<td>−0.28</td>
</tr>
</tbody>
</table>
Health behaviour:

<table>
<thead>
<tr>
<th>Item</th>
<th>Subjective wellbeing</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eat fruit daily</td>
<td>0.37 0.10</td>
<td>0.36 0.14</td>
</tr>
<tr>
<td>Eat breakfast on school days</td>
<td>-0.22 0.34</td>
<td>-0.42 0.08</td>
</tr>
<tr>
<td>Average days physically active in past week</td>
<td>0.12 0.62</td>
<td>-0.45 0.06</td>
</tr>
<tr>
<td>Overweight</td>
<td>-0.56 0.01</td>
<td>-0.72 0.001</td>
</tr>
</tbody>
</table>

Subjective wellbeing

<table>
<thead>
<tr>
<th>Item</th>
<th>Subjective wellbeing</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self rated fair/poor health</td>
<td>-0.32 0.19</td>
<td>-0.27 0.30</td>
</tr>
</tbody>
</table>

Personal wellbeing:

<table>
<thead>
<tr>
<th>Item</th>
<th>Subjective wellbeing</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life satisfaction above median</td>
<td>-0.35 0.13</td>
<td>-0.32 0.20</td>
</tr>
<tr>
<td>Feel like an outsider</td>
<td>-0.11 0.64</td>
<td>-0.04 0.85</td>
</tr>
<tr>
<td>Feel awkward</td>
<td>0.28 0.22</td>
<td>0.01 0.94</td>
</tr>
<tr>
<td>Feel lonely</td>
<td>0.45 0.04</td>
<td>-0.13 0.58</td>
</tr>
</tbody>
</table>

School wellbeing:

<table>
<thead>
<tr>
<th>Item</th>
<th>Subjective wellbeing</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Likes school a lot&quot;</td>
<td>0.07 0.77</td>
<td>0.04 0.87</td>
</tr>
</tbody>
</table>

*Where necessary, items have been reverse scored so that lower scores indicate worse outcomes throughout table.

worse in more unequal countries. Infant mortality and rates of low birth weight were higher in countries with higher levels of income inequality, as were rates of teenage pregnancy, rates of overweight children, and the proportion of children who reported having been bullied. Items in other dimensions of wellbeing that were also related to income inequality included lower maths scores, a lower proportion of young people in further education, and a lower proportion of children who find that their “peers are kind.”

There was a significant relation between lower levels of income inequality and a higher proportion of children feeling lonely. Children in countries with lower levels of income inequality were more likely to aspire to less skilled work.

Associations with percentage of children in relative poverty

Health and safety and educational wellbeing were the main Unicef dimensions of child wellbeing that were significantly worse in countries with higher levels of child relative poverty. Infant mortality and rates of low birth weight were higher in countries with more children in relative poverty, and rates of immunisation for polio were significantly lower. In such countries fewer young people participated in further education, fewer reported that “peers are kind,” teenage birth rates were higher, and a higher proportion were overweight.

Associations with average income

Educational wellbeing (but not achievement) was better in countries with higher average incomes. In richer countries, fewer children reported low levels of family affluence, more young people participated in further education, and lower proportions of children were living in single parent or step-parent families. The only other significant association with average income was that children in richer countries were more likely to report eating fruit daily.

Results among states of the US

Table 2 summarises results for the US from previously published studies and our new analyses. Income inequality at the state level was significantly correlated with rates of teenage births, juvenile homicides, infant mortality, low birth weight, child overweight, mental health problems, and high school dropouts as well as with worse educational scores. States with higher average incomes had significantly fewer teenage births and fewer children dropping out of high school, but they did no better than poorer states on the other six measures of child wellbeing.

DISCUSSION

Income inequality and the proportion of children in relative poverty measure different aspects of inequality. We included both to distinguish the effects of living in a more unequal society from the effects of being brought up in families with low relative income. Inequality and child relative poverty, however, are almost equally closely related to the Unicef measures of child health and wellbeing. Average income was unrelated to the overall index.

Among the components of the Unicef index, higher levels of one or other of our inequality measures were significantly associated with worse outcomes for infant mortality, low birth weight, polio immunisation, average maths scores, the proportion of teenagers in further education, fewer children saying their peers are kind, teenage birth rates, experience of bullying, and childhood overweight. On the other hand, in more unequal countries fewer children reported feeling lonely, and fewer had low job aspirations. The first of these is entirely driven by Japan, an outlier, with a score more than 4 SD from the mean. The second is a more robust tendency for job aspirations to be lower in more equal countries. But rather than being realistic aspirations, this may simply reflect a stronger tendency for children in more unequal countries to aspire to unattainable money and fame. We found a non-significant tendency for aspirations to be highest...
where educational achievements were lowest \((r=-0.36; P=0.12)\). In addition, there is some evidence that social mobility is lower in more unequal countries.\(^9\)

Our examination of indicators of child wellbeing among the US states largely confirmed these patterns. Outcomes on all of our indicators were significantly worse in more unequal states. In contrast, higher average income was significantly (and independently) related to lower teenage birth rates and to a lower proportion of children dropping out of high school.

Of the indicators of child wellbeing included in the Unicef index, the one most closely related to the overall index is the teenage birth rate, which has been called an “iconic” variable for this reason.\(^4\) It is also the indicator most closely related to inequality—internationally and among the US states.

Despite large differences in living standards, few measures of child wellbeing were related to average income in either the international or the US settings. Previous studies have shown that although health remains related to income within rich countries (as health inequalities testify), it is no longer related to average differences in income between them.\(^21\)\(^22\) This is consistent with the view that what matters within rich countries may no longer be absolute material standards, but income (or social position) relative to others in the same society. However, when international analyses include data for poorer countries, it is clear that among them, absolute material standards remain important for child wellbeing.\(^18\)

Analyses of units as large as whole countries or states may seem too remote from the factors that affect individual health to be informative. But given that health inequalities are typically measured across the whole social class hierarchy, a clue to the extent of the same processes of social differentiation that mark people so deeply may be gained by measuring income distribution across whole societies. This may be why, in a review of 168 analyses, we found that studies of whole societies provided overwhelming evidence that income inequality and health were related, whereas results from studies measuring inequality in small areas were equivocal.\(^3\) Deprived neighbourhoods presumably have poor health because they are deprived in relation to the wider society, not because of the inequality within them. Income distribution, as a societal variable, may be serving as a measure of the scale or importance of social stratification.

Associations, confounding, and causality
Although the associations between income inequality and child wellbeing may seem to fit well in this framework, that is not necessarily evidence of causality. Could there be confounding factors detrimental to child wellbeing that also tend to widen income differences? Consistent with the lack of association with average income, previous work suggests that relations between health and income inequality are not explained by poverty or by controlling—in multilevel models—for individual incomes.\(^21\)\(^22\)

We are sometimes asked about a possible confounding role of ethnic division or migration from poorer countries. Ram however, used international data to show that income inequality remained significantly related to health even after adjustment for an index of ethnic heterogeneity.\(^24\) In addition, although levels of child wellbeing in Sweden and the US differ so dramatically, both countries have a similar proportion of the population (around 12\%) who were born in other countries.\(^24\)\(^25\)

The provision of public services might also be a confounder. Healthcare expenditure, however, is not related to mortality in rich countries\(^26\) and an analysis of US data found that expenditure on public services among the 50 states could account for only part of the relation between income inequality and mortality.\(^27\) Among OECD countries we found that public social expenditure as a percentage of national income only slightly attenuated the relation between income inequality and the Unicef index (results not shown).

For several other outcomes related to inequality—such as obesity, homicide, and levels of trust—it is much less plausible that services might be a powerful determinant.

The UK
As the figure shows, the UK has the lowest score for child wellbeing on the Unicef index and does worse

---

**Table 2** Correlations of measures of child wellbeing with income inequality, and average income across the 50 US states (including District of Columbia)

<table>
<thead>
<tr>
<th>Measure of child wellbeing</th>
<th>Income inequality</th>
<th>Average income</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(r) (P) value</td>
<td>(r) (P) value</td>
</tr>
<tr>
<td>Teenage births(^12)</td>
<td>0.72 (\times 0.001)</td>
<td>-0.55 (\times 0.001)</td>
</tr>
<tr>
<td>Juvenile homicides(^12)</td>
<td>0.31 (0.03)</td>
<td>0.00 (0.99)</td>
</tr>
<tr>
<td>Infant mortality(^*)</td>
<td>0.55 (\times 0.001)</td>
<td>-0.20 (0.15)</td>
</tr>
<tr>
<td>Low birth weight(^*)</td>
<td>0.65 (\times 0.001)</td>
<td>-0.01 (0.99)</td>
</tr>
<tr>
<td>Educational performance (combined maths and reading scores for 15 year olds)(^*)</td>
<td>-0.69 (\times 0.001)</td>
<td>0.08 (0.58)</td>
</tr>
<tr>
<td>Dropping out of high school(^*)</td>
<td>0.66 (\times 0.001)</td>
<td>-0.28 (0.04)</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.64 (\times 0.001)</td>
<td>-0.07 (0.63)</td>
</tr>
<tr>
<td>Mental health problems</td>
<td>0.37</td>
<td>-0.14 (0.33)</td>
</tr>
</tbody>
</table>

*Similar findings have been reported elsewhere.\(^11\)\(^40\)
†Similar findings have been reported elsewhere.\(^11\)

---
RESEARCH

urgently required

Attempts to reduce inequality and the proportion of children living in relative poverty are

Young people are aware of status differentiation

Similar associations were found with eight indicators of child wellbeing in the 50 states of the

gross national income per capita

proportion of children living on less than half the median income in each country but not with

The Unicef index of wellbeing is strongly associated with income inequality and with the

WHAT THIS STUDY ADDS

A recent Unicef report measuring child wellbeing in rich countries puts the UK at the bottom

WHAT IS ALREADY KNOWN ON THIS TOPIC

The Unicef index of wellbeing is strongly associated with income inequality and with the

proportion of children living on less than half the median income in each country but not with gross national income per capita

Similar associations were found with eight indicators of child wellbeing in the 50 states of the

Young people are aware of status differentiation

Attempts to reduce inequality and the proportion of children living in relative poverty are urgently required

to their parents. These data, collected from children as old as 15, however, might be a poor reflection of family relationships in the important earlier years.

We have suggested elsewhere that greater inequality leads to increased competition and anxiety regarding social status. But are children sufficiently aware of differences in status to make the third hypothesis plausible? Research has found that before the end of primary school children are fully conscious of class differences: they can rank occupations hierarchically and are able to categorise people socially by outward indicators such as clothing, houses, and cars. There is also evidence to show how children’s performance is affected by status differentiation. For example, although tests showed that 11-12 year old Indian children from high and low castes could solve mazes equally well before they knew each other’s caste, lower caste children did much less well as soon as caste was declared. Similar effects were apparent when black and white American high school students were given cognitive tests. When told the tests were to measure ability, the black students did much less well than when they were told they were not tests of ability. White students did equally well under both conditions. Other experiments have shown how the creation of artificial differences in status can lead to differences in behaviour and performance.

The Unicef data suggest that children’s responses to inequality are remarkably similar to those found in adult populations. The data on peer relations and violence among children runs parallel to those on social capital, trust, and violence among adults. Among both, the quality of social relations is poorer in more unequal societies. When we computed a new measure of the quality of children’s relations with their peers by combining the Unicef data for involvement in fighting, experience of bullying, and the proportion of children not finding their peers kind and helpful, it correlated closely with both the inequality variables ($r=0.61$, $P<0.01$ for both). Similarly, it has been shown that juvenile homicides are, like adult homicides, correlated with inequality.

The most plausible explanation for the link between adult violence and inequality seems to be loss of face and people’s sensitivity to feeling disrespected and looked down on. Accounts of school shootings in the US suggest similar patterns. Lastly, the associations between inequality and the proportion of children who are overweight mirror relations between adult obesity and inequality.

Our finding that measures of child wellbeing are related to income inequality internationally among rich countries is supported by similar associations with child outcomes among the 50 states of the US. While our results have the usual limitations of cross sectional analyses, they cannot easily be attributed to confounding. Improvements in child wellbeing in rich countries might depend more on reductions in inequality than on further economic growth, and attempts to reduce the proportion of children in relative poverty are urgently required.
We thank Jonathan Bradshaw for helpful comments and advice and Anna Goodman, who independently discovered the association between income inequality and child mental health in the US, for helpful discussions.

Contributors: Both authors participated in the design of the study, interpretation of the results and drafting of the article. KEP conducted the data analysis. Both authors are guarantors.

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Provenance and peer review: Not commissioned; externally peer reviewed.


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Correlations among measures of quality in HIV care in the United States: cross sectional study

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ABSTRACT
Objective To determine whether a selected set of indicators can represent a single overall quality construct.
Design Cross sectional study of data abstracted during an evaluation of an initiative to improve quality of care for people with HIV.
Setting 69 sites in 30 states.
Data sources Medical records of 9020 patients.
Main outcome measures Adjusted performance rates at site level for eight measures of quality of care specific to HIV and a site level summary performance score (the number of measures for which the site was in the top quarter of the distribution).
Results Of 28 site level correlations between measures, two were greater than 0.40, two were between 0.30 and 0.39, four were between 0.20 and 0.29, and the 20 remaining were all less than 0.20. One site was in the top quarter for seven measures, but no sites were in the top quarter for six or eight of the measures. Across the eight quality measures, sites were in the top quarter no more often than predicted by a chance (binomial) distribution.
Conclusions The quality suggested by one measured indicator cannot necessarily be generalised to unmeasured indicators, even if this might be expected for clinical or other reasons.

INTRODUCTION
Efforts to measure and report the quality of care delivered by healthcare organisations are becoming commonplace. Publicly reported performance data are increasingly available for health plans, hospitals, nursing homes, and groups of physicians, and many providers are now being rewarded on the basis of measures of quality of care.1–3 These initiatives generally rely on a small set of measures, usually of processes of care but sometimes of outcomes. Common indicators of performance of health plans and physicians focus on the provision of preventive services and the management of a small number of chronic conditions, such as diabetes and asthma.

In addition to making reported quality data more comprehensible, a rationale for using a small subset of possible quality indicators is the belief that an organisation’s performance on unmeasured processes or outcomes will be similar to that on measured ones. For example, although there are many activities involved in high quality care in diabetes, it is assumed that assessment of selected processes, such as whether a yearly retinal exam is performed or whether a test for haemoglobin A1c was ordered, provides a reasonable indication of the overall quality of an organisation’s diabetes care. An extension of this logic is that monitoring care indicators for a carefully selected set of prevalent and important conditions, such as diabetes, hypertension, and heart attacks, provides valid information about the overall quality of care provided by a physician, medical group, health plan, or hospital. The use of a few indicators to assess care is consonant with systems theory, which implies that there should be relatively high correlations among quality indicators within organisations because multiple areas of performance should be influenced by common characteristics of the system.4,5

Several studies have examined the relations among quality measures for various different types of organisations, but few of these studies examined outpatient medical practices. For instance, a recent study of 11 outpatient practices that assessed measures of technical clinical quality (such as cholesterol screening), patients’ satisfaction, clinic function (such as follow-up of abnormal results of laboratory tests), and compliance with treatment for diabetes and asthma found no significant correlations between these measures.6 Similarly, Palmer et al found that correlations across cases seen by a given physician were low.8 Other studies that examined hospitals,9,10 health plans,11 and communities12 have found similarly low correlations among quality measures.

Given the large number of initiatives for measurement and improvement of quality, many of them founded on systems theory, it is surprising that so few have reported empirical assessments of the relations among quality indicators. Examining such correlations is critical for both measurement and improvement of quality. With regard to measurement, it is important to understand whether it is appropriate to draw conclusions about the overall quality on the basis of a limited set of indicators. With regard to improvement, finding strong correlations among quality measures would...
support the theory that the measures are the output of a single functional system and that efforts to improve quality should focus on characteristics of the system. Low correlations, by contrast, would suggest that multiple functionally independent systems are operating, implying that efforts to improve quality need to address these distinct systems or their integration.

We examined the relation among eight quality indicators for a single chronic medical condition in care settings in which we expected relatively high correlations—that is, organisations that deliver HIV care to outpatients. We used data from a quality improvement initiative that included HIV care sites in 30 states to see whether we could identify organisations that were “high performers”—that is, organisations that consistently scored highly across different quality measures. High performing organisations, presumably, are organised and managed in ways that allow them to achieve high quality.

### Table 1: Characteristics of patients and sites

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No (%) or mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients (n=9020)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>40.5 (8.9)</td>
</tr>
<tr>
<td>Women</td>
<td>2859 (31.7)</td>
</tr>
<tr>
<td>Psychiatric diagnosis</td>
<td>2832 (31.4)</td>
</tr>
<tr>
<td>Active substance abuse*</td>
<td>1470 (16.3)</td>
</tr>
<tr>
<td>Lowest CD4 cell count $\times 10^6/l$ during review period:</td>
<td></td>
</tr>
<tr>
<td>0-49</td>
<td>929 (10.3)</td>
</tr>
<tr>
<td>50-199</td>
<td>1912 (21.2)</td>
</tr>
<tr>
<td>200-499</td>
<td>3870 (42.9)</td>
</tr>
<tr>
<td>$&gt;$500</td>
<td>2309 (25.6)</td>
</tr>
<tr>
<td><strong>Sites (n=69)</strong></td>
<td></td>
</tr>
<tr>
<td>Region:</td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>14 (20)</td>
</tr>
<tr>
<td>Northeast</td>
<td>26 (38)</td>
</tr>
<tr>
<td>South</td>
<td>20 (29)</td>
</tr>
<tr>
<td>West</td>
<td>9 (13)</td>
</tr>
<tr>
<td>Type of clinic:</td>
<td></td>
</tr>
<tr>
<td>Community based organisation</td>
<td>11 (16)</td>
</tr>
<tr>
<td>Community health centre</td>
<td>23 (33)</td>
</tr>
<tr>
<td>Health department</td>
<td>11 (16)</td>
</tr>
<tr>
<td>Hospital</td>
<td>10 (15)</td>
</tr>
<tr>
<td>University medical centre</td>
<td>14 (20)</td>
</tr>
<tr>
<td>Mean (SD) No of full time equivalent physicians</td>
<td>5.6 (5.6)</td>
</tr>
<tr>
<td>Mean (SD) No of full time equivalent nurse practitioners and physician assistants per site</td>
<td>2.7 (2.8)</td>
</tr>
<tr>
<td>Mean (SD) No of health professionals on staff:</td>
<td></td>
</tr>
<tr>
<td>General physicians</td>
<td>4.9 (6.4)</td>
</tr>
<tr>
<td>Obstetrics and gynaecology</td>
<td>0.8 (1.7)</td>
</tr>
<tr>
<td>Fellowship trained specialists in infectious diseases</td>
<td>1.8 (3.4)</td>
</tr>
<tr>
<td>Mental health professionals</td>
<td>2.6 (4.6)</td>
</tr>
<tr>
<td>Nurses</td>
<td>7.2 (7.1)</td>
</tr>
<tr>
<td>Professionals routinely available on site:</td>
<td></td>
</tr>
<tr>
<td>Dentist</td>
<td>36 (52)</td>
</tr>
<tr>
<td>Nutritionist</td>
<td>57 (83)</td>
</tr>
<tr>
<td>Social worker</td>
<td>60 (87)</td>
</tr>
<tr>
<td>Substance abuse counsellor</td>
<td>35 (50)</td>
</tr>
<tr>
<td>HIV specialisation:</td>
<td></td>
</tr>
<tr>
<td>Specialised HIV clinic</td>
<td>43 (62)</td>
</tr>
<tr>
<td>General medicine with specialised HIV team</td>
<td>24 (35)</td>
</tr>
<tr>
<td>General medicine with no specialised HIV team</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Mean (SD) % of budget from Ryan White funds</td>
<td>48.2 (34.5)</td>
</tr>
<tr>
<td>Mean (SD) % of HIV patients with case manager</td>
<td>70.1 (35.4)</td>
</tr>
<tr>
<td>Multidisciplinary HIV care team</td>
<td>55 (80)</td>
</tr>
<tr>
<td>Mean (SD) No of team meetings in past 12 months</td>
<td>23.5 (18.6)</td>
</tr>
</tbody>
</table>

*Substance abuse noted in medical record during review period.
METHODS

Overview
Data for this study were collected as part of an evaluation of a quality improvement collaborative involving clinics that received funds through the Ryan Care Act.\textsuperscript{13,14} We abstracted information on quality of care from medical records at two times (details below).

Participants
Site selection—Of the 200 relevant sites in the United States in May 2000, 171 were eligible to participate in the study. From these, we enrolled 44 sites that were participating in the quality improvement intervention and an additional 25 sites that served as controls, giving 69 participating sites in 30 states. Details of the site selection process are described elsewhere.\textsuperscript{13,14} We previously reported that changes in quality measures did not differ significantly between intervention and control sites.\textsuperscript{13} We surveyed medical directors at each site to determine specific characteristics.

Patient selection—We randomly sampled 75 active patients from each site before the intervention and then drew a second random sample of 75 after the intervention. The intervention took place from 30 June 2000 to 31 December 2001. Patients were considered active if they visited the site at least once during the review period.

Data collection
We collected data from the medical records of each sampled patient over one year of care for the two review periods. Data abstracted included age, sex, history of HIV related illnesses, comorbid medical or psychiatric conditions including current substance abuse or psychiatric illness, screening and prophylaxis for HIV related conditions, number and timing of visits, CD4 cell counts, viral loads, and antiretroviral medications. Reviewers specified whether each visit was to a physician, a nurse practitioner or physician assistant, a nurse, or some “other” clinician (such as a nutritionist). The first review covered the year before the intervention (1 June 1999 to 31 May 2000), and the second covered the year beginning six months after the start of the intervention and ending three months after the end of the intervention (1 January 2001 to 31 December 2001).

Table 2 | Measures of quality (proportions, adjusted for patients’ characteristics) at the 69 sites studied

<table>
<thead>
<tr>
<th>Quality measure</th>
<th>Mean (range)</th>
<th>Median (IQR\textsuperscript{*})</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAART use</td>
<td>0.81 (0.57-0.93)</td>
<td>0.81 (0.77-0.86)</td>
</tr>
<tr>
<td>Non-detected HIV viral load</td>
<td>0.38 (0.01-0.60)</td>
<td>0.41 (0.30-0.48)</td>
</tr>
<tr>
<td>P\textit{carinii} pneumonia prophylaxis</td>
<td>0.70 (0.25-1.00)</td>
<td>0.75 (0.61-0.84)</td>
</tr>
<tr>
<td>Tuberculosis screening</td>
<td>0.52 (0.06-0.91)</td>
<td>0.53 (0.35-0.69)</td>
</tr>
<tr>
<td>Hepatitis C screening</td>
<td>0.81 (0.25-1.00)</td>
<td>0.87 (0.73-0.93)</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>0.60 (0.27-0.98)</td>
<td>0.62 (0.50-0.71)</td>
</tr>
<tr>
<td>Influenza vaccination</td>
<td>0.51 (0.02-0.82)</td>
<td>0.53 (0.45-0.61)</td>
</tr>
<tr>
<td>Visits in three quarters</td>
<td>0.67 (0.47-0.82)</td>
<td>0.68 (0.62-0.75)</td>
</tr>
</tbody>
</table>

*Interquartile range.

Quality of care measures
The eight measures of quality of care were based on guidelines that did not change over this time period.\textsuperscript{15-18} Our primary measures were proportion of use of highly active antiretroviral therapy (HAART) at the time of the last visit during the review period and control of HIV viral load for appropriate patients. Patients included in the denominator for the proportion of HAART use were those with CD4 cell counts less than 500×10\textsuperscript{6}/l or viral loads greater than 20 000 copies/ml, and patients already receiving HAART, as per guidelines in effect at the time.\textsuperscript{19} Viral load was considered as controlled if it was undetectable or if the total viral load was less than 400 copies/ml. We also assessed whether screening for tuberculosis, hepatitis C, and cervical cancer (for women only), appropriate prophylaxis against \textit{Pneumocystis carinii} pneumonia, and influenza vaccinations were provided during the review period. For hepatitis C, we accepted documentation of a previous positive result of a hepatitis C test. We defined appropriate access to outpatient care as actually visiting the site during at least three of four quarters. All measures at the patient level were dichotomous.

Analyses
Our unit of analysis was the care site. The site level value for each measure of quality was the proportion of patients for whom the quality indicator was documented in the reviewed medical records. Our goal was to review 75 records at each of 69 sites to give a total of 10 350 records, though the final number of records reviewed was 9986 (97%). We initially analysed the first and second review periods separately but because results were similar we aggregated data from the two periods. In 966 cases, a patient’s medical record was selected for review in both periods. For these cases we dropped the data from the second period, leaving a total of 9020 unique patients in care at 69 sites. We present descriptive statistics for the 69 sites. Because characteristics of patients vary among sites, we examined adjusted means for each of the eight quality measures. We used the GLIMMIX

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*Interquartile range.
macro in SAS (version 8.2) to produce least square means for sites using the logit link function. We adjusted for patients’ characteristics that might be related to the quality measures, including age, sex, stage of disease based on lowest recorded CD4 cell count over the period of care, active psychiatric or substance abuse problems, history of HIV related diagnoses, number of comorbid medical conditions, and review period. Adjusted least square means were then converted to proportions.

Next, we calculated the correlations among the eight adjusted quality measures. Finally, we examined the degree to which high performance on one indicator was related to high performance on the other seven. To do this, we dichotomised each quality measure at the 75th centile of the distribution across all 69 sites, and called those sites in the top quarter “high performers.” When the top fifth was used, similar results were obtained. We then examined the distribution of the number of times sites performed in the top quarter across the eight quality measures and compared it to a binomial distribution for eight independent trials with a probability of success (being a high performer) of 0.25. If the actual distribution differs from the binomial distribution, there are more high performers than expected by chance; if the two distributions are similar, this suggests that site’s performance on one quality measure is independent of its performance on others. The distributions were compared with $\chi^2$ test.

RESULTS

Characteristics of patients and sites—Thirty two per cent of patients were female, 16% reported active substance abuse, and 32% had CD4 cell counts below $200 \times 10^3$/l (table 1). The 69 sites that we studied were in 30 states in all regions of the US, representing the full spectrum of types of organisation that provide HIV care. Most sites described themselves as having HIV expertise, including 62% that were specialised HIV clinics and 35% that were general medicine clinics with specialised HIV care teams. Only 3% were general medicine clinics with no specialised HIV team. Most (80%) had multidisciplinary HIV care teams that met about twice a month.

Site level quality measures—Clinic performance on the quality measures ranged from 0.38 of patients with non-detectable viral loads (table 2) to 0.81 of eligible patients on HAART and 0.81 of patients with documented hepatitis C status. The greatest variation across clinics was for the proportion of patients who received tuberculosis screening (interquartile range of 0.35-0.69), and the least variation was seen for the proportion of eligible patients who received HAART (interquartile range of 0.77-0.86).

Correlations among quality measures—Of the 28 correlations between measures at the clinic level (table 3), the highest was the relation between proportions of HAART therapy and $P. carinii$ pneumonia prophylaxis at 0.42 ($P<0.001$). The correlation between the proportion receiving cervical cancer screening and tuberculosis screening was nearly as high at 0.40 ($P<0.001$). Two other correlations were greater than 0.30, those between the proportion receiving hepatitis C screening and tuberculosis screening (0.32, $P<0.01$), and between influenza vaccination and non-detectable viral loads (0.30, $P<0.05$). Four additional correlations were between 0.20 and 0.29, and the 20 remaining correlations were all less than 0.20.

Distribution of number of high performance areas—The number of times sites were in the top quarter (a “high performer”) for the eight quality measures ranged from none (never in the top quarter) to seven (in the top quarter for all but one measure). The figure shows the actual and expected distribution under an assumption that “high performance” on different measures occurs at random (according to a binomial distribution in which the probability of success on each trial is 0.25 and the eight trials are independent). The actual and the binomial distributions are not statistically different ($P=0.49$).

DISCUSSION

We found relatively weak associations between the assessed indicators of quality of HIV care. Of the 28 possible correlations between the eight quality measures, only two (7%) were greater than 0.40, two were between 0.30 and 0.39, and 20 (71%) were less than 0.20. This was particularly surprising because we assessed quality of care for a single chronic medical condition in sites that were specialised HIV clinics or had specialised HIV care teams. Furthermore, there were no more “high performing” organisations than were predicted by chance. Only one site was in the top quarter for seven measures, and no sites were in

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Table 3 | Correlations among adjusted quality measures (n=69)*

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HAART use</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Non-detectable HIV viral load</td>
<td>0.20</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Pneumocystis carinii pneumonia prophylaxis</td>
<td>0.42***</td>
<td>0.02</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Tuberculosis screening</td>
<td>0.13</td>
<td>0.02</td>
<td>0.18</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Hepatitis C screening</td>
<td>-0.02</td>
<td>0.10</td>
<td>0.06</td>
<td>0.32**</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Cervical cancer screening</td>
<td>-0.09</td>
<td>0.06</td>
<td>0.14</td>
<td>0.40***</td>
<td>0.05</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Influenza vaccination</td>
<td>-0.002</td>
<td>0.30*</td>
<td>0.12</td>
<td>0.18</td>
<td>0.24*</td>
<td>0.07</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>8 Visits in three quarters</td>
<td>0.03</td>
<td>0.26*</td>
<td>0.04</td>
<td>0.08</td>
<td>0.009</td>
<td>0.21</td>
<td>0.14</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.01; ***P<0.001.
the top quarter for six or eight measures. We expected that their focus on HIV care would lead some of these sites to develop systems and procedures that would positively affect multiple aspects of care. Moreover, guidelines for HIV care had been widely disseminated when these data were collected.\(^{15-27}\)

We thought that in HIV care sites the preconditions would exist for high correlations among measures, including focus on a single condition, relatively high proportions of specialisation (97%), and the presence of multidisciplinary HIV care teams (at 80% of sites). Our results suggest that specialisation and focus on a specific condition may not be sufficient to produce high quality in multiple aspects of care. Consistency may require the coordination of multiple processes and procedures. Consider, for the sake of argument, two contrasting models of the clinical processes related to the eight quality measures we assessed. In the first model, a common system connects all eight measures. Elements in this common system include the physical space, clinic staff, a phone and messaging system, medical records, regular group meetings, and shared (specialised) clinical knowledge. In the second model, each quality measure can be thought of as the outcome of an independent chain of linked processes; failure of any single process in the chain causes the desired quality event not to occur. Because each chain of processes is independent of the others, success or failure of one chain has little impact on the success or failure of a simultaneously operating or parallel chain.

For example, starting and maintaining a patient on HAART may require preparatory visits with several different providers (for example, physicians, pharmacists, and case managers) and access to these providers during the initial phases of treatment. Doing tests to screen for tuberculosis requires a provider, usually a nurse, who carries out the test, ensures that it is appropriately read 24-48 hours later, and documents the results. Ensuring regular cervical cancer screening, on the other hand, may require the cooperation of a nearby gynaecology practice. Each of these examples involves largely independent chains of processes. \(P\) carinii pneumonia prophylaxis and HAART may have been more highly correlated than most other pairs of measures because the chains of processes that produce these outcomes have several shared elements (that is, both are prescriptions given by physicians, and both are guided by CD4 cell counts).

Adapted coordination among processes is probably more difficult to achieve when quality measures assess care given by different providers at multiple care sites (such as different services in a hospital). One potential reason that studies of quality\(^{19,20}\) and quality improvement efforts\(^{15,21-23}\) have yielded less impressive results than many expected may be the difficulty of simultaneously improving and coordinating multiple systems.

During the study period there were no specific incentives in place (financial or otherwise) for the practices we studied to meet specific quality targets, nor were there any centralised or public processes to measure quality. Such measurement processes and incentives may increase correlations among quality measures, even in the absence of effective and coordinated systems and processes.

One interpretation of these data could be that providers recognise that they cannot provide uniformly high quality care and that they therefore prioritise. For example, few would debate that HAART use is clinically the most consequential of the eight measures we assessed, and the median proportion for use was among the highest the eight proportions at 0.81. Furthermore, the correlation between HAART use and \(P\) carinii pneumonia prophylaxis (also consequentially) was relatively high (0.42). On the other hand, prioritisation would not explain why the median proportion for hepatitis C screening was higher than for HAART use. High proportions of hepatitis C screening may be observed because it involves only ordering a blood test, and because once a positive result is found the test does not need to be repeated. If providers know that they have to trade off some goals of care against others, however, this is further proof that performance on one measure might imply little about performance on others, even in the setting of specialty care for a single disease. While no one advocates a healthcare system in which one measure of good care competes against another, limited resources and difficult choices are a reality in all healthcare settings.

**Study limitations**

We examined quality measures that could be assessed by reviewing medical records. All but one (non-detectable viral load) were measures of process. Our findings might have differed if we had been able to assess mortality, rates of admission to hospital, appropriate management of opportunistic infections, changes in health status, adherence to medication, or patients’ reports about care.\(^{24}\) We think that measurement of other processes or outcomes, however, would yield even lower correlations. Four of the care processes we assessed (screening for tuberculosis, hepatitis C, and cervical cancer, and influenza vaccinations) are simple to implement for anyone with basic clinical training, and the remaining four (HAART therapy, viral load control, \(P\) carinii pneumonia prophylaxis, and frequency of visits) are the subject of detailed guidelines for clinical practice.\(^{25-26}\) Guidelines for tuberculosis skin testing do not suggest yearly testing, but rather that annual repeat testing (after an initial negative test result) should be considered in populations with a “substantial risk” of exposure (such as prison inmates),\(^{18}\) which may have reduced the proportion who received tuberculosis screening. Another limitation of reviewing medical record is that processes may have been completed, but not documented, biasing our estimates downwards.

Finally, we studied patients at clinics receiving specific funding, and our findings may not generalise to other HIV care settings. Because this specific funding goes to rural and urban underserved care sites, our
findings may not generalise to sites that care for patients with, for example, higher incomes, more education, and better health insurance. The sites studied, however, receive considerable scrutiny as a condition of participation in the programme, and quality levels there might be higher than at some other HIV care sites. To the extent that our study design excludes sites with consistently low quality scores, the correlations that we report are lower than they would be in a broader sample.

Implications

Our findings have implications for efforts to monitor quality and improvement. Current policy initiatives that seek to pay physicians for their performance on a small selected set of indicators or that create tiers of physicians or hospitals may not improve quality across a broad spectrum of care or conditions. Indeed, such programmes could prompt physicians or physician organisations to channel efforts into affecting the indicators being assessed to the detriment of other aspects of quality. More empirical studies are needed on the impact of pay-for-performance initiatives and other improvement strategies on overall quality.28,29

Our results suggest that none of the sites we studied had the kinds of administrative, clinical, and human resources systems in place that are necessary to produce consistently high care quality. Continued and concerted efforts to improve healthcare systems may yield such patterns of high performance, but that goal has remained elusive to date. This should stimulate us to redouble our efforts to identify and implement the kinds of system changes that will allow us to cross the “quality chasm.”40 Focusing on the improvement and coordination of multiple systems within organisations may be a useful direction to pursue.

We thank Carol Cosenza and Patricia Gallagher of the Center for Survey Research who assisted with instrument development and survey administration and our colleagues at the Health Resources and Services Administration and at the Institute for Healthcare Improvement who participated in and facilitated the EQHIV study.

Contributors: All authors made substantial contribution to conception, design, analysis, and interpretation of data, drafting the article, and revising it critically for important intellectual content and final approval. IBW is guarantor.

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Treatment of bronchiectasis in adults

Nick H T ten Hacken, Peter J Wijkstra, Huib A M Kerstjens

Patients with bronchiectasis usually need lifelong medical support from their doctor, especially given the frequent episodes of infection. This article focuses on the treatment of bronchiectasis in adults and does not include a discussion of bronchiectasis caused by cystic fibrosis. The prevalence of bronchiectasis not linked to cystic fibrosis is unclear, but every general practitioner in the United Kingdom probably has a few patients.

How do we diagnose bronchiectasis?

Bronchiectasis refers to the permanent abnormal dilatation of the central and medium sized bronchi as a result of a vicious cycle of transmural infection and inflammation with mediator release. Symptoms include chronic productive cough, wheeze, and dyspnoea. Infective exacerbations are associated with worsening of symptoms and signs of pneumonia. Haemoptysis can occur, but amounts of blood are usually small, and serious haemoptysis requiring selective arteriography and embolisation or surgery is rare.

The most frequently used classification system distinguishes between cylindrical, varicose, and saccular or cystic bronchiectasis. Although insightful, this classification has no clinical or therapeutic uses. A modern clinical definition includes the daily production of mucopurulent phlegm and chest imaging that demonstrates dilated and thickened airways. The clinical suspicion of bronchiectasis can be confirmed by high resolution computed tomography. Characteristic findings include internal bronchial diameters greater than that of the adjacent pulmonary artery, lack of bronchial tapering, presence of bronchi within 1 cm of the costal pleura, presence of bronchi abutting the mediastinal pleura, and bronchial wall thickening.

A diagnosis of bronchiectasis should prompt an investigation of possible causes and associated conditions (table 1), some of which can be treated. Extrinsic factors, particularly childhood respiratory infections, were an important cause of permanent bronchial damage in the past. These days, especially in Western countries with early immunisation and widespread use of antibiotics, post-infectious damage is a less prominent cause of the disease, and intrinsic defects are more common causes. A study of 150 adults with bronchiectasis in the UK found that 53% of cases were idiopathic; 29% were post-infectious; 8% were caused by an immune defect, 7% by allergic bronchopulmonary aspergillosis, 4% by aspiration, 3% by Young’s syndrome, 3% by cystic fibrosis, 3% by rheumatoid arthritis, 1.5% by ciliary dysfunction, and <1% by miscellaneous causes.

How is it treated?

Bronchiectasis can be treated by pharmacological and non-pharmacological means (tables 2 and 3). The box shows an arbitrary step-up scheme that takes into account the level of evidence and safety risks.

Antibiotics

Antibiotics are used to treat acute exacerbations, to prevent exacerbations, or to reduce the bacterial burden. In general, the outcome of treatment with antibiotics depends on the severity of the disease. In mild to moderate bronchiectasis the infection can be completely eradicated, whereas in severe disease the bronchial tree remains chronically colonised. Antibiotics with a high penetrance (macrolides, azalides, and quinolones) are recommended in severe cases because high concentrations of bacteria are located intraluminally in association with mucus, and because thickening and scarring of the bronchial wall may reduce local bioavailability. Pseudomonas aeruginosa is inherently resistant to most antibiotics at concentrations that are achieved in vivo. The organism is susceptible to (oral) quinolones, but after one or two courses resistance may develop. Patients who are clinically unwell or do not respond to oral antibiotics should be admitted to hospital and given intravenous antibiotics.

Patients who relapse quickly might need prophylactic antibiotics. Three strategies have been described—a high oral dose for a prolonged period (at least four weeks), aerosolised antibiotics (for example, during alternate months), or regular pulsed courses of intravenous antibiotics (for example, two to three week courses with one or two months in between).

Suggested step-up scheme for treating bronchiectasis

Step 1: Inhaled fluticasone (500 µg twice daily)
Step 2: Physical therapy including exercise training
Step 3: Prolonged use of oral antibiotics. The choice of antibiotic should depend on sputum culture results, with a preference for clarithromycin
Prolonged use of oral antibiotics for purulent bronchiectasis was investigated in a recent meta-analysis. It identified six trials that included 302 patients. The results of five studies were positive in terms of parameters pertaining to sputum, such as volume or purulence. However, no positive effects were seen on rates of exacerbation, lung function, or death. This contradicts the findings of a recent controlled study that investigated 500 mg of azithromycin given twice a week for six months in 30 patients. Pulmonary function tests did not change, but azithromycin significantly decreased the incidence of exacerbations compared with usual care. Inhalation of nebulised antibiotics might be a better route of administration because of its favourable benefit-risk ratio. Gentamicin 40 mg inhaled twice daily for three days improved sputum production, sputum neutrophil activity, airway obstruction, exercise capacity, and nocturnal desaturation compared with placebo. Tobramycin 300 mg inhaled twice daily for four weeks eradicated _P. aeruginosa_ in 35% of patients and improved the medical condition of 62%. Cefazidine 1 g and tobramycin 100 mg inhaled twice daily over 12 months decreased the number of hospital admissions and inpatient days.

Flu vaccinations reduced the number of flu related exacerbations in chronic obstructive pulmonary disease, so vaccination might have a beneficial effect in bronchiectasis. However, randomised controlled trials of vaccination in patients with bronchiectasis are lacking.

### Mucolytics

Mucolytics target hypersecretion or the physicochemical characteristics of sputum seen in bronchiectasis. They aim to improve tracheobronchial clearance. In one study, oral bromhexine (30 mg three times daily) was added to an antibiotic during acute infective exacerbations. It improved expectoration, the quantity and quality of sputum, and auscultatory findings. In another study, nebulised recombinant human DNase I (2.5 mg once or twice a day for two weeks) was given to patients with stable bronchiectasis. The study found no improvements in spirometry, quality of life, dyspnoea, safety, or ciliary transportability of the sputum. In a large placebo controlled study, 349 patients with idiopathic bronchiectasis in a stable condition inhaled 2.5 mg recombinant human DNase I for 24 weeks. Pulmonary exacerbations were more frequent and the decline in FEV1 (forced expiratory volume in one second) was greater in patients who received DNase than in controls. These results contrast greatly with the positive effects of this drug in cystic fibrosis.

Inhaled mannitol may improve impaired mucociliary clearance by inducing an influx of fluid into the airways, and thereby changing the mucous rheology. One study found that mucociliary clearance was doubled in the central and intermediate lung regions of 11 patients with bronchiectasis directly after inhaling 300 mg mannitol. A follow-up study showed that these effects lasted for at least 24 hours. Inhalation of 400 mg mannitol once daily for 12 days improved the tenacity and hydration of sputum, as well as health status. Mannitol is therefore a promising new drug, especially as it is easier and more hygienic to inhale a dry powder than to use a nebuliser. Large randomised controlled studies are needed, however, to establish its efficacy and tolerability during long term administration.

### Anti-inflammatory agents

Inhaled corticosteroids may reduce inflammation and improve airway obstruction, as they do in asthma. To date, three randomised controlled studies have investigated this hypothesis. Inhaled fluticasone decreased the density of leucocytes and concentrations of the inflammatory mediators interleukin 1β, interleukin 8, and leukotriene B4 in sputum. However, a systematic review found no significant improvements in lung function. Recently, a large study was published in which 86 patients inhaled fluticasone 500 µg twice daily or placebo for 12 months. Twenty four hour sputum volume improved significantly in patients treated with fluticasone, but no change was seen in the frequency of exacerbations, the purulence of sputum, or lung function. Systemic corticosteroids may be better at penetrating the bronchial wall and therefore be more effective, but data from randomised controlled trials are available only for bronchiectasis associated with cystic fibrosis.

Leukotriene receptor antagonists are a new class of drugs that is effective in the treatment of asthma. These drugs may be of benefit in bronchiectasis because they inhibit neutrophil mediated inflammation. To date, no randomised controlled trials of these agents have been published, however.

Non-steroidal anti-inflammatory drugs may also be of use because they inhibit neutrophil function and the release of neutrophil elastase. In a non-controlled open study, eight patients with stable bronchiectasis...
received 25 mg oral indometacin three times daily for four weeks.\textsuperscript{13} Indometacin had a pronounced effect on two of the three neutrophil functions studied—neutrophil chemotaxis and fibronectin degradation were inhibited by more than 50%. However, lung inflammation, sputum volume, and sputum quality did not change. Interestingly, high dose ibuprofen taken consistently for four years significantly slowed the progression of lung disease in patients with cystic fibrosis.\textsuperscript{14} Ibuprofen has not yet been investigated in non-cystic fibrosis bronchiectasis.

Macrolides suppress inflammation—indepen dent of their antimicrobial actions—in airway diseases like asthma, chronic obstructive pulmonary disease, cystic fibrosis, and diffuse panbronchiolitis. Indeed, macrolides improved clinical status and lung function in a few small studies of bronchiectasis.\textsuperscript{14–18} In addition, a randomised placebo controlled trial in children showed that three months of treatment with clarithromycin decreased the total number of leucocytes, proportion of neutrophils, and the concentration of interleukin 8 in bronchoalveolar lavage fluid.\textsuperscript{18} Because bacterial growth was not eliminated the authors suggested that direct anti-inflammatory effects of clarithromycin were responsible. This contradicts a randomised placebo controlled study in adults, however, which showed that eight weeks of low dose erythromycin did not reduce the number of leucocytes or the concentrations of interleukin 1α, interleukin 8, tumour necrosis factor α, or leukotriene B4 in sputum.\textsuperscript{15}

### Table 2 | Pharmacological and non-pharmacological treatments for stable bronchiectasis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
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<td><strong>Drugs</strong></td>
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<tr>
<td>Antibiotics:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolonged use of oral antibiotics</td>
<td>1+</td>
<td>A</td>
</tr>
<tr>
<td>Aerosolised antibiotics</td>
<td>1+</td>
<td>A</td>
</tr>
<tr>
<td>Regular pulsed courses of intravenous antibiotics</td>
<td>4</td>
<td>D</td>
</tr>
<tr>
<td>Flu vaccination</td>
<td>1−</td>
<td>C</td>
</tr>
<tr>
<td><strong>Mucolytics:</strong></td>
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</tr>
<tr>
<td>Bromhexine*</td>
<td>1+</td>
<td>B</td>
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<tr>
<td>N-acetylcysteine</td>
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<tr>
<td>Recombinant human DNase aerosol</td>
<td>1+</td>
<td>A†</td>
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<tr>
<td>Mannitol inhalation powder</td>
<td>2++</td>
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<tr>
<td><strong>Anti-inflammatory or immunomodulating drugs:</strong></td>
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<tr>
<td>Oral corticosteroids</td>
<td>2+</td>
<td>D</td>
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<tr>
<td>Inhaled corticosteroids</td>
<td>1+</td>
<td>B</td>
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<tr>
<td>Oral leukotriene receptor antagonists</td>
<td>4</td>
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<tr>
<td>Indometacin or ibuprofen</td>
<td>2−</td>
<td>D</td>
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<tr>
<td>Macrolides (clarithromycin)</td>
<td>1+</td>
<td>B</td>
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<tr>
<td>Flu vaccination</td>
<td>2+</td>
<td>C</td>
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<td><strong>Bronchodilators:</strong></td>
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<tr>
<td>Short acting β2 adrenergic agonists</td>
<td>2+</td>
<td>D</td>
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<td>Long acting β2 adrenergic agonists</td>
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<tr>
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<td>D</td>
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<tr>
<td>Methylxanthines</td>
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<tr>
<td><strong>Non-pharmacological treatments</strong></td>
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<tr>
<td>Bronchopulmonary hygiene physical therapy\textsuperscript{w14 w15}</td>
<td>3</td>
<td>D</td>
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<tr>
<td>Forced expiratory technique†</td>
<td>3</td>
<td>D</td>
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<tr>
<td>Autogenic drainage‡</td>
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<td>D</td>
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<tr>
<td>Positive end expiratory pressure therapy‡</td>
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<td>D</td>
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<tr>
<td>Flutter device or RC-Cornet device‡</td>
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<tr>
<td>Postural drainage§</td>
<td>3</td>
<td>D</td>
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<tr>
<td>Mechanical vibration§</td>
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<tr>
<td>Percussion§</td>
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<tr>
<td>Intrapulmonary percussive ventilation§</td>
<td>3</td>
<td>D</td>
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<tr>
<td>High frequency chest compression§</td>
<td>3</td>
<td>D</td>
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<tr>
<td><strong>Training</strong></td>
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<tr>
<td>Exercise training with or without inspiratory muscle training†</td>
<td>1+</td>
<td>B</td>
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<tr>
<td><strong>Surgery</strong></td>
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<tr>
<td>Segmental, lobar, or lung resection</td>
<td>2+</td>
<td>B</td>
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</table>

*S* Studied in acute exacerbations; †not recommended; ‡active participation of the patient needed; §passive techniques. See table 3 for definitions of level of evidence and grade of recommendation.

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**SOURCES AND SELECTION CRITERIA**

We searched PubMed using the keywords "bronchiectasis," "diagnosis," "pathogenesis," "treatment," and "management." We also searched the Cochrane Library databases and Clinical Evidence and used references from our personal archives. Papers and reports on cystic fibrosis and childhood bronchiectasis were excluded.

**Bronchodilators**

The mechanisms of expiratory airflow obstruction in non-cystic fibrosis bronchiectasis are not clear, but may include excessive production of mucus, distortion of the bronchial wall, and constriction of smooth muscle. Increased bronchial hyper-reactivity and some reversibility of the airflow obstruction with an inhaled bronchodilator are common. As bronchiectasis may coexist with asthma or chronic obstructive pulmonary disease, some studies have a high degree of uncertainty as to whether airway obstruction is due to asthma, chronic obstructive pulmonary disease, or bronchiectasis (or a combination). Nevertheless, as many patients show signs of airway obstruction and hyper-responsiveness, they often receive bronchodilators.

One small Malaysian study gives some information about the reversibility of airway obstruction in bronchiectasis. It included 24 patients with confirmed bronchiectasis but no signs of an acute exacerbation. The study compared 400 µg fenoterol, followed by 5 mg fenoterol 30 minutes later, with 40 µg ipratropium, followed by 500 µg ipratropium.\textsuperscript{19} FEV\(_1\) increased more than 15% in response to one or both bronchodilators in 11 patients—five responded to both, three to fenoterol alone, and three to ipratropium alone. This small study suggests a significant response to bronchodilators in a subset of patients.

Cochrane reviews found no randomised controlled trials on short acting β2 adrenergic agonists,\textsuperscript{18} long acting β2 adrenergic agonists,\textsuperscript{19} anticholinergic...
therapy,20 or oral methylxanthines21 in patients with non-cystic fibrosis bronchiectasis. Good quality studies are therefore urgently needed in this field.

**Bronchopulmonary hygiene physical therapy**

Bronchopulmonary hygiene physical therapy is a form of chest physical therapy that aims to remove lung secretions in patients with acute and chronic airway diseases. Many active and passive techniques are available (table 2), and the technique chosen varies between institutes and physical therapists.w20 w21 The evidence in support of these techniques is variable and the literature is conflicting.w20 Two systematic reviews found insufficient evidence to support or refute this form of therapy.22 23

<table>
<thead>
<tr>
<th>Grade</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
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<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
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<tr>
<td>1−</td>
<td>Meta-analyses, systematic reviews or RCTs, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>2++</td>
<td>High quality systematic reviews of case-control or cohort studies; or high quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the association is causal</td>
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<tr>
<td>2+</td>
<td>Well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the association is causal</td>
</tr>
<tr>
<td>2−</td>
<td>Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the association is not causal</td>
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<tr>
<td>3</td>
<td>Non-analytic studies, such as case reports, case series</td>
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<td>4</td>
<td>Expert opinion</td>
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<th>Evidence</th>
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<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and showing overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results or extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results or extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4 or extrapolated evidence from studies rated as 2+</td>
</tr>
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</table>

RCT=randomised controlled trial.

**Exercise training**

The role of pulmonary rehabilitation and inspiratory muscle training has been investigated in only one randomised controlled trial. It compared an eight week training programme of pulmonary rehabilitation alone, pulmonary rehabilitation plus inspiratory muscle training, and a control group.w22 The authors concluded that pulmonary rehabilitation does improve exercise tolerance. Simultaneous inspiratory muscle training offered no additional benefit.

**Surgery**

If the area of bronchiectasis is localised and the patient’s symptoms are debilitating or life threatening, surgical resection has long been thought to be of benefit. This assumption was based on several non-randomised controlled studies of uncertain value. A Cochrane review updated in 2002 found no randomised clinical trials—just case series or case-control studies.24 The largest case-control study included pneumonectomy in 190 cases, lobectomy in 202 cases, bilobectomy in 23 cases, and lobectomy combined with segmental resection in 72 cases.25 Overall mortality was 3.5%, and 71% of patients had no symptoms during follow-up (four months to 10 years). The authors therefore concluded that surgery was preferable to conventional medical treatment.

**Conclusion**

The general consensus is that acute exacerbations should be treated promptly with short courses of systemic antibiotics. In stable bronchiectasis, a high level of evidence exists for the use of prolonged and aerosolised
SUMMARY POINTS

Bronchiectasis refers to abnormal bronchial dilatation caused by a vicious cycle of transmural infection and inflammation.

Symptoms include chronic productive cough, wheeze, and dyspnoea; repeated respiratory infections may dominate the clinical picture.

Diagnosis is based on daily production of mucopurulent phlegm and dilated and thickened airways on computed tomography.

Diagnosis should lead to investigation and treatment of possible causes and associated conditions.

Acute exacerbations should be treated promptly with short courses of antibiotics.

Frequent exacerbations may be treated with prolonged and aerosolised antibiotics.

The role of mucolytics, anti-inflammatory agents, and bronchodilators is not clear.

Surgery is a possibility if the area of bronchiectasis is localised and symptoms are debilitating or life threatening.

Antibiotics, but this form of treatment is mostly reserved for patients with frequent exacerbations. Because of the low level of evidence we cannot recommend the use of mucolytics, anti-inflammatory agents, or bronchopulmonary hygiene therapy on a routine basis.

Surgery may be considered if the area of bronchiectasis is localised and the patient’s symptoms are debilitating or life threatening.

Well powered studies to investigate the effects of well defined treatment regimens on important short and long term outcomes of bronchiectasis are urgently needed.

Contributors: NHTtH selected the literature and wrote all versions of the article. HAMK and PJW commented on the various drafts of the manuscript. All authors discussed the grading the levels of evidence and recommendations. NHTtH is guarantor.

Competing interests: None declared.

Provenance and peer review: Commissioned; externally peer reviewed.


An all-round thumbs up

A 43 year old street cleaner was brought to her local emergency department in the early hours of the morning by a concerned set of firefighters. The patient had inadvertently trapped her non-dominant thumb in the end of a standpipe. The activated self-locking mechanism had clamped on her thumb within the heavy weight tubing, and the fire crew had been unable to prise her free.

After the administration of a digital nerve block and some fairly hefty head scratching, a fair fetched plan came to mind. The standpipe had two holes (for a cross bar) about 10 cm from the locked thumb. By inserting a fine-bore optic naso-endoscope into one of the holes, I was able to see the pin compressing the patient’s thumb and simultaneously introduce a right angled Lahey clamp. This enabled me to retract the pin, and the patient slide her thumb free to a resounding round of applause from the attendant fire crew.

The benefits of an old fashioned basic surgical training shone through as my accident and emergency, ENT, and general surgery skills combined for an all-round thumbs up.

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brigstocke@hotmail.com
RATIONAL IMAGING

Investigating progressive unexplained renal impairment and hypertension

L A Ratnam, S R Nelson, A M Belli

Diagnosing renal artery stenosis can be difficult. This article explores possible types of imaging for this, ranging from safe, inexpensive tests to more invasive procedures.

The patient

A 79 year old hypertensive man was referred for investigation of impaired renal function. At the time of referral he was taking a single antihypertensive agent and his blood pressure measured 170/85 mm Hg. He smoked 50 g of pipe tobacco a week. He had no other medical history of note. No renal artery bruit was detected, and the remaining clinical examination was unremarkable. His serum creatinine concentration at presentation was 116 mmol/l (normal range 60-110 mmol/l), representing an estimated glomerular filtration rate of 55 ml/min. Urine analysis was normal. His serum cholesterol concentration was raised (5.9 mmol/l (normal range 3.0-5.2 mmol/l)). Over two years, his blood pressure remained raised despite an increase in his antihypertensive treatment, and his serum creatinine concentration rose to 206 mmol/l.

What is the next investigation?

Unexplained, progressive renal impairment, and hypertension that is poorly controlled despite the use of multiple drugs, warrants further investigation. The absence of blood and protein in the urine points away from intrinsic renal disease. Both a prerenal cause (such as renal artery stenosis) and obstructive uropathy are possible diagnoses. Renal artery stenosis is an important diagnosis to make as it is common, potentially treatable, and associated with a higher mortality from end stage renal failure than other causes.¹ ²

Ultrasonography

Ultrasonography is the usual first investigation as it is safe, inexpensive, and widely available. Obstruction is generally easily detected, but occasionally a calculus causing intermittent obstruction may be missed. Size difference of >1.5 cm or a solitary kidney are the potential ultrasound features of significance in renal artery stenosis. Doppler studies are conducted for renal artery evaluation in some centres. The reported sensitivity ranges from 60% to 97%, and specificity from 85% to 99%,³ but the results are highly dependent on operator expertise, and interpretation is consistently accurate only in non-atheromatous arteries. Visualisation is limited by adipose tissue and bowel gas; accessory renal arteries may be missed; and mild stenosis is difficult to detect. Given the technical difficulties and time consuming nature, Doppler studies may be replaced by other, non-invasive methods of imaging the renal arteries.

Nuclear medicine

Conventional ⁹⁹ᵐ technetium-mercaptoacetyltriglycine (⁹⁹ᵐTc-MAG3) renography allows evaluation of the split function of the kidneys (contribution of each kidney to overall function) and exclusion of functional obstruction by assessing renal excretion and drainage. In the absence of obstruction, a difference in split function may be indirect evidence of renal artery stenosis. The use of an angiotensin converting enzyme inhibitor in conjunction with renography (captopril challenge scintigraphy) removes angiotensin II mediated vasoconstriction, which increases the difference in glomerular filtration rates of the stenotic kidney and the contralateral kidney. Sensitivities of captopril renography have been reported at 90%, with specificity of 79%.⁴ A
positive scan indicates the presence of renovascular hypertension with a haemodynamically significant renal artery stenosis. False negatives arise in the presence of bilateral stenosis, overhydration, and chronic use of angiotensin converting enzyme inhibitors, and impaired renal function reduces the specificity of the examination. Owing to these limitations, renography is not widely used for non-invasive diagnosis of renal artery stenosis.

Computed tomography angiography
Non-contrast enhanced computed tomography may show a small calculus not seen by other methods if the history is suggestive. The introduction of multislice computed tomography with the possibilities of three dimensional reconstruction has made computed tomography angiography an important non-invasive means of identifying renal artery stenosis. Image interpretation may be difficult in heavily calcified arteries.

However, computed tomography angiography involves the use of ionising radiation and iodinated contrast medium. The procedure is therefore contraindicated in patients with contrast allergy and may not be tolerated by claustrophobic patients. The use of contrast in those with impaired renal function can result in contrast induced nephropathy. The most effective means of preventing this is by prior hydration. The use of various pharmacoprophylaxis agents and the benefits of iso-osmolar radiographic contrast agents remain controversial, with more evidence required. Computed tomography angiography is reported to have sensitivities of 90-98% and specificities of 85-94%.3

Magnetic resonance angiography
Magnetic resonance angiography has similar diagnostic accuracy to computed tomography angiography, with reported sensitivities of 90-100% and specificities of 88-100%.3 Comparable information is obtained about the number of renal arteries, the size of the kidneys, and the presence of anatomical variants. It has the benefits of producing angiograms without using iodinated contrast or radiation. Enhancement with gadolinium based contrast has generally replaced non-contrast enhanced techniques, but contrast associated nephrogenic systemic fibrosis in patients with moderate to end stage renal failure has been reported.5 (For further information visit www.mhra.gov.uk.) Contraindications to magnetic resonance imaging include use in patients with implants such as pacemakers, defibrillators, cochlear implants, and spinal cord stimulators. Claustrophobic patients should also be excluded.

Digital subtraction angiography
Arteriography with digital subtraction improves contrast resolution by removing background information. It is an invasive technique, carrying a small but definite risk that is related to the arterial puncture and to the manipulation of the catheter and wire. Although angiography uses iodinated contrast and entails radiation, carbon dioxide may be used as a non-nephrotoxic contrast agent in patients with renal impairment or contrast allergy. Pressure gradients can be measured across areas of stenosis to determine haemodynamic significance where there is doubt, and therapeutic procedures such as percutaneous transluminal angioplasty or stenting can be carried out at the same time, although how much such an intervention improves renal function is the subject of ongoing trials.

Outcome
Our patient had an ultrasound scan, which showed normal sized kidneys. As creatinine concentration improved and then deteriorated, 99mTc-MAG3 renography was conducted to look for functional obstruction. The renogram showed asymmetric function. As 69% of the overall function was from the left kidney, this raised the suspicion of underlying renal artery stenosis on the right (fig 1).
Magnetic resonance angiography showed single renal arteries bilaterally with bilateral stenoses and a slightly smaller right kidney (fig 2). Our patient was encouraged to stop smoking and was started on simvastatin as his cholesterol concentration remained raised.

A year later, his serum creatinine concentration had increased from 116 mmol/l to 206 mmol/l and his blood pressure remained difficult to control despite an increase in his antihypertensive treatment. In view of the rising creatinine concentration, a decision was made to proceed to angioplasty and stenting in an attempt to preserve his renal function (figs 3, 4 and 5). The left renal artery was stented, but a guidewire could not be passed across the tight stenosis in the right renal artery. His serum creatinine concentration fell from 206 mmol/l to 163 mmol/l. His blood pressure improved from 170/85 mm Hg to 130/58 mm Hg with no change in medication.

Contributors: All three authors contributed to the selection of the patient and the preparation and editing of the manuscript. AMB is the guarantor.

Competing interest: AMB has been reimbursed expenses by Boston Scientific, Johnson & Johnson, and Abbott and Gore—all manufacturers of arterial stents—for attending scientific conferences.

Provenance and peer review: Commissioned and externally peer reviewed.

Doctor only to the dead

I worked as a clinical skills assessor in a research project in Nepal. Apart from seeing the health situation in rural Nepal, I heard dozens of stories about their work from the mid-level healthcare workers who had come to be assessed.

One of them said that in his area patients do not get an opportunity to see a doctor as “only the dead can see doctors.” I asked why that was, and he replied, “As you know, in Nepal the doctors are not available in villages. The mid-level healthcare workers like me, who have 18 months of medical training, are the ones responsible for most health care. We do almost anything—like the GPs in the developed world. We prescribe medicine, perform procedures, even do minor surgery and conduct deliveries. “But we are not authorised to do a postmortem examination. At that time a doctor (the only authorised service provider) is needed to write a postmortem report. They have to come from the district headquarters or even the zonal hospital, which is days’ walk from most villages. So we have the saying that ‘only dead people can see doctors.’”

Laxmi Vilas Ghimire junior doctor, Tribhuvan University Teaching Hospital, Kathmandu, Nepal laxmivilas@gmail.com
A few lessons about drugs and gun crime

PERSONAL VIEW Ademola Odunfa

I arrived in Jamaica in April 1990 after landing a job at the Ministry of National Security in Kingston. I was there to boost the ministry’s pathology staff because of the country’s high murder rate. Jamaica has been variously described as the most violent or dangerous place on earth, although it also has one of the highest numbers of churches per square mile.

With our young family of five my wife and I were received warmly by staff. Most of my medical training had taken place in Nigeria, but we quickly settled into our new surroundings, and the work began in earnest.

Kingston is a highly volatile city of about one million inhabitants. The notorious downtown area is a place you don’t visit after 6 pm unless you are armed, ready to battle for your life, or both. Murder here was seen as just one of those things, and nobody really batted an eyelid. The only thing the relatives asked you after a postmortem examination was how many shots did he get. It was just another murder. People in Kingston were murdered in the most bizarre ways. I once conducted an autopsy on a man with only parts of his body available for examination. Another time there was just the lower half of a man—the upper part had been destroyed to make identification difficult. DNA analysis was not readily available in Jamaica in 1990. It wasn’t until a year or so later that a seminar entitled “DNA fingerprinting” was arranged for government pathologists—and many more years before the analysis actually became available.

Gang warfare and control of drug distribution in particular areas are said to be responsible for most of the crime, which was concentrated in downtown Kingston.

Murders uptown usually resulted from robberies, especially of residents returning from overseas, who were believed to have brought back huge sums of money; political killings; or accidental discharge of weapons. But these pale in comparison with what happened downtown. In the early 1990s it was very dangerous to walk downtown in Kingston; I had a police escort if I had to do a postmortem examination at the Kingston Public Hospital morgue, and even then it was still risky. You would hear sporadic gunshots as you drove through town.

There the usual weapon of choice among men was a handgun or automatic rifle. Among women, especially local women, it was a knife—sophisticated women also used handguns. Suicide was common. I remember the case of two young university lecturers, both doctors, who ended their lives because they were suspected of infidelity.

At the end of my three year contract I was seconded to the Ministry of Health and stationed at the Public Health Laboratory. At this time there was an outcry about the high number of extrajudicial killings by the armed forces and especially by the police. Local human rights groups were scouting for pathologists who were willing to risk their necks and testify against the armed forces. I accepted the challenge. Of course, this put me in the authorities’ black books, and I received death threats on many eyewitnesses are easily eliminated by cronies of the accused, usually as a result of tips from the security forces.

In 1996 I was posted back to Kingston and stationed at the Public Health Laboratory. At this time there was an outcry about the high number of extrajudicial killings by the armed forces and especially by the police. I was getting too popular with the police because I responded to their calls at any time of the day or night.

In Montego Bay I had to double as hospital pathologist and police pathologist. At the same time I was regularly called back to Kingston to attend court, usually with a police or army escort. I used to find that the crown counsels liked to play God. They would call you up at very short notice and without any apology. You couldn’t even complain to the judges, who usually took the side of the attorneys. The judge at the Gun Court, which deals exclusively with firearms cases, usually took pains to explain to the accused that the pathologist is not an eyewitness but that he is just going to relate his findings from the postmortem examination. This is important as Jamaica’s witness protection programme does not work properly, and many eyewitnesses are easily eliminated by cronies of the accused, usually as a result of tips from the security forces.

In all, in my 16 years of pathology practice in Jamaica I conducted about 1000 postmortem examinations, more than half of which were murders. Of these, 80% were gun crimes. The rest were stabtings, bludgeonings, suffocation, and strangulation.

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The bitterest pill

In 2004 I attended a parliamentary subcommittee meeting and sat with stars of the medical firmament such as Andrew Hexheimer, David Healy, and Ike Iheanacho. I was there simply as an honest witness to the excesses I had seen and to express support for the No Free Lunch group (www.nofreelunch-uk.org). I was a mere pimple on an ailing and delirious drug industry being dragged down by a virulent infection called marketing.

After all its high living, the drug industry is now hung over and needs to sort its life out—there are no more magic pills. Once the darling of the stock exchanges it now receives dire reports on its future profitability and witnesses a steep fall in the number of new drugs being approved. And under media attention it is experiencing drug induced flashbacks to the night of excess before: lap dancing clubs, Wimbledon tickets, and funds slipped to medical experts and charities, and so on.

But all this is a painful and long overdue correction—the bursting of the bubble that is the notion that societies’ social sicknesses can be cured by pills. Can we doctors help the industry? Yes: we must stop seeing pharmaceutical representatives. This is a logical move on several levels. Such contact increases costs and exposes patients to the dangers of new drugs, and the associated hospitality is inappropriate for public servants, undermining the status of doctors in the eyes of the public.

But there is also a new economic argument. The open doors to doctors’ surgeries have allowed pharmaceutical marketing departments to gain a stranglehold on business plans and stifle true innovation. It is estimated that the firms spend a third of turnover on marketing but only a fifth on research and development. Worse still, most of this research is not innovative but centred on “me too” drugs that seek merely to increase companies’ foothold in profitable established markets. But a “me too” strategy doesn’t even cut costs through true competition, for there is an unwritten agreement in the industry that undercutting of prices merely erodes overall profitability.

Preventing access of drug company representatives to doctors would help stop drug companies putting marketing above innovation and force a change in the business culture. This might result in much blood on the carpets of corporate boardrooms, but a return to innovation offers the only hope of a cure to the industry’s illness.

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Competing interests: D5 is the UK spokesman of No Free Lunch.

Now and then

He died in 1993. His book was published more than 40 years ago, has long been out of print, and isn’t widely known. So, how could he still be saying anything relevant about a field as dynamic as drugs?

Brian Inglis’s Drugs, Doctors and Disease. A Survey of the Pharmaceutical Industry appeared midway between the thalidomide scandal and the UK’s Medicines Act 1968, which provided a crucial brake on drug company activities. It is worth reflecting on just how bad things had been. Facing little or no regulation, drug companies were running riot. Products were inadequately tested before launch, misleading promotion flourished unchecked, and cartels kept some drug prices obscenely high. And, importantly, no safety culture existed that ensured disclosure of unwanted effects of treatments.

Authorities in the United States had decided that enough was enough. A congressional inquiry chaired by Senator Estes Kefauver prompted groundbreaking legislation to control approval, marketing, and promotion of medicines. Brian Inglis’s book was in part a push for a similar investigation in the UK.

Like many of the best commentators on the drug industry he was neither a healthcare professional nor a scientist. And like many of the best writers on anything he was Irish. The academic’s intellectual rigour and the skills of a natural communicator glow throughout Drugs, Doctors, and Disease. But being scholarly, lucid, and concise doesn’t account for the book’s enduring value.

It is the stunning quality of the author’s insights that makes the text so brilliant, despite the huge changes in circumstances four decades on. A few examples? He emphasised the dangers of resistance to drugs, related to inappropriate advertising and misuse of antibacterial drugs. He debunked attempts to present promotion as the supply of unbiased information, drew attention to inadequate training of medical students in pharmacology and therapeutics, poured scorn on doctors’ self deception that they were (uniquely) immune to advertising, and cautioned against the too cosy relationships that develop between the industry and those meant to regulate it. None of these issues (and many others he raised) can be considered remotely out of date.

Also, he was not especially interested in knocking drug companies. Rightly, he found much to praise about the industry but was highly critical of the environment in which it was allowed to operate.

In short, he showed how society gets the industry it deserves—a truly timeless message. In the 1960s governments, regulators, doctors, and the public could plausibly plead ignorance to such a suggestion. What excuse do we have now?

Ike Iheanacho is editor, Drug and Therapeutics Bulletin iheanacho@bmjgroup.com

FROM THE FRONTLINE
Des Spence

DRUG TALES AND OTHER STORIES
Ike Iheanacho
The God delusion

In his essay “Nature” (one of the Three Essays on Religion published posthumously in 1874), John Stuart Mill denies that one can decide on the morality or immorality of a course of action by describing it as natural or unnatural. Either the word “nature” means all that occurs in the universe; or it means all that happens in the universe with the exception of the deliberate actions of mankind. In neither sense can nature provide us with any moral guidance. This is obviously of interest to medical ethicists struggling with morality or otherwise of genetic engineering.

The following words appear in Mill’s essay: “The consciousness that whatever man does to improve his condition is in so much a censure and a thwarting of the spontaneous order of Nature, has in all ages caused new and unprecedented attempts at improvement to be generally at first under a shade of religious suspicion . . .”

In my copy, a first edition, a previous owner (a Victorian, to judge by the handwriting) has written the word “Chloroform” (sic) in the margin opposite these words. And this, of course, brings me to Sir James Young Simpson’s pamphlet, “Answer to the Religious Objections Advanced Against the Employment of Anaesthetic Agents in Midwifery and Surgery,” which he wrote in December 1847, shortly after his discovery of chloroform anaesthesia.

Simpson, a man of fairly humble background—who, showing extraordinary academic promise at an early age, was selected by his father from among his siblings for an education—was a man of wide interests, including archaeology; he loved nothing so much as a good controversy. He was a formidable pamphleteer, commanding an excellent, vigorous style in the service of relentless logic.

He argues against those who said that to give chloroform to women in labour was impiously to try to reverse God’s curse on women in Genesis, “in sorrow shalt though bring forth children.” If this part of the curse were taken literally to mean physically pain, he says, why not the other part of the curse, that “in the sweat of thy face shalt thou eat bread?” All attempts to mitigate labour, and improve the land by removing the “thorns and thistles” that it “shall bring forth to thee,” would likewise be forbidden, says Simpson. Indeed, the whole of the medical profession would be sacrilegious on the same view, because it attempted to delay man’s return to dust (“dust thou art, and to dust thou shalt return”) that was part of the same curse.

If God had not wanted man to relieve the pain of childbirth, says Simpson, he would not have made chloroform available to him. Simpson then goes on to demonstrate, by reference to Hebrew philology, that the common acceptance of the meaning of the Bible is based on a misapprehension of Hebrew words. Sorrow in the Biblical curse on women means labour, not pain. Finally, Simpson points out that the same argument from sacrilege was advanced against Jenner’s vaccination, but everyone now acknowledges that it was a ridiculous argument. Altogether, Simpson’s is a bravura performance. The only problem is that Simpson, being an avid self promoter, had made up the religious objections. He was destroying a Biblical curse on women means labour, not pain. Finally, Simpson points out that the same argument from sacrilege was advanced against Jenner’s vaccination, but everyone now acknowledges that it was a ridiculous argument. Altogether, Simpson’s is a bravura performance. The only problem is that Simpson, being an avid self promoter, had made up the religious objections. He was destroying a Biblical curse.
When Blair went to market

Blair’s Damascene conversion to market forces was one of the many differences he had with Gordon Brown, a new television series has shown. Where does that leave the NHS under Blair’s rival, asks Tony Delamothe

Explicitly about the relationship between former prime minister Tony Blair and his chancellor, Gordon Brown, this programme provided an interesting insight into some of the key moments of the Blair government’s relationship with the NHS. It also gave some hints as to what to expect from the Brown government.

First off was Blair bouncing Brown into providing five years of 5% annual increases in the NHS budget, which would bring UK spending up to the European average. Blair chose Sir David Frost’s television programme for his momentous announcement one Sunday morning in January 2000. Minutes after the programme “Number 10 hit the phones.” It being a Sunday, all the facts and figures were locked up in Whitehall offices. About the time the Department of Health’s chief economist had made the figures add up (using the sophisticated calculator of his daughter’s boyfriend) it dawned on Blair’s advisers that Blair had not told his chancellor about the biggest spending announcement they would ever make.

Even this early in his government there was a hint that Blair had to resort to guerrilla tactics to achieve what he wanted in the face of Brown’s implacability. Insiders commented: “Gordon Brown saw himself as the senior partner” . . . “For much of his time [Blair] couldn’t get his way.” Already by then Frank Field, Blair’s new broom in pensions, had been dropped: “Gordon was adamant that nothing was going to happen.” Whenever money was involved, the question of who was really boss was never properly resolved, and even led to an abortive plan to drop Brown early in the government’s third term.

Bitter divisions surfaced between Blair and Brown over how to reform health and education. True to form, both men wanted to do it their own—different—way. Before the 1997 election, Blair had anathematised the use of markets to improve public services: “First of all we’ll get rid of that Conservative internal market that has caused such much damage in the National Health Service.

We’ve had enough of running it like a supermarket—it’s not a supermarket, it’s a public service.”

But within a few years, Blair underwent a Damascene conversion, the reasons for which we’ll presumably have to await publication of his diaries. He became convinced that hospitals and schools needed market incentives to improve: “A quasi-market situation, where you can contest the service or the consumers get greater choice, injects this greater sense of dynamism. Contestability, competition—it’s basically breaking down the monolith of the old public services.”

Brown’s response to this distinctly non-Labour view was to emphasise the limits and failures of markets. “Our clear and robust defence of markets must be combined with a clear and robust recognition of their limits. In health, not only is the consumer not sovereign, but a free market in health care will not produce the most efficient price for its services, so that many market failures in health, if taken individually, challenge the adequacy of markets to provide efficient market solutions.”

Blair and his then health secretary, Alan Milburn, were pushing for foundation hospitals, with freed up management and financial controls. Brown’s response was a 50 page memorandum setting out his objections to their proposed financial regime. This time, presumably the option of announcing it as a fait accompli on Frost was out, and a compromise was thrashed out.

At the time when he might have handed the premiership to Brown, he decided he needed to stick around to carry his domestic reforms through. “There were certain things I wanted to get absolutely secure and bolted down before I left.”

How insecure and unbolted down they were became apparent in the week the programme was broadcast. Not five months after Blair handed over to Brown, the government announced that one of its main routes to inject contestability and competition into the NHS has been cut by two thirds (see News p 1066). Can a politician really believe that something can be set so firmly in stone that a successor can’t dynamite it at will?

Ultimately, “What you owe people is your conviction: you owe them the duty to do what you believe to be right.” Not necessarily “be right,” Blair was at pains to explain, just to do what you believe to be right. He said this in the programme in the context of his public service reforms but he’s said it before regarding his decision to go to war in Iraq. It begs the question: are strong convictions enough for a politician? Do we elect them just to visit their convictions on us? I can envisage what conviction based medicine would look like, and it’s not a pretty sight.

Tony Delamothe is deputy editor, BMJ|tdelamothe@bmj.com

The Blair Years: Blair and Brown (episode 1)
BBC 1, 18 November at 10 15 pm
Rating: ★★★★★

I can envisage what conviction based medicine would look like, and it’s not a pretty sight.
Hubert Campbell

Emeritus professor of medical statistics University of Cardiff (b 1920; q Durham 1959; FRCP, FSS), died from a cerebrovascular accident on 7 October 2007.

Hubert Campbell started studying mathematics at Leeds in 1938 but in 1940 joined the Air Ministry and then the Admiralty in operational research. After the war he completed his degree at the University of London while working as a trainee actuary. He then joined Durham University Medical School in Newcastle as the only lecturer in medical statistics. In 1963, after qualifying in medicine, he joined the Welsh National School of Medicine in Cardiff as a joint appointment with Archie Coltrane’s MRC Epidemiology Unit. In 1970 he became the foundation professor of medical statistics in Cardiff and was editor of the *Journal of Epidemiology and Community Health*. After retirement he began a second career as a county councillor for South Glamorgan. He leaves three children and eight grandchildren.

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Alexander Murray Farrell

Consultant immunologist Glasgow (b 1959; q Liverpool 1982; FRCPath), d 18 April 2007.

Initially attracted to surgery, Alexander Murray Farrell developed an interest in tissue typing and then immunology. After a brief locum consultant post in Leicester, he became the consultant immunologist in Glasgow in 1992, running both the immunology and histocompatibility and immunogenetics laboratories, one of the last to be qualified in both disciplines. Alex fought hard for his service and spent the past decade planning a new joint department of immunology and tissue typing to unite the two components. He also set up the clinical primary immunodeficiency and home immunoglobulin therapy programmes and contributed nationally through roles with the Royal College of Pathologists. His many interests included a love of languages—he was learning Japanese and was a fluent Welsh speaker. He leaves a partner, Christina, and two children.

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Basil Seltzer

Former general practitioner Maryhill, Glasgow (b 1926; q Glasgow 1948; MRCP), died from renal failure and ischaemic heart disease on 7 February 2007.

After house jobs in London and Lancashire, Basil Seltzer went into practice in one of the less affluent areas of Glasgow. He became one of the driving forces in setting up Glasgow’s Prince and Princess of Wales Hospice, which opened in 1983, when hospices were still a novelty. As chair of the friends of the hospice, he promoted the idea of palliative care, as well as raising funds. After retiring, he travelled extensively until forced to stop by ill health, but his capacity for inventive thought and lengthy conversation persisted. He leaves his second wife, Fiona, and a daughter by his first marriage.

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Nicholas Thomas

Obituary

David Eric Worsley

Former commander Army Medical Services, Territorial Army (b 1929; q Bristol 1952; DIH, MFOM, FPPh), died from adenocarcinoma of the lung complicated by vasculitis on 21 December 2006. Initially a reluctant conscript to the army for national service, David Eric Worsley readily took a permanent commission in the Royal Army Medical Corps in 1955. Early in his career he published on chloroquine resistance, and researched the physiology of climate stress and disturbance in circadian rhythm. David became director of army health in 1980 with responsibility for preventive medicine and training involved staff; he was also course organiser for several training modules for membership of the Faculty of Community Medicine, and a Queen’s honorary physician. He resigned from his last post in 1987, unhappy with the reduction in RAMC staff to what he considered to be unsafe levels. He leaves a wife, Sylvia; three children; and seven grandchildren.

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Simon D Worsley

Sylvia N Worsley

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The ill effects of social isolation could in part be hormonally mediated. In mice kept in total isolation for four weeks, expression of 5α-reductase type I—the brain enzyme responsible for producing the stress relieving hormone alloprogrenanolone—was halved. The enzyme acts on the parts of the brain involved in emotional learning, fear, and stress responses. The researchers say this may account for the anxiety, aggression, and memory impairments that are sometimes seen in socially isolated people (Proceedings of the National Academy of Science 14 November 2007).

No matter how fancy and sophisticated surgical technology and procedures become, the tenets of good teaching remain the same. Surgical training still “relies heavily on mentorship, support, and role modelling by committed postgraduate trainers,” says an otolaryngologist in the Bulletin of the Royal College of Surgeons of England (2007;89:346-7). He says: “You need to be aware of what the trainees’ worries or concerns are. They won’t always tell you directly so you need to be able to spot the signs.” Just as with patients.

Some studies have indicated that the concentration of fetal haemoglobin (HbF), a possible marker of hypoxaemia before birth, is higher than normal in babies who have died from sudden infant death syndrome. Attempting to resolve this question using optimal technical methods, a US based team now reports that the percentage of fetal haemoglobin in infants who fulfilled rigorous criteria for sudden infant death and in control cases was not significantly different at autopsy (Journal of Forensic and Legal Medicine 2007;14:456-60).

Last week Minerva mentioned the EQUATOR network for helping researchers access guidelines for optimal reporting. There’s also an easy way to look up the STROBE (strengthening the reporting of observational studies in epidemiology) statement directly, as discussed in the BMJ recently (2007;335:806-8)—go to www.strobe-statement.org/Checklist.html.

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