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EDITORIALS

Assertive community treatment in psychiatry
May not reduce inpatient visits, but its success in engaging marginalised patients should not be ignored

Assertive community treatment is a specific model of intensive community mental health care and a key component of the national service framework for mental health in England. Over 220 new teams using this model have been implemented since 1999.1 Assertive community treatment originated in the United States, evolving from a pioneering approach to delivery of treatment for people with mental health problems in the community.2 The treatment has been extensively researched. Good evidence exists for its efficacy outside the United Kingdom,3 but results in England have been disappointing.4-7 Possible reasons for this include differences in adherence to assertive community treatment and differences between the US and the UK in the comparison group of standard community mental health care.8 9 However, even in the UK, clients seen as being “difficult to engage” (those with whom community mental health services have found it difficult to arrange meetings) find assertive community treatment more acceptable than standard community care in terms of satisfaction with services and the amount of contact they have with them.3 7

In this week’s BMJ a systematic review of randomised controlled trials by Burns and colleagues compares the impact on the use of inpatient services of various forms of intensive case management (including assertive community treatment) compared with standard community mental health care. It finds that the way in which the team organises its approach to the work and whether it is implemented in an area with high use of inpatient services accounts for the differences in findings regarding inpatient service use.

The assessment of the organisation of the team was based on whether the team was the primary therapy for its clients; was based off the hospital campus; met daily; had a team leader who was also a case manager; and offered services without a time limit. The authors state that these features reflected the extent that case managers worked as a team rather than as independent practitioners. This aspect of assertive community treatment is often referred to as the “team based approach,” facilitated by the team working extended hours in shifts such that several different staff are involved in a client’s care. Also, daily team meetings take place to discuss the work plan and share ideas about clinical problems. Burns and colleagues suggest that similarities in the organisation of the team between community mental health teams and assertive community treatment teams could explain the lack of efficacy in the UK, and they conclude that case managers should work as teams rather than as individuals when caring for severely mentally ill individuals.10

However, another important component of home treatment models, including assertive community treatment, is “in vivo” work,11 where contact occurs at the client’s home or elsewhere in the community rather than in the team office. Although home treatment teams in the US have been reported to make more in vivo visits than UK teams, community mental health teams in the UK make more in vivo visits than standard care comparison teams in the US.9 This may also explain the lack of efficacy reported in the UK studies.

Despite these similarities between assertive community treatment and community mental health care, the finding that the former is more acceptable to a particularly marginalised group of clients should not be ignored. This may result from differences in styles of client engagement, with assertive community treatment using more recovery based practice approaches,12 such as collaborating on agreed tasks and therapeutic risk taking rather than the more autocratic community mental health care approach of delivering treatment. This has potentially far reaching consequences for reducing social exclusion for this group. The team based approach seems to be a particularly important component for staff in assertive community treatment teams in providing supportive and constructive containment in working with challenging clients (unpublished data).

In the current financial context of the National Health Service in England, assertive community treatment is vulnerable, and the National Forum for Assertive Outreach has many examples of teams being disbanded and/or having their practitioners redeployed to provide the treatment within community mental health care teams. This makes little sense now that the critical success factors seem to have been identified (team based approach; extended hours; high proportion of in vivo visits). It is unfeasible to deliver these factors within a community mental health care team for three reasons. Firstly, the size of a community mental health care team’s caseload makes shared caseloads and daily team meetings impractical. Secondly, a quorum of staff is required to work shifts to provide an extended hours service. Thirdly, protection of low caseloads is difficult in the pressured environment of a community mental health care team but necessary to ensure a high proportion of in vivo visits.
The problem for assertive community treatment in England is that reducing the use of inpatient services is seen as the main measure of success. This correlates with the cost of the service, but its great success in enabling staff to work with clients that community mental health care teams had failed to engage for years seems to be being ignored. The model is popular with staff working in assertive community treatment and with clients. With an increasing focus across all health specialties to provide services in the community, it seems premature to dismantle assertive community treatment teams now that we really know how they should work.

2 Stein LI, Test MA. Alternatives to mental hospital treatment. Arch Gen Psychiatry 1990;37:392-7.

Umbilical cord clamping after birth
Better not to rush

Early clamping and cutting of the umbilical cord is widely practised as part of the management of labour, but recent studies suggest that it may be harmful to the baby. So should we now delay the clamping? Early clamping of the cord was one of the first routine medical interventions in labour. Its place in modern births was guaranteed by its incorporation into the triad of interventions that make up the active management of the third stage of labour. The earliest references are clear about the other two components of active management—oxytocin to contract the uterus and prevent postpartum haemorrhage, and controlled cord traction to prevent retention of the placenta. But early cord clamping had no specific rationale, and it probably entered the protocol by default because it was already part of standard practice. When this package was shown to reduce postpartum haemorrhage in the 1980s early cord clamping became enshrined in the modern management of labour.

But it has not been accepted everywhere. In Europe, although 90% (1052/1175) of units recommend uteroton prophylaxis, only 66% (770/1175) recommend early cord clamping and 41% (481/1175) recommend controlled cord traction. The rate of early cord clamping varies from 17% (4/23) of units in Denmark to 90% (98/109) in France.

So what is the evidence behind cord clamping? For the mother, trials show that early cord clamping has no effect on the risk of retained placenta or postpartum haemorrhage. Evidence from a Cochrane review supports this result—prophylactic oxytocin reduces the risk of postpartum haemorrhage whether the rest of the active management package is adopted or not.

But what about the baby? Initially, the cord blood continues to flow, sending oxygenated blood back to the fetus while respiration becomes established, ensuring a good handover between the respiratory systems. At the time of the first fetal breath, however, the reduction in intrathoracic pressure draws blood into the lungs from the umbilical vein. So long as the cord is unclamped the average transfusion to the newborn is 19 ml/kg birth weight, equivalent to 21% of the neonate’s final blood volume (figure). The final amount is unaffected by the use of oxytocics or the position of the baby relative to the placenta. Three quarters of the transfusion occurs in the first minute after birth. The rate of transfer can be increased by the use of intravenous uterotonics (to 89%), or by holding the newborn 40 cm below the level of the placenta.

For the term baby, the main effect of this large autotransfusion is to increase iron status and shift the normal curve of the neonatal haematocrit to the right. This may be life saving in areas where anaemia is endemic. Here, late cord clamping increases the average haemoglobin concentration by 11 g/l at four months. In the developed world, however, there...
have been concerns that it could increase the risk of neonatal polycythaemia and hyperbilirubinaemia. Trials show this is not the case. Delayed cord clamping seems to drive up mean haematocrit values and serum concentrations of bilirubin, without increasing the number of infants needing treatment for jaundice or polycythaemia. 

For preterm babies the beneficial effects of delayed cord clamping may be greater. Although the studies are smaller, delayed clamping is consistently associated with reductions in anaemia, intraventricular haemorrhage, and the need for transfusion for hypovolaemia and anaemia. The one exception may be growth restriction babies who are already at risk of hypoxia induced polycythaemia.

How should we approach cord clamping in practice? In normal deliveries, delaying cord clamping for three minutes with the baby on the mother’s abdomen should not be too difficult. The situation is a little more complex for babies born by caesarean section or for those who need support soon after birth. Nevertheless, it is these babies who may benefit most from a delay in cord clamping. For them, a policy of “wait a minute” would be pragmatic. Indeed, this first minute is already largely spent on neonatal assessment. This could be done in warmed towels on the birthing bed or the mother’s abdomen after vaginal delivery, or on the mother’s legs at caesarean section. Cord clamping need only take place when transfer to the resuscitation trolley is required. For medical purposes it will be important to document the time at which the cord was clamped, as delayed clamping reduces pH values in umbilical artery blood samples.

There is now considerable evidence that early cord clamping does not benefit mothers or babies and may even be harmful. Both the World Health Organization and the International Federation of Gynecology and Obstetrics (FIGO) have dropped the practice from their guidelines. It is time for others to follow their lead and find practical ways of incorporating delayed cord clamping into delivery routines. In these days of advanced technology, it is surely not beyond us to find a way of keeping the cord intact during the first minute of neonatal resuscitation.


Obstructive sleep apnoea

Trials are under way to determine the still unclear associations between sleep apnoea and cardiovascular outcomes

The prevalence of obstructive sleep apnoea in its severe form is about 2% and 0.5% in middle aged men and women respectively. Pharyngeal collapse during sleep causes recurrent frustrated inspiratory efforts, oscillating levels of blood oxygen, and disturbed sleep, which may, or may not, lead to excessive daytime sleepiness. The main treatment for moderate to severe obstructive sleep apnoea and excessive daytime sleepiness (obstructive sleep apnoea syndrome) is nasal continuous positive airway pressure applied during sleep. A meta-analysis clearly showed that this treatment is highly effective in preventing apnoea in such patients, thus relieving symptoms and improving self assessed quality of life.

The main debate over treatment is whether obstructive sleep apnoea is also an important independent risk factor for vascular disease (such as myocardial infarction, heart failure, and stroke), both in those with and without current vascular problems. Some of the potential mechanisms suggested include acute and long term effects on blood pressure, endothelial dysfunction, deoxygenation-reoxygenation injury, increased swings in pleural pressure causing cardiac loading, and increased platelet coagulation. Unfortunately, obstructive sleep apnoea coexists with many features of the metabolic syndrome. Indeed, the condition is common in type 2 diabetes, with a prevalence of 20%, and such patients tend to share a similar body shape. Obesity of the upper body provokes obstructive sleep apnoea through deposition of fat in the neck, compromising pharyngeal patency, and visceral obesity also provokes insulin resistance, as well as being a better predictor of vascular risk than general obesity.

This means that cross sectional and cohort studies, apparently linking obstructive sleep apnoea and vascular disease, cannot prove causation (especially as simple indices such as waist to hip ratio do not fully control for visceral fat), and thus can only generate hypotheses. Obstructive sleep apnoea probably acts partly as a marker for the metabolic syndrome in such studies.

Non-randomised interventional trials have suggested
survival advantages from continuous positive airway pressure, but the control populations were those who showed poor compliance with the treatment. Unfortunately, patients who are poor compliers with trial treatments have a higher mortality anyway, presumably because of poorer compliance with other treatments. Because of the imperative to treat symptomatic patients, most randomised controlled trials of treatment in obstructive sleep apnoea have been short term, looking only at surrogate end points for vascular disease, such as blood pressure, insulin resistance, inflammatory markers, and cardiac function. Hence they have not yielded robust evidence for an independent effect of obstructive sleep apnoea on vascular outcomes.

Several studies have shown a fall of up to 10 mm Hg in mean 24 h blood pressure in patients treated with continuous positive airway pressure compared with controls; the largest reductions occurred in the most severe and symptomatic patients. Furthermore, echocardiography and gated nuclear scanning have shown improvements in left ventricular ejection fraction and indices of diastolic function. However, treatment with continuous positive airway pressure does not seem to improve insulin resistance or glycaemic control in patients with both obstructive sleep apnoea and type 2 diabetes.

Such surrogate end points can only hint at potential additional vascular morbidity and mortality. Thus, the recent appearance of the first mortality study in patients with heart failure (with left ventricular ejection fraction ≤ 45%) and obstructive sleep apnoea is interesting, even though treatment was non-randomised. This paper compared mortality in three groups: 113 patients with heart failure, but little or no obstructive sleep apnoea; 37 such patients with untreated moderate to severe obstructive sleep apnoea; and 14 with obstructive sleep apnoea treated with continuous positive airway pressure.

The presence of untreated obstructive sleep apnoea seemed to double mortality from heart failure over five years from 12% to 24%, and there were no deaths in the small group treated with continuous positive airway pressure. Although this study would have been subject to unrecognised confounders and non-randomisation bias, the size of the effect suggests that people looking after patients with heart failure should be more aware of the detrimental impact of obstructive sleep apnoea.

How can robust long term evidence be collected in this area? Patients with moderate to severe symptoms cannot be entered into placebo controlled trials because they should be offered treatment. Because no robust evidence indicates that patients with asymptomatic obstructive sleep apnoea should be treated to reduce vascular risk, clinicians can ethically randomise such patients to long term trials of continuous positive airway pressure versus no treatment. Such trials are in their infancy, and outcomes for morbidity and mortality will take a long time to gather. But without them we will not know whether to offer this treatment for vascular benefits to patients with asymptomatic obstructive sleep apnoea.

**Effects of air pollution on health**

Quantifying the effect alone is not enough to change policy and improve health.

The term “smog”—a combination of smoke and fog—was invented by a British doctor a century ago. In 21st century Europe, air pollution has greatly improved by most measures but is still a substantial health problem, responsible for the early deaths of hundreds of thousands of people each year. Estimates of mortality attributable to long term exposure to fine particles are now widely accepted as a key policy indicator of the effect of air pollution. A draft UK government report, written by the Committee on the Medical Effects of Air Pollution and currently open for public review, re-examines the scientific evidence underpinning these estimates.

The most directly applicable evidence is provided by follow-up of large populations exposed to different long term average levels of air pollution. Findings of the first cohort studies by the American Cancer Society have been confirmed and extended by additional years of follow-up and extensive reanalyses, and with cohort studies in Canada and Europe. Studies of cities that have experienced substantial reductions in exposure...
Competing interests: SH has acted as an expert witness on health effects of air pollution for Environment Canterbury, Christchurch; Campaign for a Better City, Wellington; Nelson Transport Strategy Group; Nelson; and the People’s Inquiry, Auckland.

Provenance and peer review: Commissioned; not externally peer reviewed.

to air pollution as a result of policy changes (such as Dublin2 and Hong Kong6) provide convincing evidence that the effects are real and not the result of unmeasured confounding.

Time series studies, although not suited to assessing effects of long term exposure,10 provide further evidence that day to day changes in air pollution have measurable health effects at population scale, even at very low levels of ambient exposure. Slowly varying factors such as socioeconomic status or smoking history, which might bias the results of cohort studies, cannot explain the short term associations between air pollution and health seen in time series studies.

The best estimate from the Committee on the Medical Effects of Air Pollution, based on the American Cancer Society’s follow-up study,2 is a 6% (95% confidence interval 2% to 11%) increase in all cause mortality per 10 μg/m² increase in fine particle exposure (measured as PM). The authors also report a probability distribution of a “plausible” dose response (range 0-1.5%). This was based on a Delphi survey that used the expert judgment of committee members to capture uncertainties in the coefficient. The committee recommends using Monte Carlo analysis to sample from the plausible dose response range when applying their findings to assessment of air pollution policy. In practice, the use of statistical confidence intervals would probably give similar results, as the distribution of plausible dose response coefficients is clustered within the range of the statistically derived confidence intervals.

The report by the Committee on the Medical Effects of Air Pollution is well argued and supported by working papers discussing the key uncertainties, although a few areas warrant more discussion. Firstly, the American Cancer Society’s study excluded those under age 30 years,3 and so the results do not apply to younger adults and children. Other studies that have linked infant mortality with exposure to air pollution11 12 are included in a table but not discussed in the main text. Secondly, most epidemiological studies of air pollution have been conducted at the scale of whole cities. More recent studies, conducted at a smaller geographic scale, have reported substantially larger effects.5 6 13 These studies have important implications for estimates of years of life lost.

Finally, evidence that the effects of air pollution are modified by social factors14 should be reflected in health impact assessments. In the American Cancer Society’s study, the effects of air pollution seemed greater in those with lower educational status. The distribution of effects between rich and poor communities is important from a social justice perspective, independently of the overall effect on health.

Quantifying the direct effect of air pollution on mortality is an important step towards effective interventions to improve health. However, policy makers need a wider perspective than that provided by the Committee on the Medical Effects of Air Pollution so that they can take into account the indirect, long term health implications of energy and transport policies. Global climate change will have major effects on health that are difficult to measure using conventional approaches that look at individual aspects rather than the problem as a whole. Coal fired power stations and vehicles are major emitters of carbon dioxide, the main driver of climate change. Energy efficiency measures can have simultaneous benefits through reductions in local air pollution (particulates) and global carbon dioxide emissions. It is becoming increasingly clear that we need to stop burning fossil fuels and that we cannot afford another decade of scientific enquiry, let alone another century, before we act. Rigorous scientific assessments—exemplified by the Committee on the Medical Effects of Air Pollution’s report—have an important place but are only part of the policy equation.

12 Woodruff TJ, Parker JD, Schoenfeld KC. Fine particulate matter (PM)</dd>

Developing nurse prescribing in the UK
Prescribing should be integrated into education for advanced nursing practice

The United Kingdom has seen a recent major expansion in the scope of nurse prescribing, reflecting government policy and the international trend towards advanced nursing practice. In the 1990s it became possible for community based nurses to prescribe independently from a limited formulary, thereby facilitating their traditional roles such as wound management and bowel care. From 2000, further changes in legislation radically altered the professional restrictions on prescribing, and since May 2006 independent nurse prescribers in England have been able to “prescribe any licensed medicine for any medical condition within their competence.”

Each stage of the development of nurse prescribing in the UK has had its advocates and detractors, but this recent initiative has proved the most controversial, fueling debate about the adequacy of training of nurse prescribers and risks to patient safety.

The training for independent nurse prescribers consists of a standalone course of 26 days of theory, 12 days of mentored practice, and five assignments. More than 8000 nurses in the UK have now been trained as independent or supplementary prescribers and thus have access to the full formulary that doctors use, and many more district nurses and health visitors prescribe from a restricted formulary. Nevertheless, in England in 2005 just 0.6% of prescription items came from nurses working in the community; this proportion increased to almost 0.9% in April to September 2006. Figures for this later period show that those nurses with access to the full formulary were prescribing drugs previously restricted to doctors, including antimicrobial agents, asthma drugs, nicotine replacement products, and statins.

Comparative figures for secondary care are not available.

Early international analyses of nurse prescribing indicate that nurses prescribe within their areas of competence and according to guidelines. These findings were echoed by a study of independent nurse prescribing in the UK in which an expert panel judged the appropriateness of prescribing decisions made during consultations. Nevertheless, detractors are ready to pounce on any contrary findings, and an example is a recent study of independent nurse prescribing in the UK in which an expert panel judged the appropriateness of prescribing decisions made during consultations. This study, 25 nurse prescribers were presented with a number of prescribing scenarios. Only a minority were able to identify more than half of the pharmacological problems relevant to each case and to suggest an appropriate course of action. This led Pulse (a weekly newspaper for general practitioners) to state that “nurses are ‘floundering’ in their new prescribing role.” In contrast, the authors suggest that the participants would have referred patients to the general practitioner for matters that were outside their area of competence.

This type of problem is at the heart of the current debate about independent nurse prescribing in the UK. On the one hand, the training and competence of nurse prescribers continues to be called into question.

On the other, it is argued that nurses can diagnose and treat conditions safely and effectively within their areas of competence. While it is possible to dismiss some of the criticisms as due to doctors’ concerns about nurses encroaching on their traditional territory, we believe that for nurse prescribing to contribute more to patient wellbeing in the future, certain educational and practice problems need to be dealt with.

A further expansion of nurse prescribing in the UK is likely in coming years, but the extent to which it develops will depend partly on National Health Service trusts and general practices having confidence in the safety and effectiveness of nurse prescribers and their value in meeting patient needs. Some issues will be clarified by current research studies and local experiences, but concerns are likely to remain about the adequacy of the standalone training module.

To deal with these concerns and bring about a further step change in nurses’ contribution to health care we believe that the “task” of prescribing should be incorporated within the broader framework of the internationally recognised clinical role of nurse practitioners. The current short training course for independent nurse prescribers was designed to allow rapid expansion of a prescribing workforce among experienced practitioners. It is now time to build prescribing into the development of advanced nursing practice so that it becomes a complementary part of training in assessment, diagnosis, clinical decision making, audit, evaluation, and referral. This would provide a firmer foundation for nurse prescribers and help to strengthen the case for nurses having a greater role in prescribing.

Incentives help vulnerable patients to stay well

In the head to head debate, Shaw says that to pay patients to take medication would create perverse incentives, but in her discussion she dismisses a particularly complex group of patients, with tuberculosis, despite the public health issues involved. This is a group of patients for whom payment, or other forms of incentive, are of critical importance, at both the individual and the public health level. For these patients, health is very low on their list of priorities—they tend to be those suffering from social exclusion, often with histories of offending, substance abuse, mental health problems, and homelessness. They require the most complex care and are least likely to complete treatment, particularly when the course of treatment is lengthy.

It is common practice in tuberculosis teams to carry out a standard risk assessment with each patient and to offer incentives to those who would be at high risk of non-completion of treatment. Shaw asserts that even in the case of infectious tuberculosis, the disadvantages of financial incentives outweigh the benefits. However, the reasons she cites for non-compliance with TB medication do not correspond to the attitudes that we find in our high risk patients, for whom the daily business of finding a place to sleep, eat, inject, or sell their bodies comes well before whether to take their medication. Different teams vary in the types of incentive they will offer these patients, and although research shows that money is the incentive proved to be most effective for adherence, other interventions, such as social support, free meals, bus passes, and food tokens, are effective. Unlike in New York, where direct payments of $10.00 are made, financial incentives are not permitted in the NHS. However, through the use of social care incentives, completion rates for TB treatment in this at-risk group of patients are far better than would otherwise be the case.

Drug misusers are likely to abuse the system

I am a forensic physician working in the east end of Glasgow, and I write with reference to the debate by Burns and Shaw. A high percentage of detainees are on opiate substitution programmes. From my own personal observations, nearly all are using “top-up” heroin.

Additionally, alcohol consumption while receiving methadone treatment is high. It is obvious that a £2 shopping voucher could easily be diverted into paying for two litres of cider to fund a dual addiction.

I also find it ridiculous in a cash strapped NHS service, where we are unable to fund life saving or life extending medications, we are able to pay addicts to “comply” with a treatment that offers no treatment benefit other than to “reduce harm.”

Management skills need to be systematically learnt

I share Nicholson’s belief that NHS organisations will have an improved chance of dealing successfully with the complex challenges they face if led by people who have substantial personal experience of providing clinical care to patients.

However, management skills are not necessarily intuitive. Currently, too many clinicians with management roles rely on innate instinct and gut feeling, honed by variable experience on the job, when dealing with issues and situations that require more than this. Those clinicians who really wish to provide high quality leadership to NHS organisations need to become more familiar with the existing body of management evidence and theory at both operational and strategic levels.

Having been directly involved with healthcare management for the last dozen years, in the United Kingdom and United States, my experience has been that, until becoming formally acquainted with current management thinking by undertaking an MSc in strategic management, my approach was based largely on a set of well intentioned, but vaguely random, principles. Learning systematically from current academic thought in areas such as negotiation, innovation, leadership, marketing, strategic development, and financial management has provided a rigorous and robust platform on which to think and operate.

There are no shortcuts to successful leadership in NHS organisations, as the Gerry Robinson experience showed when the business guru tried to cut waiting lists at an NHS hospital for a recent TV programme. Clearly, not all potential clinician managers need to study management theory to degree level, but by carefully selecting developmental opportunities that make use of the large body of management thinking and evidence currently available, and by targeting these at those clinicians who have the desire to contribute in this way, skilful, clinically experienced and patient focused
leadership could realistically be given the driving seat at the top table of NHS organisations very soon. Sean W O’Kelly, interim medical director Northern Devon Healthcare Trust, Barnstaple, Devon EX31 4JB swokelly@aol.com

Competing interests: None declared.


**ABCD OF DIGNIFYING CARE**

We need imaginative approaches to training

Chochinov’s framework may help health professionals to provide more compassionate and respectful care for our patients. However, great ideas alone don’t always lead to better practice, even when supported by training and re-training.

We are all taught good practices as students but usually conform with the habits of colleagues and bosses once we enter the “real world” of work. Unfortunately bad habits contribute to the culture of our parent organisations and are engrained and very hard to change. Replacing a bad culture with a better one requires will, leadership, and good strategic planning, but, as is often said in business circles, “culture eats strategy for breakfast.”

So how might we persuade people to adopt new and better habits? An interesting approach is suggested by Fred Lee in his book, *If Disney Ran Your Hospital.* He explains how exercises in imagination are crucially important components of staff training at Disney (world leaders in customer satisfaction). Lee adapted Disney’s technique to training healthcare workers. He reports the case of a surly radiology department receptionist with bad interpersonal skills. Lee persuaded her to imagine that a patient had been dealt with by a receptionist with bad interpersonal skills.

Chochinov has described a better world, but real work is needed to get us there. New habits will overcome bad cultures only if better ways of learning are accepted.

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Competing interests: None declared.


**MEDICINES FUNDING**

Value for money is nothing new

Pursuing value for money in medicines funding is neither tough nor new.1 PHARMAC (New Zealand’s funder) has focused strongly on it for 14 years. We are mindful of funding trade-offs through explicit use of a fixed budget—a desirable and powerful incentive to ensure that value for money remains paramount.2

PHARMAC has used the tools referred to by Jack for several years, including reference pricing, tendering, rebates, and risk sharing arrangements.3 4 Built around a strong core of independent clinical and economic assessment, the strategies have successfully improved value for money, freeing up resources for funding of other medicines or health services.

The idea of an individual refund for ineffective treatments is interesting, but one PHARMAC hasn’t implemented because of definitional and monitoring concerns. The mechanism is an attempt to deal with a fundamental mismatch between pricing and value (health outcomes) to populations—an issue that can generally be more cost effectively managed in other ways.

Matthew Brougham, acting chief executive PHARMAC, PO Box 10 254, Wellington 6143, New Zealand matthew.brougham@pharmac.govt.nz

Competing interests: None declared.

1 Jack A. No cure, no cost. BMJ 2007;335:122-3. (21 July.)

**UVULA ANGIO-OEDEMA**

ENT form of Saturday night palsy

Davidson et al present a case of uvula angio-oedema associated with the recreational drug ecstasy.5 Referrals of patients to our ENT unit in Scotland with isolated uvula angio-oedema are not uncommon. However, on occasion the aetiology seems to differ from the causative factors which the authors discuss.

Many of these patients give a history of alcohol ingestion and heavy snoring thereafter (often corroborated by their partner). Most quickly settle with no intervention and do not receive steroids or antihistamines. It has been postulated that the snoring itself is responsible, worsened by the sedative and desensitising effects of the alcohol, and relative dehydration. The anaesthesia literature includes reports of uvula oedema after deep sedation and heavy snoring.

Clearly it is important to consider the other aetiologies that the authors discuss, and in severe cases follow the management plan that their case necessitated. Quincke’s oedema is an important differential diagnosis.

However, we write to highlight a subgroup of patients who may simply be manifesting a relatively innocuous ENT equivalent of the “Saturday night palsy” and will settle with reassurance, oral rehydration, and no further intervention.

David P Crampsey, specialist registrar, otolaryngology head and neck surgery Garthwaite General Hospital, Glasgow G12 0YN
Sarah A Little, specialist registrar, otolaryngology Ninewells Hospital and Medical School, Dundee DD1 4HJ
David Crampsey@NorthGlasgow.Scot.NHS.UK

Competing interests: None declared.

1 Davidson J, Patel RB, Emlyn A, Bennett AMD, Minerva BMJ 2007; 335:216. (28 July.)

**THE PROFESSION’S FUTURE**

Is the BMJ fit for purpose?

Where is the evidence for Jones’s statement that the shipman, Bristol, and Alder Hey inquiries, and a litany of errors, shook the foundations of public trust and professional confidence?2 My attempts to elicit such evidence from him have so far been unsuccessful. I am aware, however, of a MORI poll that suggested that confidence in the medical profession had not been dented.2

In this evidence based age, the journal’s editor should ensure that her editorialists provide evidence for their assertions. False premises make for unreliable conclusions.

One basis for stating that Shipman has dented patient confidence is that the government wants it to be so, because this serves to promote the wasteful non-starter called revalidation.

Oliver R Dearlove, consultant anaesthetist Royal Manchester Children’s Hospital, Manchester M27 4HA o.dearlove@m-an.ac.uk

Competing interests: ORD has received a warning from the GMC and therefore is considered fit to practise.

1 Jones R. The future of the medical profession. BMJ 2007;335:53. (14 July)
2 Medical scandals leave trust in doctors unshaken. http://society.guardian.co.uk/nhsperformance/story/0,6487617,00.html
High Court backs NICE’s decision on Alzheimer’s drugs

Owen Dyer LONDON

Campaigners and drug makers failed last week in their High Court bid to overturn guidance recommending only limited coverage on the NHS of drugs to treat Alzheimer’s disease. This was the first major legal challenge to guidance issued by the National Institute for Health and Clinical Excellence (NICE), the body that recommends which drugs are available on the NHS in England and Wales.

Mrs Justice Dobbs ordered NICE to amend the existing guidance, having ruled that its diagnostic criteria breached the Disability Discrimination Act and the Race Relations Act. NICE undertook to make the relevant changes within 28 days—but the core of the guidance will remain unchanged.

The guidance recommends against the use of donepezil (Aricept), rivastigmine (Exelon), and galantamine (Reminyl) in patients with mild to moderate Alzheimer’s disease and against the use of memantine (Ebixa) in moderately severe to severe disease.

The core of the guidance will remain unchanged taking the drugs, however, will continue to receive them under an arrangement made in 2006, when NICE reversed its previous recommendation that the drugs be covered.

The judge rejected claims by the Alzheimer’s Society that NICE’s deliberative process failed to take adequately into account the potential benefits to carers and failed to reflect the full costs of long term care. The court also dismissed a claim from the manufacturer of donepezil, Eisai, and its UK distributor, Pfizer, alleging that NICE acted unfairly in releasing a “read only” version of its economic model document in which changes could not be tracked.

Mrs Justice Dobbs also rejected a claim that NICE’s assessment of data from research into Alzheimer’s disease was irrational.

But she upheld the claim of the Alzheimer’s Society that the questionnaire NICE recommends for diagnosing the severity of Alzheimer’s disease, the mini-mental state examination, potentially discriminates against non-English speakers and people with learning disabilities.

The claimants were ordered to pay 60% of the case’s legal costs and were denied leave to appeal.

NICE delays decision on drugs for macular degeneration

Caroline White LONDON

The National Institute for Health and Clinical Excellence (NICE) has had to delay its final decision on two drugs for age related macular degeneration after mounting pressure from charities and healthcare professionals.

NICE, which advises health authorities in England and Wales on the treatments to use on the NHS, issued preliminary guidance in June on the use of ranibizumab (marketed as Lucentis) and pegaptanib (Macugen) for the treatment of the disease. Both drugs are already available in Scotland.

It argued that pegaptanib should not be used at all and that ranibizumab should be prescribed only to the one in five people with the neovascular or “wet” form of the disease and only where both eyes were affected and in the better seeing eye only.

Both drugs target vascular endothelial growth factor, high concentrations of which can prompt excess blood vessel formation and fluid leakage in the eye.

Around 26 000 people develop the wet form of age related macular degeneration every year in the United Kingdom, and 245 000 people are blind or visually impaired as a result.

NICE’s conclusions sparked a wave of protest from patients and healthcare professionals that continued after the statutory consultation period closed, following a campaign spearheaded by the Royal National Institute for the Blind (RNIB).

The Royal College of Ophthalmologists and the Royal College of Nursing had both pressed for the drugs to be made available to NHS patients. The Drug and Therapeutics Bulletin, published by the BMJ Publishing Group, called NICE’s stance “unacceptable.”

The institute said at the time of its initial decision that both drugs were very expensive and that most people with age related macular degeneration sought help only once their second eye was affected. But last week it decided to postpone its deliberations until the autumn while it reviews the figures for the projected costs to the NHS.
Audit Scotland wants more effective care for long term illness

Bryan Christie EDINBURGH

Decisions on managing long term medical conditions in Scotland are being made on limited evidence of what works for patients, says a report from the public service watchdog, Audit Scotland.

The report calls for better information to be provided urgently on the cost, quality, and scope of such services to ensure the best use of resources and the most appropriate service provision in the future.

The report says that managing long term conditions is one of the biggest challenges facing healthcare systems worldwide. In the United Kingdom these conditions account for 80% of all GP consultations and 60% of hospital bed days. The number of people with long term conditions is expected to rise markedly over the next 20 years, in line with the ageing of the population.

The watchdog looked in particular at two diseases: chronic obstructive pulmonary disease and epilepsy. The report found that services are improving but that progress could still be made.

The current policy is to develop community based services to look after people with long term conditions. This requires the redesign of existing care and the transfer of resources from hospital to community services. The report says, however, that decisions on the best use of resources are currently being made on limited evidence and that there is little information at a national or local level on activity levels, costs, and effectiveness of services. “This gap urgently needs to be filled,” it says.

The report recommends that the Scottish Executive Health Department, NHS boards, and local authorities should collect better information and should agree targets on the best use of resources and the scope of such services to ensure the best use of resources and the most appropriate service provision in the future.

Managing Long Term Conditions is available at www.audit-scotland.gov.uk

GMC looks into complaints about overseas trained doctors

Peter Moszynski LONDON

The General Medical Council has commissioned new research to establish why UK doctors who trained overseas seem to be disproportionately represented at its fitness to practise hearings.

Figures released by the GMC last month show that of the 3086 complaints lodged against doctors in 2006 where the doctor’s country of training was known, nearly 40% referred to overseas trained doctors—roughly in proportion to their numbers in the NHS workforce—but the percentage of overseas trained doctors who were then referred to hearings was twice that among UK graduates (34% versus 16%). However, in a further 1279 complaints made about doctors the doctor’s place of training was not given.

Of those 3806 inquiries, 2334 related to UK trained doctors, 1143 were “international,” 309 from the European Union, and 20 were “other European.” Overseas trained doctors also seemed more likely to be struck off: of the 54 doctors removed from the medical register last year, 35 of them had trained abroad.

The figures only refer to whether a doctor graduated abroad (either within the European Union or in other countries) or in the UK so do not give details of nationality, language, or ethnicity. A British doctor who trained in Australia would appear as an overseas graduate, while an Iraqi who trained in the UK would appear in the British statistics.

Paul Philips, the GMC’s director of standards and fitness to practise, said, “The number of fitness to practise cases we deal with is going up year on year. Doctors with a primary medical qualification from overseas or within the EU are disproportionately represented, and more are being referred to us than we should be seeing, without a good explanation.”

The GMC began to investigate the issue last November after similar findings from the 2005 statistics, and the Economic and Science Research Council, the UK’s leading research funding and training agency, has initiated a number of research projects into the implications of these findings as part of a larger programme examining the links between career transitions and medical performance.

The GMC says that the studies are “designed to help understand the experiences of doctors from different backgrounds and the contexts within which concerns about doctors are referred to us.”

The GMC says “recent international research points to performance problems occurring as a result of the transition process, from . . . one country to another, from one stage of training to another, and so on.”

Overseas trained doctors more likely to be struck off

A Bangladeshi woman pulls a makeshift raft, carrying drinking water
South African health minister sacked after attending AIDS conference

Pat Sidley JOHANNESBURG
President Thabo Mbeki of South Africa last week fired his outspoken deputy minister of health, Nozizwe Madlala-Routledge. The sacking unleashed an unusually vigorous wave of support for her among opposition parties, trade unions, doctors, and AIDS activists as well as a torrent of criticism against the minister of health, Manto Tshabalala-Msimang, and the president.

Ms Madlala-Routledge had flown to an AIDS conference in Madrid in June, which Mr Mbeki says she did not have permission to attend. She told a radio station after being sacked that she had been invited to address the International AIDS Vaccine Initiative (IAVI) meeting and believed she had permission to go before leaving. When told she did not have permission she flew back to South Africa without delivering her speech.

Much of the criticism of the sacking has its background in the president’s views on HIV and AIDS—he has questioned the link between the virus and AIDS (bmj.com, 14 Oct 2006, News Extra).

The president was eventually forced to release the letter of dismissal to her giving reasons for her firing. It referred to her previous stint as deputy minister of defence and said, in part, “I have, during the period you served as deputy minister of defence, consistently drawn your attention to the concerns raised by your colleagues about your inability to work as part of a collective, as the constitution enjoins us to.” It continued: “You travelled to Madrid despite the fact that I had declined your request to undertake this trip. It is clear to me that you have no intention to abide by the constitutional prescriptions that bind all of us.”

Extreme weather affects half a billion people

Peter Moszynski LONDON
In the wake of unprecedented flooding across the world, humanitarian agencies are appealing for immediate help and warning that serious planning efforts must be made to mitigate disasters, given the likelihood of increasing devastation from the effects of global warming.

The International Federation of the Red Cross and Red Crescent Societies said, “Severe flooding has affected tens of millions of people around the world in recent weeks and months, including Bangladesh, China, Colombia, India, Indonesia, Nepal, Pakistan, and Sudan. From Dhaka to Khartoum, officials say they are seeing the heaviest rains in decades and, in some cases, recent memory.”

The federation estimates that 35 million people have been affected in South Asia, while a “staggering” 200 million people have been affected by the floods in China. It is feared that a lack of clean drinking water will result in widespread outbreaks of waterborne diseases, such as diarrhoea, skin infections, and malaria.

Cholera is reported to be spreading in Bangladesh, where local authorities report that more than a million homes have been destroyed by floodwaters in recent weeks. In India doctors have been asked to forgo their August holidays to help cope with the consequences of record monsoon rainfall across wide areas. See www.oxfam.org.uk and www.reliefweb.int.

UK heart surgeons improve patients’ survival rates

Toby Reynolds BMJ
Heart surgeons in the United Kingdom have raised the standards expected of them, figures published last week by the Healthcare Commission show.

The data on survival of patients after heart surgery, issued by the independent healthcare regulator in England, cover 38 of the 39 hospitals in the UK that carry out major heart surgery (St Mary’s Hospital, London, was unable to supply the data in the format required). The figures show that 96.5% of the 35064 patients who underwent any kind of heart surgery in the year to March 2006 survived (left the hospital alive).

The commission looked in particular at survival of patients after the two most common heart operations: heart bypass and aortic valve replacement.

Survival after heart bypass operations remained better than expected, said the commission. In the UK 20773 such operations were performed between April 2005 and March 2006. Of these patients 98.4% survived, above the expected range of 97.7% to 98.3%.

The survival rate of 98% among the 3504 patients undergoing aortic valve replacement operations was within the expected range of 96.6% to 98.2%.

The overall survival rate was similar to the 96.6% seen in the previous year.

The main change this year is in what the website shows as an expected standard alongside the actual survival data for individual hospitals. The site compares actual survival with a predicted rate calculated from patients’ characteristics, so that hospitals or surgeons who take more difficult cases are not disadvantaged. This year a new and more exacting UK algorithm that gives higher expected survival rates has been added to the Euroscore model that was used last year.

The Healthcare Commission first published cardiac surgery survival data on its website last year to help patients make more informed choices about their care.

The UK rates of survival after heart surgery are at http://heartsurgery.healthcarecommission.org.uk.
FDA needs more funding, journal says, amid questions about antidiabetes drug

Janice Hopkins Tanne NEW YORK
The US Food and Drug Administration needs more funding to do its job, say two articles in the New England Journal of Medicine (NEJM) related to reports of an increased cardiovascular risk associated with rosiglitazone (marketed as Avandia), used to treat type 2 diabetes.

Earlier this year the FDA placed its most serious “black box” warnings on rosiglitazone, which is made by GlaxoSmithKline, and pioglitazone (Actos), made by Takeda, saying that they increased the risk of congestive heart failure (BMJ 2007;334:1237).

Clifford Rosen, who chaired the FDA advisory committee that looked into the drug, has written a commentary in the NEJM (doi: 10.1056/NEJMp078167). “The basic plot of the rosiglitazone story quickly became obvious to the . . . committee: a new ‘wonder drug,’ approved prematurely and for the wrong reasons by a weakened and underfunded government agency subjected to pressure from industry, had caused undue harm to patients.”

Earlier this month the committee recommended keeping rosiglitazone on the market, because it might help patients, but that it should carry stronger warnings (BMJ 2007;335:223, 4 Aug). Dr Rosen said that the rosiglitazone studies were mostly short (about six months) and that adverse events might be classified differently in some studies. The committee lacked information about the other glitazone drug, pioglitazone, because the FDA had not completed reviewing the manufacturer’s data.

Dr Rosen, an endocrinologist, is a senior staff scientist at St Joseph Hospital in Bangor, Maine, and the Jackson Laboratory in Bar Harbor, Maine. He told the BMJ that the FDA needed more funding and should undergo a “sea change” in the way it evaluates drugs.

Instead of relying on surrogate end points such as glycaemic control or lipid concentrations it should look at clinical events such as myocardial infarction, he said.

More funding would enable the FDA to increase its staff and design longer studies that would yield better results, such as two year, prospective, randomised controlled trials, he added.

Skin cancer is on the increase—but lung cancer is falling

Adrian O’Dowd MARGATE
The incidence of some cancers is rising in the United Kingdom because of people’s lifestyle choices, says Cancer Research UK.

The charity has published new statistics showing steady rises in the numbers of cases of some types of cancer that are linked to excessive exposure to sun, alcohol consumption, smoking, and obesity.

The number of new diagnoses of malignant melanoma—the most dangerous form of skin cancer—rose from 5783 in 1995 to 8939 in 2004, making it the fastest rising cancer in the UK. This represented an increase in incidence per 100 000 people, adjusted for age, of 43%.

The incidence of oral, uterus, and kidney cancers has also risen in the 10 years to 2004, says Cancer Research UK. And it adds that around half of all cancers could be prevented if people modified their lifestyle.

The new figures, published by the charity and the UK Association of Cancer Registries, show that:

- From 1995 to 2004 the number of new diagnoses of oral cancer rose from 3696 to 4769 (six cases in every 100000 people in the UK population), an increase in age standardised incidence of 23%
- Cancer of the uterus rose from 5018 to 6438 (16.8 per 100000), a 21% increase in age standardised incidence, and
- Cancer of the kidney rose from 5636 to 7044, a 14% increase in age standardised incidence.

Together these four types of cancers account for almost 10% of all the 284 560 new diagnoses of cancer in the UK in 2004.

Over the same period, however, the incidence of cervical cancer fell from 3478 in 1995 to 2726 cases in 2004 (a fall in age standardised incidence of 24%) and those of lung cancer fell from 40787 to 38313 (13%). However, lung cancer, with an incidence of 47.6 per 100000 in 2004, is still the commonest cancer.

Ian Fentiman, professor of surgical oncology at Guy’s, King’s and St Thomas’ School of Medicine, London, said the new statistics were important but had to be considered in context.

“These are certainly not the biggest cancers out there,” he said. “The things we should still be panicking about are things like smoking, because lung cancer is still a mega-killer.”

Details of the incidence of cancers in the UK in 2004 are at http://info.cancerresearchuk.org/cancerstats/incidence.

UK INCIDENCE OF KIDNEY, LUNG, AND ORAL CANCERS AND MALIGNANT MELANOMA

Lung cancer is still a bigger killer than skin cancer

Source: Cancer Research UK
MRI may be better than mammography for early detection of breast cancer

Mammography is widely regarded as the gold standard for detecting ductal carcinoma in situ, but a new study challenges this belief. More than 7300 women who were referred to a national breast cancer centre over five years underwent magnetic resonance imaging (MRI) and mammography, the results of which were independently double read by four experienced breast radiologists. Of the 167 women with a pathologically confirmed diagnosis of ductal carcinoma in situ, 93 (56%) were picked up by mammography and 133 (80%) by MRI (P<0.0001).

MRI was also more sensitive for detection of high grade carcinoma in situ, which is more likely to progress to invasive carcinoma than low grade lesions. Almost a third of carcinomas detected by mammography, and almost all detected by mammography alone, were low grade, whereas 60% of those caught by MRI alone were high grade. Positive predictive value was also better with MRI (59%) compared with 55% for mammography.

These results are in contrast with previous studies, but the authors discuss how selection bias and lack of specific diagnostic criteria might have led to previous misleading conclusions. The linked comment (pp 439-60) states that MRI outperforms mammography for detection of breast cancer in its earliest stage. We now need a large multicentre screening trial that would confirm these unexpected results in the general population.


Screening for osteoporosis may pay off in some groups of older men

In ageing populations, bone fractures and impaired quality of life caused by osteoporosis increasingly affect not only women, but also older men. Densitometry screening programmes for men, and treatment with oral bisphosphonate as appropriate, are sparse and understudied.

A recent modelling study used data from large cohort studies, US national databases, and systematic reviews to better inform decisions on the cost effectiveness of screening men for osteoporosis. With costs of bisphosphonate at their current level, screening might be cost effective at the threshold of $50 000 (£25 000; €36 000) for men aged 65 years with a previous self reported bone fracture, and for men aged 80 years or older without previous fracture.

It seems that universal screening of all men aged 70 years or older, based on expert opinion, would only be cost effective if society was willing to pay $100 000 per year for a quality adjusted life year gained, or if the cost of oral bisphosphonate treatment became less than $500 per year. This might happen in the United States when alendronate loses patent protection in 2008.

*JAMA* 2007;298:629-37

Geriatric conditions are prevalent and disabling, but neglected

In the United States, a nationally representative survey of 11 093 adults aged 65 years or older assessed the prevalence of self reported geriatric conditions and their association with impairment in some activities of daily living (bathing, dressing, eating, toileting, and transferring). Almost half of the respondents had at least one geriatric condition—defined as falls resulting in injury, incontinence, body mass index of less than 18.5, persistent or troublesome dizziness or lightheadedness, vision impairment, hearing impairment, or cognitive impairment. In this study, researchers weren’t able to gather data for delirium, pressure sores, frailty, or failure to thrive.

After adjustment for age, sex, ethnicity, marital status, education, net financial worth, and major chronic diseases (all known to affect activities of daily living) having one geriatric condition doubled the risk for dependency in the studied activities of daily living. The risk increased 3.6-fold with two geriatric conditions and 6.6-fold with three or more conditions.

The authors argue that the high prevalence of geriatric conditions and their link with dependency indicate that geriatric conditions largely go unrecognised when they could be prevented or delayed, managed, and sometimes treated. Moreover, their presence should have an impact on treatment or management of coexisting diseases and disabilities.

*Ann Intern Med* 2007;147:156-64

Women with diabetes miss out on mortality improvements 1971 to 2000

Reduced mortality from cardiovascular disease has been a major public health success in industrialised countries, but how has this improvement extended to patients with diabetes? A study of mortality trends across three large US cohorts found that men have benefited more than women over the last three decades.

All cause mortality rates for men with diabetes fell by 43% between 1971 and 2000 (from 42.6 to 24.4 deaths per 1000 persons per year, P=0.03), which is a similar relative fall to that seen in men without diabetes. A reduction in mortality from cardiovascular causes in men with diabetes paralleled this trend (26.4 to 12.8, P=0.06).

**MORTALITY RATES AMONG US POPULATION, 1971-2000**

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Adapted from *Ann Intern Med* 2007;147:149-55

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**SHORT CUTS**

**WHAT’S NEW IN THE OTHER GENERAL JOURNALS**

Kristina Fister, associate editor, *BMJ* kfister@bmj.com

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**OSTEOPOROSIS SCREENING AND TREATMENT IN OLDER MEN**

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No intervention

Densitometry and treatment

Adapted from *JAMA* 2007;298:629-37

**MORTALITY RATES AMONG KOREAN POPULATION, 1971-2000**

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<td>30</td>
</tr>
<tr>
<td>2007</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

Adapted from *Ann Intern Med* 2007;147:149-55
Neither the all cause nor the cardiovascular mortality rates fell over the time period for women with diabetes, and the difference between all cause mortality in women with diabetes and without diabetes doubled (from a difference of 8.3 deaths to 18.2 deaths per 1000 persons per year, $P=0.04$).

The lack of improvement in women is hard to explain. A linked editorial (pp 208-10) says evidence indicates women with coronary heart disease and diabetes are less likely to receive appropriate care. It adds, however, that risk factors for cardiovascular disease might be more common, more severe, or more likely to cluster in women with diabetes than in men. *Ann Intern Med* 2007;147:149-55

Another neuroprotective drug fails to make its mark

**NYX-059 FOR ACUTE ISCHAEMIC STROKE**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>Placebo better</th>
<th>NXY-059 better</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 hours</td>
<td>0.91 (0.78 to 1.06)</td>
<td>0.98 (0.79 to 1.22)</td>
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</tr>
<tr>
<td>&gt;4 hours</td>
<td>0.99 (0.74 to 1.30)</td>
<td>0.97 (0.82 to 1.15)</td>
<td></td>
</tr>
<tr>
<td>Use of alteplase</td>
<td>0.99 (0.74 to 1.30)</td>
<td>0.97 (0.82 to 1.15)</td>
<td></td>
</tr>
<tr>
<td>No use of alteplase</td>
<td>0.85 (0.69 to 1.05)</td>
<td>0.92 (0.74 to 1.13)</td>
<td></td>
</tr>
<tr>
<td>NIHSS* 6 to 9</td>
<td>1.14 (0.83 to 1.52)</td>
<td>1.00 (0.71 to 1.41)</td>
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</tr>
<tr>
<td>NIHSS 10 to 14</td>
<td>0.92 (0.74 to 1.13)</td>
<td>0.97 (0.82 to 1.15)</td>
<td></td>
</tr>
<tr>
<td>NIHSS 15 to 19</td>
<td>0.85 (0.69 to 1.05)</td>
<td>0.92 (0.74 to 1.13)</td>
<td></td>
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<tr>
<td>NIHSS ≥20</td>
<td>0.99 (0.74 to 1.30)</td>
<td>0.97 (0.82 to 1.15)</td>
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</tbody>
</table>

* NIHSS: National Institutes of Health Stroke Scale

Adapted from *N Engl J Med* 2007;357:562-71

Few treatments are available for acute stroke, and new ones are needed urgently. Several drugs thought to help protect neurones from ischemic injury have been tried, but none have been effective in clinical trials. A study has found that the free radical trapping drug NXY-059, for which earlier trial results had been promising, is also ineffective.

NXY-059 had been shown to improve outcome relative to placebo if given within six hours of the onset of symptoms. A larger, randomised double blind placebo controlled trial set out to confirm these results, examining disability scores at 90 days. Based on 3195 patients from 362 centres across 31 countries who were included in the efficacy analysis, there was no difference in disability score distribution on the modified Rankin scale between 1588 people treated with NXY-059 and the 1607 treated with placebo ($P=0.33$, odds ratio 0.94, 95% CI 0.83 to 1.06). Mortality and adverse event rates were similar in the two groups. *N Engl J Med* 2007;357:562-71

D-dimer test might help exclude deep vein thrombosis in pregnancy

D-dimer values increase during pregnancy, and although a D-dimer test has high specificity in women suspected of having deep vein thrombosis who are not pregnant, it is thought to have limited value in pregnant women. Previous studies confirmed that rapid enzyme linked immunoabsorbent assay D-dimer tests and latex agglutination tests yielded too many false positive results to be of clear diagnostic value in pregnant women.

A recent study that looked at the diagnostic accuracy of the SimpliRED assay seems to give more encouraging results. Among 149 pregnant women suspected of having deep vein thrombosis, a detailed diagnostic procedure that included compression ultrasonography and three months of clinical follow-up confirmed the diagnosis in 13 (8.7%) of the women.

The SimpliRED assay was positive in all these women, and also had an acceptable specificity of 60%. Still, because of the low number of cases and wide confidence intervals, these results need to be interpreted cautiously. Doctors will particularly need to take into account clinical presentation, which is made difficult by the lack of a validated, structured clinical prediction rule for pregnant women. *Ann Intern Med* 2007;147:165-70

Rituximab works for severe pemphigus but there are serious side effects

Twenty one patients with severe pemphigus who didn’t respond to treatment with corticosteroids or in whom treatment with corticosteroids was contraindicated were given four weekly infusions of rituximab—a monoclonal antibody directed against the CD20 antigen of B lymphocytes. The drug had been shown to be effective against several other autoimmune diseases and pemphigus, but only in combination with intravenous immunoglobulin and when given in multiple cycles.

At three months, 18 out of 21 people had a complete remission. Of these, 12 people had pemphigus vulgaris and six had pemphigus foliaceus. Two more patients had a complete remission at 180 or 360 days of follow-up, leaving only one patient with pemphigus foliaceus not responding to treatment. At three years of follow-up, 18 patients were still in full remission, with eight of them not receiving any treatment with corticosteroids.

Two patients had serious side effects. One developed pyelonephritis one year after the treatment, and another died of septicemia a year and a half after treatment with rituximab. Other side effects of rituximab, previously reported in the literature, include death from pneumocystis infection, toxic epidermal necrolysis, and progressive multifocal leukoencephalopathy. *N Engl J Med* 2007;357:545-52

How best to save joints in severe haemophilia A

A trial randomised 65 boys with severe haemophilia A, up to 30 months old at recruitment, to receiving prophylactic regular infusions of recombinant factor VIII every other day or to episodic treatment at the time of clinically evident joint haemorrhage. After a median follow-up of 49 months, at 6 years of age, 25 of the 27 boys who were randomised to prophylaxis and completed the trial had no damage to ankle, knee, or elbow joints, as assessed by magnetic resonance imaging, compared with 16 of 29 boys in the episodic treatment group. Boys randomised to prophylaxis also had fewer clinically evident joint haemorrhages (median 0.2 v 4.4 occurrences per participant per year) and fewer total haemorrhages (median 1.2 v 17.1 occurrences per participant per year).

Despite clinical benefits, which fit well with previous evidence, the major factor limiting widespread uptake is the high cost of recombinant factor VIII—estimated at an average of $300 000 per patient per year. Still, the linked editorial (pp 603-5) reminds that, untreated, severe haemophilia A incurs great costs to the health systems later on in boys’ lives, such as costs of replacing joints. In the absence of relevant trials and any formal cost effectiveness analyses, the optimal prophylaxis regimen still eludes us. *N Engl J Med* 2007;357:535-44
Mediterranean diet reduces child asthma and allergy

A survey of 93% of the 857 children and teenagers aged 7-18 years living on the Greek island of Crete suggests that eating grapes, oranges, apples, and tomatoes is protective against wheezing and rhinitis. Margarine had the opposite effect, whereas a high nut intake was inversely associated with wheezing. Of the 690 children for whom data were complete, 80% reported eating fruit twice daily, and 68% ate vegetables twice daily.

The investigators conclude that the local diet, high in antioxidants, may be responsible for the relatively low prevalence of allergic symptoms in the Cretan population. Thorax 2007;62:677-83

Carvedilol less diabetogenic than metoprolol

Patients with chronic heart failure are more likely to develop diabetes if treated with metoprolol than carvedilol. A double blind trial (COMET) recruited 3029 patients with heart failure and left ventricular systolic dysfunction to receive one or the other β blocker as well as their standard treatment. Among the 2298 not diabetic at trial entry, diabetes developed in 264 (11.5%) during 47-72 months of follow-up. As expected, this was more likely in those with a high body mass index, history of hypertension, and more severe heart failure. However, it was less likely in those treated with carvedilol than metoprolol (119/1151 (10.1%) and 145/1147 (12.6%) respectively, hazard ratio 0.78 (95% CI 0.61 to 0.99)).

Of those patients not diabetic at study onset and taking metoprolol, 38.1% (95% CI 35.1% to 41.2%) died during follow-up, compared with 32.7% (29.8% to 35.7%) of those taking carvedilol. Heart 2007;93:968-73

Adalimumab maintains remission in Crohn’s disease

Patients with moderate to severe Crohn’s disease who had achieved remission after a four week regimen of the cytokine inhibitor adalimumab (CLASSIC I trial) went on to a placebo controlled trial of maintenance treatment for a year. Those who had not responded received the drug on a ‘down-staging’ basis. Of the 55 patients randomised, 8/18 who received placebo were in remission at 56 weeks compared with 15/19 who received adalimumab 40 mg subcutaneously every other week and 15/18 who received it weekly. The remission rate at 56 weeks in the remaining 204 patients, who had not responded at four weeks, was 46%. Treated patients were more likely to have reduced their corticosteroid dose and have an improved quality of life.

Adverse events were commoner with placebo than active drug, the most usual being upper respiratory symptoms. The investigators conclude that adalimumab is an important new therapeutic agent (currently not licensed for treating Crohn’s disease in the UK). Gut 2007 doi: 10.1136/gut.2006.106781

Chlamydia infection increases risk of premature delivery

A retrospective, population based, cohort study of all 851 women in Washington State, USA, listed as having Chlamydia trachomatis on routine screening during pregnancy in one year has shown they were more likely to have premature rupture of the membranes (PROM) and preterm delivery than a comparison group of 3404 women who had screened negative. This was despite them and their partners receiving appropriate treatment.

After adjustment for maternal age and education, chlamydia infection was associated with a relative risk of preterm delivery of 1.46 (95% CI 1.08 to 1.99) and of premature rupture of the membranes of 1.50 (1.03 to 2.17). Infected patients were not more likely to have babies of low birth weight, nor was there a greater risk of infant death. The investigators are concerned that the organism remained a risk factor even after screening and treatment. Sex Transm Infect 2007;83:314-8

Television soap operas set a poor example

Alcohol related behaviour frequently appears on the four most popular UK television soap operas (EastEnders, Coronation Street, Emmerdale, and Hollyoaks), but not drink-driving or drinking or smoking during pregnancy. Researchers had the pleasure of watching recordings of all 80 episodes screened during April and May 2005 and observed 959 instances of “health behaviours of interest,” as derived from current national guidelines on health promotion.

Alcohol related behaviour occurred 19.3 times per programme hour, unhealthy eating 6.1 times/hour, healthy eating 2.9 times/hour, and exercise 0.9 times/hour. Smoking was shown rarely. Perhaps surprisingly, the most alcoholic soap was Emmerdale and the least alcoholic was EastEnders.

The authors speculate that engaging programme makers in a health promotion agenda may be fruitful. J Epidemiol Community Health 2007;61:575-7

In September 2007, we release the full online legacy archive for Heart, our international cardiology journal. The legacy archive will contain articles dating back to 1939 and all content older than 12 months will be available FREE. Visit the website at www.heart.bmj.com

WHAT’S NEW IN BMJ JOURNALS

Harvey Marcovitch, BMJ syndication editor h.marcovitch@btinternet.com
Iraq’s beleaguered government has sought outside help to run its troubled health ministry—in the form of a Kent psychiatrist. Dr Sabah Sadik, who until recently was medical director of Kent and Medway NHS and Social Care Trust, will take on a ministry heavily infiltrated by the political faction loyal to Shiite cleric Moqtada al-Sadr and its feared militia, the Mahdi Army. “A lot of people—especially Iraqis—have told me I’m crazy to go,” he said.

Six Sadrist ministers quit the government in April, including Ali al-Shemari, the health minister. Iraq’s government saw an opportunity to break the militia’s grip on the health system, says Dr Sadik. “That’s the main reason why I’ve decided to accept this job now. There seems to be a new determination to get the sectarianism out of the ministries and appoint neutral technocrats. If that is serious, I’m willing to be one of them.”

Dr Sadik qualified in Baghdad in 1974, and has worked in Britain for nearly three decades. He comes from a “very liberal Shiite family,” but lived from age 10 in Baghdad’s heavily Sunni Kharq district, attending the same secondary school as Saddam Hussein. He spent a year in Iraq in 2004-5, working as national adviser for mental health.

Unstable system
Five health ministers have come and gone since the 2003 invasion, but Iraq’s health system has continued its long slide into disrepair. A report published by Oxfam last week showed every public health indicator heading in the wrong direction.1

The health ministry’s problems, however, go far beyond a lack of resources. As the Sadrist’s grip tightened throughout 2006, the ministry descended into gangsterism. In an effort at inclusiveness, Sunni parties were allowed to nominate one deputy health minister. Their candidate, Ali al-Mahdawi, entered the health ministry last June for an appointment with the minister, Mr al-Shemari. He and his bodyguards have never been seen since.

Last summer, horrific stories began to emerge of Shiite death squads prowling Baghdad’s hospital wards. It’s unclear to what extent the health ministry controls these men. Many wear the uniforms of the Facilities Protection Service, ministerial private armies staffed with party militia. The service is particularly notorious, and numbers about 15 000 armed men.

Last autumn, the health ministry became embroiled in a violent feud with the Sunni controlled Ministry of Higher Education, culminating in armed attacks on both ministry headquarters.

Restoring confidence
Will Dr Sadik purge the ministry? “It’s fair to say,” he acknowledges, “that the Sadrist influence runs through the ranks. In Iraq, everyone expects the new man to clean everyone out and replace them with his own people. They expect a dictatorial leadership style. I prefer not to operate that way. I think everyone deserves a chance to show that they can look beyond sectarian loyalty and work for all Iraqis. But if someone can’t do that, then yes, ultimately they must go.”

Some have already gone. A kidnap ring operating from the heart of the ministry was shut down last August when US forces arrested seven bodyguards of Mr al-Shemari. But in November, deputy health minister Ammar al-Saffar was kidnapped from his home. He has never been found. The next day, two bodyguards of another deputy health minister, Hakim al-Zamili, were killed when his convoy was ambushed. “We as health ministry officials have become targets,” Mr al-Zamili told reporters.

This February, US forces named a suspect in Mr al-Saffar’s disappearance—his fellow health minister Mr al-Zamili, whom they arrested in his office along with five bodyguards. Mr al-Zamili was also accused of diverting ministry funds to the Mahdi Army.

Dr Sadik is aware of these incidents, but he is not deterred. “Certain political groups may be unhappy with my appointment. But there is always the knowledge that if you don’t do it, who will?”

“I’m under no illusion that progress will be quick or easy. But I think there are some quick fixes available. Communications within the government can definitely be improved,” says Dr Sadik, who recounts that during his year as Iraq’s national adviser for mental health, he never met his health minister. “My first priority will be to go to the hot spots myself. People won’t trust their government if it won’t show its face.” He plans an early visit to the bitterly divided province of Diyala.

Dr Sadik does not dispute the widespread claim that more than half of Iraq’s doctors have fled the country. “There were 150 psychiatrists in Iraq in 2003. Now there are 65. I believe that’s representative. But no doctors are getting jobs in neighbouring countries any more, as they’ve stopped giving work visas.”

“My greatest concern is for those who can’t afford to travel, who must stay and face difficult conditions.” He worries about nurses, whom he considers key to rebuilding the health system. “We must quickly raise salaries for both doctors and nurses,” he says.

On the US led invasion, Dr Sadik pronounces himself “ambivalent.” He is critical of reconstruction efforts and describes casualties in Iraq as “unknowable but unacceptably high.”

He is awaiting confirmation by Iraq’s parliament, which is now in recess for August and has recently been short of a quorum because of walkouts by members of parliament.

When he does leave for Iraq, his British born wife and four sons will stay in Kent. “They will visit later,” he says, “when things settle down a bit.”

Owen Dyer is a journalist owen_dyer@hotmail.com


Owen Dyer talks to the new minister about the challenges

Running Iraq’s health department is not only logistically difficult but dangerous.

Owen Dyer

Kent psychiatrist, Sabah Sadik

Kent psychiatrist, Sabah Sadik
In a July hearing of the US Congress the immediate past US surgeon general, Richard Carmona, testified about the problem of political meddling in what he saw as the proper functions and activities of his office.

Carmona spoke generally about repeated interference by the Bush administration (which appointed him) in his attempts to speak out on controversial issues, such as stem cell research, abstinence only sex education, and the emergency contraceptive pill (BMJ 2007;335:114). His speeches were scrubbed of any mention of these matters, even when his comments were based on science.

The former surgeon general also said that he was told by an unnamed senior official that he didn’t “get it” when it came to the political basis for scientific reports which had to agree with the administration’s political agenda or they would not be approved. Two other former surgeons general—C Everett Koop, from the Reagan years, and David Satcher, from the Clinton presidency— also testified and cited similar examples from their own tenures but said that the censorship seemed to be getting worse.

The testimony brought a swift response from the Bush administration and Washington’s punditocracy. The administration dismissed Carmona’s charges, saying that it had given him all the support and opportunities he needed and that it was disappointing “if he failed to use his position to the fullest extent.” The pundits either praised him for coming forward with his story or questioned his courage for waiting until he had left office before speaking out.

Carmona’s general accusations became specific at the end of July, when the Washington Post said in a front page story that one of the reports Carmona was complaining about was a 2006 global health study. It was never released, because Carmona would not make political changes demanded by a Bush official named William Steiger. A godson of the first President Bush, Steiger had no medical or public health background when he was appointed director of the government’s Office of Global Health Affairs. (He still occupies this post while he awaits Senate confirmation as ambassador to Mozambique.) It is common practice in the United States for presidents to appoint well connected but inexperienced allies to key policy posts. Although they can be depended on to follow the president’s political agenda, they often have little or no substantive knowledge about the agencies they administer.

Steiger maintained that the global health report should focus mainly on the steps that the Bush administration had taken to improve health worldwide. Carmona wanted to release a version drafted by international health experts that reviewed the links between poverty and ill health and advocated that disease prevention and treatment become a part of the US’s foreign policy. When Steiger wouldn’t approve this report, which he called “often inaccurate and out of date,” and Carmona refused to release the administration’s version, the report was cancelled.

The Bush administration seems more likely than most to suppress scientific information to further political ideology, with recent complaints surfacing from disgruntled employees at the National Institutes of Health, the Food and Drug Administration, and NASA. Such meddling happens in all administrations, though, and it raises two issues that transcend administration and subject matter: what happens when an official disagrees with an announced policy, and what to do when scientific expertise is disregarded and evidence is manipulated or ignored.

In the first of these cases the traditional advice to political appointees has been to advocate for their opinions strongly in private discussions but support whatever policy eventually emerges. A well known example of this was when President Clinton’s health and human services secretary, Donna Shalala, strongly disagreed with making a major change in welfare payment policy that would result in many people being thrown off the welfare lists. But when the president endorsed it she went along publicly, despite opposition from her liberal constituency. Most now agree that it was, on balance, an important and successful reform.

The second issue is trickier. Carmona complained that political ideology was trumping science when, for instance, he was not allowed to advocate any type of sex education for young people except abstinence, even though scientific reviews showed clearly that abstinence only sex education curriculums don’t work. It was reminiscent of an episode in the Reagan administration when Surgeon General Koop was ordered to prepare a report on the adverse psychological effects of abortion. After reviewing the literature Koop refused, saying that he had found none. As a conservative surgeon whose appointment was opposed by liberals, he had enough stature and support to weather the storm.

Clearly an administration should be allowed to attempt to set its agenda, to focus on what it thinks are important issues, and to prioritise. It also, of course, has a right to tout its accomplishments and take credit for even the serendipitous achievements that have taken place during its tenure. But when officials knowingly cite inaccurate or misleading information or bend the rules of science or evidence in pursuit of a political agenda or policy, it is time for honourable officials—whether career status or political appointees—who are unable to convince the administration to desist from such distortions to call attention to them in the only way they can: resignation.

Douglas Kamerow is former US assistant surgeon general and a BMJ associate editor}

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It is normal to feel depressed. In our study of 242 teachers, the 1978 baseline questionnaire defined depression as “a significant lowering of mood, with or without feelings of guilt, hopelessness and helplessness, or a drop in one’s self-esteem or self-regard.” Ninety-five per cent reported such feelings (with a mean of six episodes a year), showing the ubiquitous nature of a depressed mood.

A low threshold for diagnosing clinical depression risks treating normal emotional states as illness, challenging the model’s credibility and risking inappropriate management. When the first antidepressant (imipramine) was developed, manufacturer Geigy was reluctant to market it, judging there were insufficient people with depression. Now, antidepressant drugs have a large share of the drug market. Reasons for the overdiagnosis include lack of a reliable diagnostic model and marketing of treatments beyond their true utility in a climate of heightened expectations.

Fifty years ago, clinical depression was either endogenous (melancholic) or reactive (neurotic). Endogenous depression was a categorical biological condition with a low lifetime prevalence (1-2%). By contrast, reactive depression was exogenous—induced by stressful events affecting a vulnerable person. Thus, it is normal to feel depressed. In our study of 242 teachers, 95% reported such feelings (with a mean of six episodes a year), showing the ubiquitous nature of a depressed mood.

Minor DSM-III depressive disorder (dysthymia) homogenised less severe chronic conditions, requiring even fewer and less substantive symptoms such as crying, decreased productivity, and feeling sorry for yourself. This model was extended by proposing a less severe condition, subsyndromal or subclinical depression. Its one year prevalence in a US community database was nearly triple that of major depression, encouraging those investigators to argue for its “clinical and public health importance” and treatment.

How low do we go?

Determining caseness for any dimensional construct requires imposing a cut-off, risking underdiagnosis of true cases or overdiagnosis of non-cases. By 1993, 79% of teachers in our cohort had met the criteria for major, minor, or subsyndromal depression (unpublished data). Although it was necessary to redress psychiatry’s earlier weighting to melancholia, the dimensional model risks medicalising normal human distress and viewing any expression of depression as mandating treatment.

That many people with substantive clinical depression do not have their condition diagnosed does not mean that depression is underdiagnosed. Such boundary concerns have parallels. For example, the diagnosis of attention-deficit/hyperactivity disorder is often missed; conversely, it is often falsely diagnosed in children with other disruptive behaviours.

Does overdiagnosis matter?

Does current looseness matter if a low diagnostic threshold destigmatises depression, encouraging people to seek help? After all, breast screening programmes may lead to detecting more malignant lumps. However, false positives results generated by breast screening are filtered out by refined assessment, and harm rarely occurs. For false positive detection of depression, many of psychiatry’s leaders mandate treatment, which for those with less severe conditions raises hopes but results in ineffective and inappropriate treatments.

The ease of diagnosing clinical depression has rebounded on psychiatry, blunting clarification of causes and treatment specificity. As Hickie, who argues here against overdiagnosis, observed elsewhere: DSM-III defined major depression has failed “to demonstrate any coherent pattern of neurobiological changes or any specific pattern of treatment response outside in-patient treatment settings.”

Meta-analyses show striking gradients favouring antidepressants over placebo for melancholic depression. Yet trials in major depression show minimal differences between antidepressant drugs, evidence based psychotherapies, and placebo. The benefit of treatment for minor and subsyndromal depression is even more unclear. Extrapolating management of the more severe biological conditions to minor symptom states reflects marketing prowess rather than evidence.

Depression will remain a non-specific “catch all” diagnosis until common sense prevails. As American journalist Ed Murrow said: “Anyone who isn’t confused doesn’t really understand the situation.”

Competing interests: GP is executive director of Australia’s Black Dog Institute and has served on pharmaceutical advisory boards and spoken at meetings convened by drug companies.
Rates of diagnosis of depression have risen steeply in recent years. **Gordon Parker** believes this is because current criteria are medicalising sadness, but **Ian Hickie** argues that many people are still missing out on lifesaving treatment.
Potential of electronic personal health records

Novel methods for helping patients to access and manage their personal electronic health data are emerging in the UK and internationally. Claudia Pagliari, Don Detmer, and Peter Singleton examine their potential benefits and challenges.

Public demand for flexible access to health information and services is growing, encouraged by internet trends and policies promoting patient rights and empowerment. In parallel, unprecedented global investment in healthcare information and communication technologies has been dominated by efforts to implement electronic health records, which promise improved quality and efficiency through better maintenance and availability of patient data. There is considerable international interest in the potential of electronic personal health records to bridge these agendas, and NHS HealthSpace is set to become the world’s first fully national system, although its capabilities are still limited in comparison with some European and US examples. We consider the potential of electronic personal health records and factors that are likely to influence their adoption in the UK, drawing on a new report from the Nuffield Trust.

What are electronic personal health records?

Although no universally agreed definition of an electronic personal health record exists, it has been described as “an electronic application through which individuals can access, manage and share their health information… in a private, secure and confidential environment.” Models vary in the extent to which the content of the record and rights of access are controlled by the patient or the healthcare provider, the range of tools that accompany it, and their interactivity. Simpler models include patient generated health and lifestyle records that are stored and managed using personal computer or web applications, and passive access to provider held records through waiting room kiosks, the internet, or digital copy (such as on a CD or smart card).

However, personal health record systems are becoming increasingly complex (box 1). Some are integrated with providers’ information systems to combine personal record keeping, access to current electronic health records, and a range of information and communications functions. For example, patients of the US managed care organisation Kaiser Permanente have access to HealthConnectOnline, which offers records of allergies, immunisations, future appointments, diagnoses, instructions from past visits, and laboratory results as well as allowing patients to book appointments, reorder prescriptions, and communicate with healthcare professionals by email (figure).
### Current UK experience with electronic personal health records

#### Primary care
Online access to the full electronic primary care record is being piloted in practices associated with a major system supplier. Patients of some eligible practices also have access to online appointment booking, prescription reordering, and secure email. Waiting room kiosks providing secure access to records and related patient information have been introduced in several general practices and are now available commercially through Healthecard.co.uk. Some practices have offered patients copies of their electronic record on CD or USB memory stick for several years.

Smart cards are currently being marketed, on to which patients can upload their general practice record, for a fee, and view it using personal computing software through healthecard.co.uk. Access to record via mobile phone and BlackBerry smart phone is also being piloted.

#### Secondary care
Patient portals offering access to more specialised records, some with a range of additional features, exist or are being developed in several areas, including:
- Nephrology ([www.renalpatientview.org](http://www.renalpatientview.org))
- Paediatric intensive care ([www.babylink.info/Edinburgh/BabyLink/Intro_page.asp](http://www.babylink.info/Edinburgh/BabyLink/Intro_page.asp))
- Diabetes ([www.dmag.org.uk/bird/aboutthisproject.asp](http://www.dmag.org.uk/bird/aboutthisproject.asp))
- Maternity care ([www.nhshealthquality.org/nhsqis/229.htm](http://www.nhshealthquality.org/nhsqis/229.htm))

Patient-provider email and remote submission of symptoms to electronic health records are also being tested in both sectors.

### What are the possible benefits and for whom?
Electronic personal health records have the potential to empower patients through greater access to personal data, health information, and communications tools, which may aid self care, shared decision making, and clinical outcomes. They may increase patient safety through exposing diagnostic or drug errors, recording non-prescribed medicines or treatments, or increasing the accessibility of test results or drug alerts. They may also reduce geographical barriers to patient care and act as a point of record integration, particularly in fragmented health systems, thus improving continuity of care and efficiency.

Although the number and quality of studies remains limited, existing research suggests improvements in communication and trust between patients and professionals, confidence in self care, compliance in chronic disease, and accuracy of records. Patients particularly value online reordering of prescriptions, laboratory results, disease management plans, trend charts, drug lists, and secure messaging.

Surveys indicate that most patients would like to be able to access their health records, however, the most frequent users of electronic personal health records, and those for whom the greatest benefits can be expected, are likely to be patients with long term conditions, who have the most need to track their illness and treatments, and patients experiencing episodic periods of care or treatment that generate new needs for information or communication (such as in vitro fertilisation).

The emergence of mobile and wireless applications that allow remote submission of data to a shared record offer new possibilities for patient monitoring and real time decision support. Additionally, electronic records may help to promote partnership between carers and health professionals through sharing information, or allow relatives to monitor the care and progress of elderly parents or children in hospital from a distance.

### Factors influencing UK adoption and effectiveness

#### Privacy and security
Anxieties around security and confidentiality have been expressed in most studies of patient attitudes to personal electronic records, particularly in regard to mental and sexual health data. This does not seem to have been a barrier where access to general practice records has been tried in the UK, however, some patients may wish to keep sensitive information off the central NHS record (called the spine).

Although encryption technologies can help to prevent unauthorised access, the risk of privacy invasions may be greatest at the family level, whether the intent is supportive or malign (for example, in spousal abuse), which is difficult to control for. Growing experience

<table>
<thead>
<tr>
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<th>Current UK experience with electronic personal health records</th>
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<tbody>
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<tr>
<td><strong>Secondary care</strong></td>
<td>Patient portals offering access to more specialised records, some with a range of additional features, exist or are being developed in several areas, including: - Nephrology (<a href="http://www.renalpatientview.org">www.renalpatientview.org</a>) - Paediatric intensive care (<a href="http://www.babylink.info/Edinburgh/BabyLink/Intro_page.asp">www.babylink.info/Edinburgh/BabyLink/Intro_page.asp</a>) - Diabetes (<a href="http://www.dmag.org.uk/bird/aboutthisproject.asp">www.dmag.org.uk/bird/aboutthisproject.asp</a>) - Maternity care (<a href="http://www.nhshealthquality.org/nhsqis/229.htm">www.nhshealthquality.org/nhsqis/229.htm</a>) Patient-provider email and remote submission of symptoms to electronic health records are also being tested in both sectors.</td>
</tr>
</tbody>
</table>
of online services in other sectors and traditionally high levels of trust in healthcare professionals are likely to help ease concerns about confidentiality.

Digital divide
Electronic personal health records have the potential to contribute to health inequalities through uneven internet access, although rising ownership of mobile phones and digital TV may help to ameliorate this if developers include these alternative media. Attention also needs to be paid to usability and training in order to overcome access disparities resulting from poor technical skills—for example, among elderly people. If these problems are effectively addressed, such records may reduce healthcare exclusion through flexible access to information and services.20

Choice of model
Although patients may welcome passive access to records, the greatest benefits are likely to come from multifunctional, interactive systems that are integrated with providers’ record systems and can support education, self care, and communication with the health service.2 However, this increased utility may decrease security, and patients will have to decide whether this risk is acceptable for them.3 It also creates an imperative for standards to ensure transparency of contributorship and access. Growing availability and use of digital health monitoring devices may create new sources of data that can be included in the record, although this information is unlikely to be beneficial unless clinicians are available to interpret and respond to it.13

In view of individuals’ differing requirements from an electronic personal health record and the associated security issues, HealthSpace’s cautious approach to access and interactivity is appropriate. Systems offering more comprehensive patient records or interactive support tools are likely to be pursued as optional supplements to HealthSpace, ideally integrating with local general practice or disease specific records systems. It is unclear whether wholly patient managed records will be adopted because the NHS is in a unique position to create joined-up health records for all citizens, reducing the advantages of patient managed systems seen in more disaggregated healthcare systems such as in the US.

The business case for personal electronic records in the UK has not been well established, and it remains to be seen which optional services patients and local care providers will be prepared to pay for. However, evidence that the UK is faring worse than comparable Western countries in meeting patients’ wishes for easy access to their records suggests an unmet demand.16

Technical considerations
Incompatibility between different systems and databases remains a barrier to integrated records, although this will diminish with the adoption of consistent technology and data standards. Further work is required to ensure effective management of interactivity between patient and provider records and the balance between live and historical data. Methods of effectively managing interfaces between independent systems and HealthSpace will also need to be established.

People and organisational factors
To realise their potential, electronic personal health records must be integrated within care processes. This will require efforts to develop policies, conventions, and incentives for using such records as well as changes in attitudes and expectations regarding appropriate modes of transaction and the rebalancing of information and status differentials in the doctor-patient relationship.

Although no adverse effects have yet been reported in UK pilots, some patients may be distressed by what they read in their electronic health record.21 Healthcare professionals will need to be sensitive in their use of clinical terms and delay entering threatening diagnoses or test results until after speaking to the patient. Public education on the value of internet hygiene and password secrecy will also encourage more secure and appropriate use of online records.

Professionals and patients should be involved in the design, development, implementation, and evaluation to generate a sense of ownership and ensure that systems meet users’ needs and are easy to operate. More immediately, measures to increase awareness of the potential value of personal health records to patients and the NHS are needed if these systems are to be adopted in the UK.

Future priorities
Current views on the value and risks of electronic records are highly polarised in the UK.22 23 Studies comparing responses to alternative models of personal health records in diverse consumer groups may help to shed light on acceptable boundaries and trade-offs and hence suggest ways of tailoring such systems to patients’ needs. Ethnographic studies of usage by patients with different clinical and access needs would also be of value. Evidence of the impact of electronic personal health records on clinical, safety, economic, and psychosocial outcomes is urgently required. Although research conducted in other countries is useful, implementation of technology is highly context dependent and research within the UK is essential to inform strategic decision making. As the first fully nationalised electronic personal health records system, the implementation of NHS HealthSpace offers unique opportunities to inform the evidence base on this topic.

Contributors and sources: CP chairs the Edinburgh and Lothian eHealth Research Network. DO is president and chief executive officer of the American Medical Informatics Association. PS is a senior associate of the Judge Business School, University of Cambridge, and director of Cambridge Health Informatics Limited. All are actively involved in health informatics research, with longstanding interests in electronic personal health records. CP drafted the article, with input from DO and PS. All cowrote the Nuffield Trust report on which this article draws, which was based on a workshop organised by CP and facilitated by DO with PS as rapporteur. CP is guarantor.

Funding: The Nuffield Trust.
Competing interests: None declared.

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


16 McKinstry BH. Vulnerable people have most to lose from online access. BMJ 2007;334:599.


20 Winfield W. For patients’ sake don’t boycott e-health records. BMJ 2007;333:158.

Medical education research remains the poor relation

Research into medical education is stagnating and urgently needs the resources to become more rigorous and relevant say Mathew Todres, Anne Stephenson, and Roger Jones

The requirement that clinical practice should be based on the best available evidence has been paralleled by calls for medical education to become more evidence based. This has resulted, among other initiatives, in the establishment of the Best Evidence for Medical Education (BEME) Collaboration and the Campbell Collaboration, an off-shoot of the Cochrane Collaboration. The BEME initiative includes dissemination of best evidence to support medical education and the encouragement of a culture capable of nurturing more rigorous and better funded research.

Evidence from the United States suggests such nurturing is much needed. In 2004, Carline analysed reports of medical education research in two major North American journals (Academic Medicine and Teaching and Learning in Medicine) and found that only a minority of studies were supported by external research grants. She was critical about the quality, rigour, and generalisability of most of these studies. Her concerns were echoed last year by Chen and colleagues, who advocated moving the focus of medical education research from learners to patient oriented clinical outcomes, thus increasing the relevance and its likely attractiveness to funders. A review of 290 medical education studies published during 2002 and 2003 found that only one quarter had received external funding; the median amount of

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Accepted: 4 June 2007

Table 1 | Details of medical education research published in three journals during 2004-5

<table>
<thead>
<tr>
<th>Study design</th>
<th>No (%) of studies (n=387)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational, cross sectional</td>
<td>267 (69)</td>
</tr>
<tr>
<td>Longitudinal cohort</td>
<td>31 (8)</td>
</tr>
<tr>
<td>Before and after studies</td>
<td>31 (8)</td>
</tr>
<tr>
<td>Other</td>
<td>58 (15)</td>
</tr>
<tr>
<td>Focus of research</td>
<td></td>
</tr>
<tr>
<td>Undergraduate medical curriculum</td>
<td>240 (62)</td>
</tr>
<tr>
<td>Continuing medical education</td>
<td>85 (22)</td>
</tr>
<tr>
<td>Postgraduate medical training</td>
<td>43 (11)</td>
</tr>
<tr>
<td>Other</td>
<td>19 (5)</td>
</tr>
</tbody>
</table>
funding obtained was $15 000 (£7700; €11 500) with an interquartile range of $5000 to $66 500. Private foundations, as opposed to federal institutions, were the most common source of these research grants.

Recent medical education research
We were unable to find any recent information about the state of published medical education research in the UK and Europe. We therefore reviewed research published in 2004 and 2005 in two general medical journals, the BMJ and Lancet, and the two leading medical education journals, Medical Education and Medical Teacher. We included only primary research papers and secondary research studies (systematic reviews and meta-analyses).

During 2004 and 2005, none of the 390 research papers published in the Lancet was in the field of medical education. Only 11 of the 399 papers published in the BMJ related to medical education. We combined these with the research papers in Medical Education (207) and Medical Teacher (169) for further analysis.

Research topics, methods, and funding
Most of the research papers used observational, cross-sectional survey designs, and less than 10% reported longitudinal cohort and before and after studies (Table 1). Of the 210 (54%) studies that used questionnaires, 178 (85%) provided no details of the validation of survey instruments. Very few papers reported studies using experimental designs, with case-control studies and randomised controlled trials each accounting for less than 3% of the sample. We did not find any meta-analyses.

The research focused predominantly on the undergraduate medical curriculum, with the remaining papers dealing mostly with continuing medical education and postgraduate medical training. Table 2 shows the range of research topics. Student examinations and assessment, curriculum design, professional development, learner characteristics, and teaching methods accounted for 70% of studies. We found little research on potentially important topics such as selecting students for medical school (12 studies), patient issues in medical education (eight), and career choices for medical graduates (four). Most of the research was conducted in the UK, continental Europe, and North America.

The research was largely unfunded. Only 30% (116) of the papers stated that the study had external funding; 47 had internal funding and 224 gave no information on funding, which we assumed meant that there was none. Less than half of these studies (170) were collaborative ventures between two or more institutions. Collaborative studies were more likely to receive external funding than non-collaborative studies (53% v 47%; χ²=4.44, P<0.05), and papers published in Medical Education were more likely to be externally funded than those in Medical Teacher (39% v 20%; χ²=17.85, P<0.001). We were unable to identify any other associations between publication type, study design, and funding source.

Randomised controlled trials
We identified 10 randomised controlled trials. Most were published in Medical Education and most concerned undergraduate medical education. These studies largely reported comparisons between different methods of teaching and used a range of assessments and end points. Many of them fell short of the criteria developed by the International Committee of Medical Journal Editors for reporting randomised controlled trials. Several did not include a clear a priori hypothesis, accurately specified end points, or a sample size calculation. Type II statistical errors were common, and CONSORT diagrams indicating the flow of subjects in the control and experimental groups were generally absent.

Problems for research
This review suggests that research into medical education has not moved on, in terms of funding and methods, over the past five to ten years despite repeated initiatives to inject greater methodological rigour and to find better ways of funding studies.

Whether the absence of medical education research from the Lancet and the small number of studies published in the BMJ are causes for concern is debatable. It might be argued that the research should appear in specialist medical education

Table 2: Topics for reported studies in medical education, 2004-5

<table>
<thead>
<tr>
<th>Research topics</th>
<th>No (% of studies) (n=387)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment or examinations</td>
<td>64 (17)</td>
</tr>
<tr>
<td>Curriculum design</td>
<td>62 (16)</td>
</tr>
<tr>
<td>Professional development</td>
<td>56 (14)</td>
</tr>
<tr>
<td>Learner or student characteristics</td>
<td>52 (13)</td>
</tr>
<tr>
<td>Teaching methods</td>
<td>46 (12)</td>
</tr>
<tr>
<td>Technology in medical education</td>
<td>23 (6)</td>
</tr>
<tr>
<td>Teacher development</td>
<td>22 (6)</td>
</tr>
<tr>
<td>Other</td>
<td>62 (16)</td>
</tr>
</tbody>
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research journals and be read by medical educationists, but research on topics such as examinations, student selection, predictors of academic success, and professional trajectories in medicine is of wider relevance and deserves larger audiences. The publications in *Medical Education* and *Medical Teacher* reflect slow progress in terms of developing methods and attracting funding, with observational designs and unfunded studies still being the rule.

The research landscape in medical education is reminiscent of primary care and health services research 20 years ago, when we lacked a cadre of trained researchers, used primitive research methods, and struggled for funding. The fortunes of applied medical researchers began to improve when funders began to understand the importance of a firm evidence base for clinical care and the delivery of services. It is unclear whether the funders of medical education (the Department for Education and Skills, through the Higher Education Funding Councils) or its providers (the universities and medical schools) are convinced of the importance of a carefully built evidence base to ensure best practice. Even when medical education research is funded, the source of funding is often a charity or foundation rather than a publicly supported funding council. Although several large UK medical research charities provide funding for educational training fellowships, only the Arthritis Research Campaign supports fellowships in medical education research.

The situation is made more difficult by the lack of appreciation of research into medical education in our medical schools. One of the effects of the research assessment exercise (used to allocate research grants in the UK) has been to prioritise the laboratory based sciences over behavioural and applied sciences and research over education, with commensurate shifts in staffing, funding, and academic kudos. This has further disabled medical educators, who are now working harder than ever to keep up, often in the context of high student numbers and increasing bureaucratic complexity. One positive development, however, is that the 2008 assessment exercise will include medical education research.

The medical education research community needs to mobilise support for its mission to provide the best education for medical students. This means thinking of imaginative ways to create a critical mass of educational researchers so that cross-centre, inter-institutional, and multidisciplinary studies can be conducted. Such studies are more likely to produce generalisable results than current research. When these studies can be directly linked to meaningful outcomes, such as the quality of care provided by qualified doctors, they will become more attractive to funders. Critical topics in medical education, such as criteria for selecting medical students, predictors of success and failure at medical school, the development of a mature professional outlook and of personal and interpersonal skills appropriate to various branches of medicine, are all amenable to high quality research.

**SUMMARY POINTS**

- Medical education research lacks methodological rigour and support from funding councils
- Most studies focus on the undergraduate medical curriculum
- Important topics such as patient issues in medical education, selection of students, and career choices are under-researched
- Multicentre studies using good experimental designs are needed

Undergraduate and postgraduate curriculum reforms over the past 20 years have resulted in major changes in the way that our students and postgraduates are taught, often on the basis of nothing more than pragmatism, fashion, and whim. Not all of these have been good for medical education or for the doctors that it produces—unwieldy student numbers, poorly developed web-based learning introduced as a substitute for direct personal contact, and an obsession with vertical and horizontal integration that led to the destruction of valuable free-standing courses in subjects such as pathology and therapeutics. We must ensure future changes will be beneficial.

**Contributors and sources:** MT has been a research associate in medical education since July 2006. Before that he worked as a project manager and research assistant on an action research project in social enterprise development. AS has been a medical educationalist for 25 years with a particular interest in factors which predict success and failure in undergraduate medical education. RJ has helped to develop undergraduate medical curriculums and assessment methods for over 20 years, and has a particular interest in factors which predict success and failure in undergraduate medical education. RJ and AS had the original idea for the systematic review. MJ conducted the review. RJ evaluated the randomised controlled trials. RJ and AS supervised the review process, and all of us contributed to writing the paper. RJ is the guarantor.

**Competing interests:** None declared.

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

Use of intensive case management to reduce time in hospital in people with severe mental illness: systematic review and meta-regression

Tom Burns, professor of social psychiatry, Jocelyn Catty, research fellow, Michael Dash, research assistant, Chris Roberts, statistician, Austin Lockwood, research nurse, Max Marshall, professor of community psychiatry

ABSTRACT

Objectives To explain why clinical trials of intensive case management for people with severe mental illness show such inconsistent effects on the use of hospital care.

Design Systematic review with meta-regression techniques applied to data from randomised controlled trials.

Data Sources Cochrane central register of controlled trials, CINAHL, Embase, Medline, and PsychINFO databases from inception to January 2007. Additional anonymised data on patients were obtained for multicentre trials.

Review methods Included trials examined intensive case management compared with standard care or low intensity case management for people with severe mental illness living in the community. We used a fidelity scale to rate adherence to the model of assertive community treatment. Multicentre trials were disaggregated into individual centres with fidelity data specific for each centre. A multivariate meta-regression used mean days per month in hospital as the dependent variable.

Results We identified 1335 abstracts with a total of 5961 participants. Of these, 49 were eligible and 29 provided appropriate data. Trials with high hospital use at baseline (before the trial) or in the control group were more likely to find that intensive case management reduced the use of hospital care (coefﬁcient −0.23, 95% conﬁdence interval −0.36 to −0.09, for hospital use at baseline; −0.44, −0.57 to −0.31, for hospital use in control groups). Case management teams organised according to the model of assertive community treatment were more likely to reduce the use of hospital care (coefﬁcient −0.31, −0.59 to −0.03), but this finding was less robust in sensitivity analyses and was not found for staffing levels recommended for assertive community treatment.

Conclusions Intensive case management works best when participants tend to use a lot of hospital care and less well when they do not. When hospital use is high, intensive case management can reduce it, but it is less successful when hospital use is already low. The benefits of intensive case management might be marginal in settings that have already achieved low rates of bed use, and team organisation is more important than the details of staffing. It might not be necessary to apply the full model of assertive community treatment to achieve reductions in inpatient care.

INTRODUCTION

Modern mental health services try to ensure that people with severe mental illness spend the minimum amount of time in hospital because unnecessary hospital care is wasteful, stigmatising, and disliked by patients. To achieve this goal, mental health services increasingly use intensive case management to care for severely mentally ill people at high risk of readmission. Such programmes have been set up across the United States healthcare system and widely adopted in Canada, Australia, and Europe. In the United Kingdom, the national service framework has authorised the setting up of 170 high fidelity assertive outreach teams.

Assertive outreach was previously referred to in the UK as intensive case management, a somewhat broader term emphasising small caseloads. It is the term used for the UK application of the North American service assertive community treatment, a carefully speciﬁed approach to case management, which includes daily team meetings, case sharing, 24 hour availability, and multidisciplinary working with doctors as full team members.

Under intensive case management, each person with severe mental illness at high risk of readmission is allocated a nurse, social worker, or other clinician (a “case manager”) who carries a small caseload of between 10 and 20 patients. This case manager takes primary responsibility for keeping contact with the patient, assessing their needs, and ensuring that these needs are met. Intensive case management is one of the most thoroughly evaluated non-pharmaceutical interventions in psychiatry, but numerous trials over the past 35 years have failed to show that it consistently reduces the use of hospital care. While some trials have shown a large reduction, others have found no effect, and some have shown a significant increase.

This inconsistent effect on hospital care might be explained by differences in the contexts in which the...
We aimed to test all these hypotheses by applying meta-regression techniques to data from randomised controlled trials of intensive case management.

**METHODS**

**Data sources**

We identified randomised controlled trials available for review by January 2007 that had compared intensive case management (caseload up to and including 20) with standard care (from a community mental health team or outpatient clinic) or low intensity case management (caseload greater than 20) in people with severe mental disorder living in the community. We defined severe mental disorder as schizophrenia or schizophrenia-like disorder, bipolar disorder, or depression with psychotic features. The search strategy (see www.psychiatry.ox.ac.uk/socpsych/bmjmrtable) was updated from that of two previous reviews.12 13 We searched CINAHL (January 1982-January 2007), the Cochrane central register of controlled trials (issue 4, 2006), Embase (January 1980-January 2007), Medline (January 1966-January 2007), and PsycINFO (January 1872-January 2007) and examined the reference lists of all relevant studies and reviews.

**Study selection**

We excluded trials in which the experimental intervention was an acute crisis team or if the control condition was hospital admission, remaining in hospital, or an alternative form of intensive case management. We also excluded those in which most participants were aged under 18 or over 65 or had a primary diagnosis of organic brain disorder or learning disability. Two authors (MM and AL or JC and MD) screened each abstract and sought potentially relevant articles. They independently reviewed articles and constructed a table of included studies. Any disagreements were resolved by discussion with a third reviewer (JC or TB, respectively). We categorised each included trial for allocation concealment according to the Cochrane Collaboration Handbook14 and included only trials rated A or B.

**Data extraction**

The dependent variable in the meta-regression was time in hospital, defined as mean number of days per month in hospital. Data on the dependent variable were eligible only if provided on an intention to treat basis and available for more than half the trial participants. Two independent reviewers (MM and AL or JC and MD) extracted data from trial reports and cross checked data by double entry. If possible, we calculated the...
dependent variable on the basis of a 24 month follow-up period as this offered the best trade off between length of follow-up and attrition of participants. When a trial did not report 24 month data, we calculated the dependent variable from the nearest available follow-up point. When a trial reported a mean but no SD, we imputed the missing parameter using a regression analysis of SD against mean, based on data from trials that provided SDs.

We also noted the degree of low intensity case management in the control group (all, some, or none), the country where trial took place (US or non-US); mean days per month in hospital for participants in the two years before the study began (baseline hospital use); the year the study began; trial size; and a rating of fidelity of the intervention to assertive community treatment on the “team membership” and “team structure and organisation” subscales of the index of fidelity to assertive community treatment (IFACT). This index was derived from a survey of 20 clinical experts in assertive community treatment and validated in a survey of 18 programmes. The team membership subscale comprises four items: ratio of patients to staff, total size of the team, and the extent of psychiatric and nursing input to the team. The structure and organisation subscale comprises seven items: whether the team is the primary source of care for its patients, is situated away from the hospital, sees daily, shares responsibility for caseloads, is available 24 hours a day, has a team leader who is also a case manager, and offers unlimited time for its services. We chose the index because the subscales are brief and can be completed from published data. For each item on the index, a score of 1 indicates high fidelity to the model. Fidelity data were obtained from published and unpublished trial reports; direct contact with trialists (who either completed the scale from memory or supplied fidelity data collected contemporaneously); and data previously obtained directly from trialists by a previous review. Two raters (MM and AL) independently combined these data into a single fidelity score. Discrepancies were resolved by discussion and, if necessary, by contacting trialists. Items for which no data were available were assigned a null value because we assumed that trialists would report their efforts to achieve fidelity to the assertive community treatment model.

Multicentre trials of intensive case management often struggle to implement a uniform approach, with centres operating at different degrees of fidelity to assertive community treatment. We exploited this to increase the power of the meta-regression by disaggregating multicentre studies into component centres with outcome and fidelity data for each. Trialists provided data either in summary form or as anonymous data on individual patients with the permission of their institutional review boards. We verified independently calculated centre data against original trial reports.

### Data synthesis

The box shows the relation between the covariates and the hypotheses tested. We also included trial size as a covariate to check for publication bias. We used Stata to carry out a random effects meta-analysis with random effects for variation between centres and between studies using a three level random effects model with a numerical constraint on the level 1 variation. This was fitted with generalised linear latent and mixed models (GLLAMM), a Stata algorithm with Gaussian quadrature based maximum likelihood estimation.

Initially, we excluded baseline hospital use as a covariate as this was not available for all centres. Subsequently, we repeated the meta-analysis including only centres for which we had baseline data on hospital use. To reduce the possibility of type 2 errors, this second analysis included only covariates that were found to have a significant association with mean number of days in hospital in the first analysis.

We then carried out two sensitivity analyses on the full dataset to verify our findings. Firstly, we included the mean of the control group as a covariate instead of...
the baseline measure of hospital use. This had the advantage of being available for all centres but was potentially flawed because of mathematical coupling and regression to the mean. Therefore we carried out a second sensitivity analysis by modelling the means of the treatment group rather than the intervention effect. In this model, the relation between the intervention effect and the underlying effect can be assessed by including a random intercept, which assesses the underlying mean for that study or centre, and a random coefficient for intervention whose variance is equivalent to the variance between studies in a conventional meta-analysis of intervention effects. For the covariance between these random effects we can estimate a regression coefficient for the relation between intervention effect and the control group mean.

Finally, we performed two further sensitivity analyses: the first excluded trials with imputed SDs; and the second excluded trials where the Cochrane randomisation category was B.

RESULTS

Figure 1 summarises the selection of studies for inclusion. The initial search detected 1335 abstracts from which 42 eligible trials, involving 5961 participants, were identified. Twenty nine of these trials provided data on mean days per month in hospital (see www.psychiatry.ox.ac.uk/socpsych/bmjrmtable); 42 centres provided data on use of inpatient care before the trial. The 10 centres that did not report it included two services exclusively treating patients with their first psychotic breakdown.

A preliminary meta-analysis showed a small but significant effect in favour of intensive case management but with significant heterogeneity between centres (pooled intervention effect −0.46, 95% confidence interval −0.84 to −0.08, P=0.019; variation between centres 0.32, variation between trials 0.32).

Meta-regression on days in hospital

Table 1 shows the meta-regression of mean difference in days per month in hospital (unstandardised) against all covariates except baseline days in hospital (as this covariate was not available for all centres). It shows that the more a case management team is organised like an assertive outreach team, the better it is at reducing time spent in hospital. The regression coefficient for team organisation indicates a decrease of 0.59 days per month in hospital per unit increase in fidelity index (mean total fidelity score 6.6, 95% confidence interval 7.16 to 6.02; maximum score 11, see www.psychiatry.ox.ac.uk/socpsych/bmjrmtable); 42 centres provided data on use of inpatient care before the trial. The 10 centres that did not report it included two services exclusively treating patients with their first psychotic breakdown.

Table 2: Summary of meta-regression analysis of days in hospital per month (42 centres) based on treatment effect estimates: centres with baseline data on hospital use

<table>
<thead>
<tr>
<th>Fidelity score</th>
<th>Coefficient* (days/month)</th>
<th>SE</th>
<th>95% CI for coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisation</td>
<td>−0.31</td>
<td>0.14</td>
<td>−0.59 to −0.03</td>
<td>0.029</td>
</tr>
<tr>
<td>Hospital use at baseline</td>
<td>−0.23</td>
<td>0.07</td>
<td>−0.36 to −0.09</td>
<td>0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>1.81</td>
<td>0.63</td>
<td>0.57 to 3.05</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*Variation between centres was 0.53. No variation between trials.
of 0.44 (95% confidence interval 0.72 to 0.17) days in hospital per month for each one point increase on the index organisation scale. The scatter plot of organisation subscore versus mean days in hospital (fig 2) shows that the effect of intensive case management on hospital use is negligible if the team organisation fidelity score is low. No other covariates were significant, including the index team membership subscale (fig 3), and there was no evidence of variation within trials between centres. There was, however, continuing evidence of variation between trials, suggesting that differences on the organisation subscore did not entirely explain the heterogeneity between trials.

Table 2 shows the effect of including the covariate of mean days per month in hospital for participants before the trial (available for 42 of the 52 centres). In this model, baseline levels of hospital use and index team organisation subscore were both significant, although the strength of the association between index score and hospital use was reduced compared with that observed in the previous model. There was negligible variation between trials.

In the first sensitivity analysis, we replaced baseline levels of hospital use with mean in the control group as a covariate (see www.psychiatry.ox.ac.uk/socpsych/bmjmrtable). This analysis showed a strong effect of control group mean (−0.44; 95% confidence interval −0.57 to −0.31, P<0.001), with no other covariates being significant. As this analysis is potentially problematic, we performed a second sensitivity analysis, which modelled means of treatment group rather than the treatment effect with a random intercept and a random coefficient for treatment at the centre and trial level (see www.psychiatry.ox.ac.uk/socpsych/bmjmrtable).

When this model was fitted, there was evidence of a strong correlation between the treatment effect and the underlying level of hospital use. The treatment effect was estimated to decrease by 0.31 bed days for each mean bed day difference between centres, in the analysis within studies. The treatment effect decreased by 0.11 bed days for each difference of one bed day between studies. Index organisation score affected the intervention (−0.47, −0.78 to −0.17, P=0.002). No other covariates had significant interactions with intervention group.

When we dropped centres with an imputed SD from the analysis, index organisation score and baseline level of hospital use were no longer significant. This was because a reduction in the number of data points increased the influence of an outlying centre visible in figures 4 and 5. When we omitted this centre from the analysis the effects remained (see www.psychiatry.ox.ac.uk/socpsych/bmjmrtable).

**DISCUSSION**

For severely mentally ill patients, intensive case management works best in trials where participants tend to use a lot of hospital care and less well in trials where they do not. When hospital use is high, intensive case management tends to succeed in reducing it, but it is less successful when hospital use is already low. This is the main reason why the findings of trials on case management are inconsistent. We also found that fidelity to the structure and organisation aspect of the assertive community treatment model explained some of the variation in hospital use between trials. In sensitivity analyses, however, this finding was less robust than explanations based on participants’ use of hospital care. Fidelity to the staffing practices of the assertive community treatment model did not, however, explain variation between trials. It is precisely these extra staffing features that have been authorised in the NHS plan for assertive outreach teams. Some of the control groups in trials of assertive outreach teams with high fidelity might have shared some of their
WHAT IS ALREADY KNOWN ON THIS TOPIC

Intensive case management is designed to reduce unnecessary admissions to hospital in severely mentally ill people

Randomised controlled trials of intensive case management have conflicting findings: some have shown reductions in hospital care, while others have found no effect

WHAT THIS STUDY ADDS

Intensive case management works best in trials where participants tend to use a lot of inpatient care

The effectiveness of intensive case management teams is increased as their organisation reflects the assertive community treatment model, but there is less evidence for the benefits of increased staffing levels

organisational features, which may account for the limited effect on the use of inpatient care in some studies.20,21

Strengths and weaknesses

We made maximum use of the available data, not only by identifying all eligible randomised trials but also by obtaining previously unpublished fidelity data directly from trialists and substantial amounts of data on individual patients to facilitate the disaggregation of multicentre trials into their component centres. However, our fidelity data were only 95% complete. Nine of 14 trials with missing fidelity items had lower hospital use in the intervention arm, so if all these items had received a positive rating, this could have strengthened the relationship between fidelity to the model and reduction of days in hospital. We also found it necessary to use imputed SDs for the data provided by 16 of the 52 centres, and a sensitivity analysis without these centres reduced the strength of some of the observed associations.

Notwithstanding these reservations, our study applies an empirical test to the key hypotheses that have been advanced to explain why intensive case management is so inconsistent in reducing hospital care. We have shown that hypotheses based on where and when the trial was conducted can be discounted. We have also shown that fidelity to the assertive community treatment model, insofar as it is important, relates only to aspects of the model concerned with team organisation (in essence, the extent to which case managers work as a team rather than as independent practitioners). Specific staffing features of the assertive community treatment model (such as team size, low caseloads, and professional make up of the team) are not important in reducing hospital use among the team’s patients.

Implications of findings

Why is it that the level of hospital use among a trial’s participants is so important in determining the effectiveness of intensive case management? We think that low levels of hospital use are a proxy for good community services. Where community services are good, hospital care is used sparingly and only when absolutely necessary. Under such circumstances even intensive case management teams find it difficult to have an impact on hospital use. When community services are poor, it is usually fairly easy for patients to spend long periods of time in hospital, and intensive case management teams find it relatively easy to reduce such wastefulness. There are, however, other explanations. Firstly, low levels of hospital use might indicate that a trial’s participants are less severely ill and hence less likely to benefit from intensive case management. Secondly, low levels of hospital use may indicate that it is difficult to obtain admission within the setting in which the trial is being conducted, leaving little scope for the intensive case management team to achieve further reductions.

The main clinical implication of our study is that the introduction of intensive case management teams will not lead to substantial reductions in hospital use in settings where average hospital use is already low. Teams can optimise their ability to reduce hospital use by organising themselves in the manner recommended for assertive community treatment, and by focusing on patients with a history of high hospital use. Replicating staffing requirements of assertive community treatment does not confer measurable benefits. Our study confirms a growing recognition that we should research the practices of teams rather than their labels.22-29

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Contributors: TB is guarantor. TB and MM conceived the review. JC, MD, MM, and AL retrieved the papers and contacted authors. MM and AL prepared the tables and figures. MM, AL, and CR extracted the data, calculated estimates of effects, and dealt with the statistics. All authors read and commented on the paper.

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Competing interests: None declared.

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Probiotics for treatment of acute diarrhoea in children: randomised clinical trial of five different preparations

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ABSTRACT

Objective To compare the efficacy of five probiotic preparations recommended to parents in the treatment of acute diarrhoea in children.

Design Randomised controlled clinical trial in collaboration with family paediatricians over 12 months.

Setting Primary care.

Participants Children aged 3-36 months visiting a family paediatrician for acute diarrhoea.

Intervention Children's parents were randomly assigned to receive written instructions to purchase a specific probiotic product: oral rehydration solution (control group); Lactobacillus rhamnosus strain GG; Saccharomyces boulardii; Bacillus clausii; mix of L delbrueckii var bulgaricus, Streptococcus thermophilus, L acidophilus, and Bifidobacterium bifidum; or Enterococcus faecium SF68.

Main outcome measures Primary outcomes were duration of diarrhoea and daily number and consistency of stools. Secondary outcomes were duration of vomiting and fever and rate of admission to hospital. Safety and tolerance were also recorded.

Results 571 children were allocated to intervention. Median duration of diarrhoea was significantly shorter (P<0.001) in children who received L rhamnosus strain GG (78.5 hours) and the mix of four bacterial strains (70.0 hours) than in children who received oral rehydration solution alone (115.0 hours). One day after the first probiotic administration, the daily number of stools was significantly lower (P<0.001) in children who received L rhamnosus strain GG and in those who received the probiotic mix than in the other groups. The remaining preparations did not affect primary outcomes. Secondary outcomes were similar in all groups.

Conclusions Not all commercially available probiotic preparations are effective in children with acute diarrhoea. Paediatricians should choose bacterial preparations based on effectiveness data.

Trial registration number Current Controlled Trials ISRCTN56067537.

INTRODUCTION

The management of acute diarrhoea consists of the replacement of lost fluid with glucose-electrolyte oral rehydration solution. This solution, however, reduces neither the severity nor the duration of diarrhoea. The search for such agents started over 20 years ago. Probiotics, defined as micro-organisms that exert beneficial effects on human health when they colonise the bowel, have been proposed as adjunctive therapy in the treatment of acute diarrhoea. Several micro-organisms are effective in reducing the severity and duration of acute diarrhoea in children: Lactobacillus rhamnosus (formerly “Lactobacillus casei strain GG” or “Lactobacillus GG”), L plantarum, several strains of bifidobacteria, Enterococcus faecium SF68, the yeast Saccharomyces boulardii, and preparations containing a mix of strains. Several trials with probiotic preparations have been conducted in different settings and with different end points. Meta-analyses of probiotic efficacy, including a Cochrane review, are also available.

Few of these studies, however, meet the criteria of properly controlled trials.

In a recent study of Italian children with diarrhoea, probiotics were the most commonly prescribed treatment. With the increasing availability and widespread use of probiotics, it is important to identify the most effective preparations. We evaluated the efficacy of five probiotic preparations for the treatment of acute diarrhoea in children.

METHODS

The study was a prospective single blind randomised controlled trial in which parents of children with acute diarrhoea received written instructions to purchase a specific brand of probiotic. The trial was performed in collaboration with family paediatricians, who in the Italian public health system care for children up to 12 years of age. We discussed the study design with six family paediatricians in three meetings. Diarrhoea was defined as three or more outputs of loose or liquid stools a day. Eligible children were those aged 3-36 months who were seen in paediatricians’ offices from October 1999 to
September 2000 because of diarrhoea. We included in the study all children with diarrhoea lasting less than 48 hours for whom parents gave informed consent. Exclusion criteria were malnutrition as judged by the ratio of weight to height, clinical signs of severe dehydration, clinical signs of coexisting acute systemic illnesses (meningitis, sepsis, pneumonia), immunodeficiency, underlying severe chronic diseases, cystic fibrosis, food allergy or other chronic gastrointestinal diseases, use of probiotics in the previous three weeks, use of antibiotics or any antidiarrhoeal medication in the previous three weeks and during the study, and poor compliance (defined by administration of less than four doses of the study medication).

All children were given oral rehydration solution for three to six hours and then fed with full strength formula containing lactose or cows’ milk, depending on age. Microbiological investigation was performed only if required for specific clinical reasons. Children were also randomised to oral rehydration alone; Lactobacillus GG; S boulardii; Bacillus clausii; Ld delbrueckii var bulgaricus, Streptococcus thermophilus, L acidophilus, and Bifidobacterium bifidum; or E faecium strain SF68. Table 1 shows the main characteristics of the probiotic preparations.

Patients were allocated to each group according to a computer generated randomisation list. Random allocation was made in blocks of six to obtain groups of similar size. The sequence was concealed until treatments were assigned. The researchers responsible for enrolling the patients allocated the next available number on entry into the trial, and the parent of each child received written instructions to purchase the assigned probiotic product.

Probiotic preparations were prescribed for five days and administered orally in 20 ml water according to the manufacturers’ instructions. All the probiotic products used in this study were available only in pharmacies and had a similar brand image and price. Each pack of probiotic preparation was sufficient for the entire therapeutic course. The group of children who received only oral rehydration served as controls.

The primary outcome measures were the total duration of diarrhoea and the number of stools a day. Table 1 shows the main characteristics of the probiotic preparations.

## Table 1 | Micro-organism load (according to product label when the study was performed), administration, and main characteristics of preparations analysed

<table>
<thead>
<tr>
<th>Groups</th>
<th>Micro-organisms</th>
<th>Strains</th>
<th>Dose (twice daily)</th>
<th>Brand*</th>
<th>Price (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Lactobacillus casei</td>
<td>Rhamnosus GG</td>
<td>6×10⁹ CFU/dose</td>
<td>Dicoflor 60</td>
<td>10.50</td>
</tr>
<tr>
<td>3</td>
<td>Saccharomyces boulardii</td>
<td>S boulardii</td>
<td>S, O/C84, N/R84, T8A, SIN84</td>
<td>5×10⁹ live micro-organisms/dose</td>
<td>Codeox</td>
</tr>
<tr>
<td>4</td>
<td>Bacillus clausii</td>
<td>O/C84, N/R84, T8A, SIN84</td>
<td>10⁹ CFU/dose</td>
<td>Enterogermina†</td>
<td>6.50</td>
</tr>
<tr>
<td>5</td>
<td>L delbrueckii var bulgaricus, L acidophilus, Streptococcus thermophilus, B bifidum</td>
<td>LMG-P17550, LMG-P 17549, LMG-P 17503, LMG-P 17500</td>
<td>10⁷ CFU, 10⁷ CFU, 10⁷ CFU, 5×10⁸ CFU/dose</td>
<td>Lactogermina†</td>
<td>10.50</td>
</tr>
<tr>
<td>6</td>
<td>Enterococcus faecium</td>
<td>SF 68</td>
<td>7.5×10⁷ CFU/dose</td>
<td>Bioflorin†</td>
<td>10.50</td>
</tr>
</tbody>
</table>

CFU = colony forming units.
*All sold in coloured cardboard boxes.
†Composition, brand name, and costs of these probiotic preparations have changed since study ended.
day and their consistency. Duration of diarrhoea was the time in hours from the first to the last abnormal (loose or liquid) stools preceding a normal stool output. Stool consistency was evaluated through a score system, as previously described,\(^1^5\) and faeces were graded as 1 (normal), 2 (loose), 3 (semiliquid), and 4 (liquid). Secondary outcome measures were the incidence and median duration of vomiting, fever (>37.5°C), and the number of hospital admissions in each group. We also investigated safety and tolerability.

On enrolment we identified each child, determined the duration and severity of diarrhoea, assessed associated clinical features (fever, vomiting, dehydration), and established nutritional status and previous treatment. Parents received a coded reporting form on which to record clinical data. They were instructed to record daily the number of faecal outputs and their consistency, the type and doses of probiotic preparation taken by the child, the presence of vomiting and fever, any necessity for hospital admission, and all adverse events.

The study was performed according to a multicentre single blind and controlled design. Because of the problems of performing a double blind study of commercially available products in a large population, we used the third party blind observer method to assess efficacy. To ensure unbiased assessment, the family paediatricians, who were in charge of treatment allocation, gave written instructions to the parents to purchase a brand of probiotic and verified compliance on the reporting form, whereas the investigators collecting the reporting forms were blinded to the assigned treatment. All reporting forms were delivered to the coordinating centre at the Department of Paediatrics for analysis. This procedure was applied in previous studies of the efficacy of anti-diarrhoeal treatments.\(^1^5\)\(^1^6\) All parents of enrolled children gave informed consent.

**ESTIMATE OF SAMPLE SIZE**

To obtain the required power (95%, type I error = 0.05, two tailed test) we needed 45 participants in each group. This estimate assumes a mean difference in duration of diarrhoea of 24 hours between the treated and control children (corresponding to means of 120 and 96 hours) with an SD of 30 hours within the group. This computation was based on the results of a preliminary open trial.\(^1^5\) To investigate the secondary outcomes, we doubled the number of patients. Our estimation of sample size allowed for a drop out of up to 10%.

**STATISTICAL ANALYSIS**

A statistician blind to allocation performed the statistical analyses. We used \(\chi^2\) test for categorical variables and Mann-Whitney U test for continuous variables by analysing differences between group 1 and groups 2-6. All analyses were conducted on an intention to treat basis with SPSS version 15.0.0 for Windows (SPSS, Chicago, IL).

### Table 2 | Baseline features of children with diarrhoea allocated to study treatments

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>No (% of boys)</th>
<th>Median (IQR) age (months)</th>
<th>Median (IQR) weight (kg)</th>
<th>Median (IQR) duration of diarrhoea before treatment (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (92)</td>
<td>41 (44)</td>
<td>17 (11-28)</td>
<td>11.9 (9.9-12.7)</td>
<td>9 (4-13)</td>
</tr>
<tr>
<td>2 (100)</td>
<td>60 (60)</td>
<td>20 (13-25)</td>
<td>12.1 (9.1-13.2)</td>
<td>10 (5-18)</td>
</tr>
<tr>
<td>3 (91)</td>
<td>44 (48)</td>
<td>18 (10-27)</td>
<td>11.5 (9.2-14.0)</td>
<td>11 (6-18)</td>
</tr>
<tr>
<td>4 (100)</td>
<td>49 (49)</td>
<td>19 (10-24)</td>
<td>12.3 (9.4-13.4)</td>
<td>10 (4-15)</td>
</tr>
<tr>
<td>5 (97)</td>
<td>49 (50)</td>
<td>16 (10-28)</td>
<td>12.7 (9.5-14.2)</td>
<td>9 (5-17)</td>
</tr>
<tr>
<td>6 (91)</td>
<td>39 (42)</td>
<td>15 (8-22)</td>
<td>12.2 (10.3-13.5)</td>
<td>10 (5-16)</td>
</tr>
</tbody>
</table>

IQR=interquartile range.

### Table 3 | Primary outcome index: duration of diarrhoea (hours) in study groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Median (IQR) duration (hours)</th>
<th>Estimated difference (95% CI)*</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oral rehydration solution alone</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td><em>Lactobacillus casei subsp rhamnosus GG</em></td>
<td>115.5 (95.2-127)</td>
<td>−32 (−41 to −23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td><em>Saccharomyces boulardii</em></td>
<td>105.0 (90-104.5)</td>
<td>−5 (−13 to 5)</td>
<td>0.38</td>
</tr>
<tr>
<td>4</td>
<td><em>Bacillus clausii</em></td>
<td>118.0 (95.2-128.7)</td>
<td>1 (−7 to 8)</td>
<td>0.76</td>
</tr>
<tr>
<td>5</td>
<td><em>L debriuecii var bulgaricus, L acidophilus, Streptococcus thermophilus, B bifidum</em></td>
<td>70.0 (69-101)</td>
<td>−37 (−47 to −25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6</td>
<td><em>Enterococcus faecium SF 68</em></td>
<td>115.0 (89-144)</td>
<td>2 (−5 to 11)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

IQR=interquartile range.

*Compared with oral rehydration solution alone.
†Mann-Whitney U test. P value for comparison with oral rehydration solution alone.
RESULTS
The figure shows the flow of children through the study. A total of 600 children with acute diarrhoea were eligible for inclusion: 29 were excluded and 571 were randomised to receive intervention and contributed data to the intention to treat analysis.

The baseline features of the patients enrolled in the six groups were similar (table 2). The total duration of diarrhoea was significantly lower in children receiving Lactobacillus GG (group 2) and in those receiving the bacterial mix (group 5) than in patients receiving oral rehydration alone (group 1) (table 3). The three other probiotic preparations had no effect on diarrhoea, and the duration of diarrhoea in groups 3, 4, and 6 was similar to that in the group receiving only oral rehydration (table 3). Daily stool output was significantly lower (P<0.001) in groups 2 and 5 (table 4), starting the day after the first probiotic administration. Median stool outputs per day did not differ between groups 2 and 5 (table 4). Stool consistency, as judged by the scoring system, differed significantly (P<0.001) with preparations 2 and 5 versus the other groups (table 5). The median daily scores did not differ between groups 2 and 5 (table 5). Microbiological investigations were requested in only a few instances, and the results did not provide useful information.

None of the secondary outcome measures we evaluated was significantly modified in children receiving probiotic preparations or in the control group (table 6). All parents purchased the product indicated by the paediatrician. The probiotic preparations included in the study were well received by nearly all the children, and no adverse events were observed.

DISCUSSION
Main study findings
In an evaluation of five probiotic preparations in children with diarrhoea we found substantial differences in efficacy. Two preparations reduced the duration and severity of diarrhoea, whereas the three others had no significant effect. A recent Cochrane meta-analysis of 23 randomised controlled trials found mild therapeutic benefit from probiotics that was generally reproducible regardless of organism.10 In the only comparative trial reported previously, three preparations were tested in 46 children.17

Acute infectious diarrhoea is still a major cause of childhood morbidity. It is also a source of anxiety to families of affected children and represents a heavy economic burden for families and for society as a whole.18 19 Drugs that affect intestinal motility, ion transport and absorptive moieties, and living bacteria have been used in the attempt to reduce the duration of diarrhoea.16 20 Probiotics have progressively gained in credibility for the treatment of diarrhoeal diseases.21 22

In most countries, however, micro-organisms purported to have probiotic properties are considered to be food additives rather than drugs. Consequently, only safety features and not proof of efficacy are required for marketing.23 In addition, the term

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### Table 4: Primary outcome index: median (IQR) daily stool outputs from the first day of probiotic administration

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oral rehydration solution alone</td>
<td>1</td>
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<td>2</td>
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<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td><em>Lactobacillus casei subsp rhamnosus GG</em></td>
<td>1</td>
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<tr>
<td></td>
<td></td>
<td>2</td>
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<td>6</td>
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<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>Saccharomyces boulardii</td>
<td>1</td>
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<td>2</td>
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<tr>
<td></td>
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<td>7</td>
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<tr>
<td>4</td>
<td>Bacillus clausii</td>
<td>1</td>
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<td>2</td>
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<tr>
<td>5</td>
<td><em>L delbrueckii var bulgaricus, L acidophilus, S thermophilus, B bifidum</em></td>
<td>1</td>
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<td></td>
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<td>2</td>
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</table>

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### Table 5: Primary outcome index: median (IQR) daily stool consistency score from first day of probiotic administration

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oral rehydration solution alone</td>
<td>1</td>
</tr>
<tr>
<td></td>
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<td>2</td>
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<td>6</td>
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<tr>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td><em>Lactobacillus casei subsp rhamnosus GG</em></td>
<td>1</td>
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<tr>
<td>3</td>
<td>Saccharomyces boulardii</td>
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<td>4</td>
<td>Bacillus clausii</td>
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<tr>
<td>5</td>
<td><em>L delbrueckii var bulgaricus, L acidophilus, S thermophilus, B bifidum</em></td>
<td>1</td>
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<td>6</td>
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<td>7</td>
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</tbody>
</table>

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*Stool consistency score system: 1=normal; 2=loose; 3=semiliquid; 4=liquid.15

†P<0.001 or ‡P<0.001 v oral rehydration solution alone at same time point by Mann-Whitney U test.

*On days 2 and 5 estimated difference (95% CI) compared with oral rehydration solution alone = −1 (<1 to 0).
“probiotic” is often improperly used and information about specific probiotic properties of the strains contained in the products is not exhaustive.24 We did not conduct a qualitative and quantitative study of the microbial content of the probiotic preparations in this trial because we wanted to carry out a field trial of the clinical effectiveness of commercially available probiotic products that had been prescribed by the paediatrician.

*Lactobacillus* GG was associated with a shorter duration of diarrhoea, which was not unexpected because proof of efficacy of this strain has been obtained in children in hospitals and outpatients in both industrialised and developing countries.25-27 The results that we obtained with *Lactobacillus* GG closely resembled those obtained in a similar setting with the same strain.15 The other effective preparation was a mix of four strains. A formula with *St thermophilus* and *B bifidum*, two of the four bacterial species in the effective preparation, protected against diarrhoea in chronically sick children aged below 24 months.2 The three other preparations we evaluated had no or little clinical effect. This was unexpected in the case of *S boulardii* because a previous controlled trial showed it to be beneficial in children admitted to hospital for diarrhoea20—that is, with a more severe condition than the mild to moderate diarrhoea in the children in our trial—which could explain the different results obtained in the two studies. A previous trial with *Streptococcus faecium* strain SF68 resulted in clinical improvement in children with diarrhoea associated with respiratory infection and treated with parenteral antibiotics,28 though it had no effect in adults with diarrhoea.29 Finally, the *B clausii* preparation had no effect. None of the preparations had a significant effect on secondary outcomes, probably because of the relatively low incidence of fever, vomiting, and hospital admissions in our children. No side effects were recorded.

Diarrhoea in developed countries is usually self-limiting, and active treatment is not generally recommended. Over the counter drugs or preparations, however, are widely used. We did not consider the cause of the diarrhoea. Probiotics are generally prescribed without a specific indication. All the children enrolled in our study were outpatients, and microbiological investigations were performed only in a few.

### Table 6 | Secondary outcomes in children with diarrhoea according to treatment group

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (%) admitted to hospital</td>
<td>4 (4.3)</td>
<td>1 (1.0)</td>
<td>4 (4.4)</td>
<td>4 (4.0)</td>
<td>2 (2.1)</td>
<td>4 (4.4)</td>
<td>0.68*</td>
</tr>
<tr>
<td>Fever:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (%) of children</td>
<td>32 (34.8)</td>
<td>30 (30.0)</td>
<td>27 (29.7)</td>
<td>29 (29.0)</td>
<td>30 (30.9)</td>
<td>36 (39.6)</td>
<td>0.61*</td>
</tr>
<tr>
<td>Median (IQR) duration (days)</td>
<td>2 (1-2)</td>
<td>1 (1-2)</td>
<td>2 (1-2)</td>
<td>1 (1-3)</td>
<td>1 (1-3)</td>
<td>2 (1-3)</td>
<td>0.10†</td>
</tr>
<tr>
<td>Vomiting:</td>
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</tr>
<tr>
<td>No (%) of children</td>
<td>34 (37.0)</td>
<td>31 (31.0)</td>
<td>24 (26.4)</td>
<td>32 (32.0)</td>
<td>34 (35.1)</td>
<td>36 (39.6)</td>
<td>0.47*</td>
</tr>
<tr>
<td>Median (IQR) duration (days)</td>
<td>2 (1-2)</td>
<td>1 (1-2)</td>
<td>2 (1.0)</td>
<td>1.5 (1-2)</td>
<td>1 (1-2)</td>
<td>1.5 (1-2)</td>
<td>0.25†</td>
</tr>
</tbody>
</table>

IQR=interquartile range.
*P<0.05 test.
†Mann-Whitney U test.

Based on the findings of a large study conducted in Italy,31 it is reasonable to assume that most of the children were affected by viral acute gastroenteritis.

### Possible confounding

We cannot exclude the possibility that expectations of parents confounded our results. The brands investigated were among the most widely used probiotic preparations in Italy when the study was conducted. These products were not advertised in the press or on television, there were no remarkable differences in their brand image, and they were available only in pharmacies at the time of the study. Preconceptions within the general public about their efficacy are therefore unlikely. Similarly, in Italy it is unlikely that the public would perceive one micro-organism to be more effective than another. The lack of preconceptions about the efficacy of treatment seems to be supported by our finding that only one of the two most widely used probiotic brands in Italy was effective (group 2) whereas the other was not (group 4). A high or low cost might have affected expectations either positively or negatively, but parents were probably unaware of the comparative costs of the products investigated. From these observations, it seems unlikely that parents advised to purchase one product would have higher or lower expectations than parents assigned to purchase another product, though we cannot exclude this.

In conclusion, the efficacy of probiotic preparations for the treatment of childhood acute diarrhoea is related to the individual strains of bacteria. We believe that probiotic preparations should be classified as drugs, and physicians should select preparations for which evidence of efficacy, in a given clinical condition, is supported by solid data.

#### WHAT IS ALREADY KNOWN ON THIS TOPIC

Several probiotic products are marketed in many European countries for the treatment of acute diarrhoea in children.

#### WHAT THIS STUDY ADDS

The efficacy of probiotic preparations for the treatment of children with acute diarrhoea is related to the strain of bacteria.
We are grateful to Jean Ann Gilder for editing the text. The research was not sponsored by any pharmaceutical or food company, including yoghurt companies.

Contributors: RB and AG designed the study, coordinated the research team, and wrote the first draft of the report. PC, FA, LC, MIS, ADeV, and AP cared for the patients and contributed to the final version of the report. GDeM and GT performed the data analyses and FM contributed to the design of the study, developed the computer generated randomisation list, and performed statistical analyses. AG is guarantor.

Competing interests: None declared.

Funding: None.

Ethical approval: Ethics committee of University of Naples Federico II. Provenance and peer review: Non-commissioned, externally peer reviewed.

1 Alam NH, Ashraf H. Treatment of infectious diarrhea in children. 


Accepted: 18 June 2007
Carpal tunnel syndrome

Jeremy D P Bland

Why should I read this article?
Carpal tunnel syndrome (CTS) is the commonest peripheral nerve problem in the United Kingdom and has considerable employment and healthcare costs. If recognised early it is readily treatable. No established UK guidelines exist for diagnosis and management, but the American Academy of Neurology issued guidelines in 1993, which remain current as no major recent advances have occurred.

What causes carpal tunnel syndrome?
Carpal tunnel syndrome results from compromise of median nerve function at the wrist caused by increased pressure in the carpal tunnel, an anatomical compartment bounded by the bones of the carpus and the transverse carpal ligament. Although the ends of the tunnel are in free communication with the surrounding tissues, tissue pressure in the tunnel is much higher in patients with CTS (32-110 mm Hg, depending on wrist position) than in patients with normal wrists (2-31 mm Hg). Pressures are raised by wrist flexion and extension, and finger flexion.

Interruption or sustained high tissue pressure in the tunnel impairs microvascular circulation in the median nerve and leads to spurious generation of action potentials, local demyelination, and ultimately axonal loss. It may also stimulate the proliferation of subsynovial connective tissue in the tunnel, according to pathological studies of CTS. Anything that reduces the dimensions of the tunnel or increases the volume of its contents will predispose to CTS, and many medical associations have been reported, but most cases are idiopathic.

A study of 4488 individuals recruited from the St Thomas’ UK adult twin registry found genetic predisposition to be the single strongest factor in predicting the development of the syndrome. Obesity is a risk factor in younger patients. The role of occupational and recreational hand use in causation remains controversial. If overuse of the hands does contribute, it may be a relatively minor factor, though most patients report that heavy use of the hands aggravates the symptoms. A Scandinavian survey found population prevalences of 14.4% for median nerve distribution paraesthesias, 3.8% for CTS diagnosed on clinical grounds, 4.9% for neurophysiological focal impairment of the median nerve at the wrist, and 2.7% for neurophysiologically confirmed clinical CTS.

Incidence peaks in the late 50s, particularly in women, and the late 70s, when the sex ratio is more equal. It is also common, transiently, in late pregnancy. Elderly people tend to present with more severe CTS for the same length of history, with 59% of patients aged over 65 having thenar atrophy at presentation compared with 18% of younger patients. CTS in older patients is easily confused with other, less treatable, disorders.

When should I suspect CTS?
Although the syndrome encompasses a range of severity (from transient subjective sensory symptoms to irreversible thenar wasting and sensory loss) it should be recognised before permanent deficits develop. Patients woken by paraesthesias or pain—the distribution of which includes median nerve territory (the thumb and first two and a half fingers)—have CTS until proved otherwise. Some patients will also complain of sensory disturbance in the whole hand or pain radiating up the arm to the shoulder. Patients whose paraesthesias are limited to the ulnar side of the hand are unlikely to have CTS. About 55%-65% of cases are bilateral at first presentation and most patients present first with the dominant hand.

Daytime symptoms may be noticed with particular activities, particularly those that involve holding the arms raised. Patients may complain of a perception of swelling of the hand or fingers, but visible swelling is rare and should prompt consideration of other conditions with secondary CTS. Sensory loss in median nerve territory and weakness and wasting of the median innervated thenar muscles are reliable but late indicators of CTS.

The American Academy of Neurology’s guidelines state that the likelihood of a diagnosis increases with the number of standard symptoms and provocative factors present [box 1]. The most widely used provocative physical tests are Phalen’s sign (the provocation of median paraesthesias by flexion of the wrist to 90° for 60 seconds) and Tinel’s sign (the provocation of paraesthesias by tapping over the carpal tunnel). These

Sources and selection criteria
Evidence for the efficacy of treatment comes mainly from reviews conducted by the Cochrane Collaboration. I also searched Medline, used a personal reference archive, and analysed the computerised records of over 20 000 patients with suspected carpal tunnel syndrome in east Kent.
Box 1 | Standard symptoms of carpal tunnel syndrome*

- Dull, aching discomfort in the hand, forearm, or upper arm
- Paraesthesia in the hand
- Weakness or clumsiness of the hand
- Dry skin, swelling, or colour changes in the hand
- Occurrence of any of the above in the median distribution
- Provocation of symptoms by sleep
- Provocation of symptoms by sustained hand or arm positions
- Provocation of symptoms by repetitive actions of the hand or wrist
- Mitigation of symptoms by changing hand posture or shaking the wrist

*According to the American Academy of Neurology's guidelines

Box 2 | Conditions that may be confused with carpal tunnel syndrome

- Cervical radiculopathy (especially C6/7)—look for local neck pain on movement and neurological signs outside the territory of the distal median nerve
- Unlar neuropathy—this can also produce nocturnal paraesthesias; the distribution will usually be to the medial side of the hand.
- Raynaud's phenomenon—this should be recognisable from a history of symptoms related to cold exposure
- Vibration white finger—suspect this if the patient uses vibrating hand tools at work
- Osteoarthritis of the metacarpophalangeal joint of the thumb—this can produce a spurious appearance of thenar wasting but not true weakness or sensory deficit
- Tendonitis—specific tests may help in diagnosis, such as Finkelstein's test for De Quervain's tenosynovitis
- Generalised peripheral neuropathies—these should be recognised from the wider distribution of symptoms and reflex changes
- Motor neurone disease—this can present with wasting in one hand but does not produce sensory symptoms
- Syringomyelia—features such as prominent loss of temperature sensation in the hands should give a clue
- Multiple sclerosis—this should be recognised from the presence of neurological abnormalities disseminated in location and time

Signs have been compared with nerve conduction studies as a diagnostic gold standard in many studies. In such studies, Phalen's sign has sensitivity ranging from 10% to 73% and specificity from 55% to 86%. Tinel's sign has sensitivity ranging from 8% to 100% and specificity from 55% to 87%, the wide ranges probably reflecting the difficulty in standardising the test methods. Both signs are less reliable in advanced CTS.10

On general examination of the patient, be alert for signs of endocrine disease and connective tissue disorders, which can predispose to CTS, and other hand problems such as Raynaud's phenomenon, vibration white finger, trigger finger, and Dupuytren's contracture, which can all coexist with CTS. Many conditions have been mistaken for CTS; box 2 lists some important differential diagnoses.

What laboratory investigations are needed?

Plain x ray examination of the hand is not cost effective in idiopathic CTS—an American study concluded that costs were $5869 (£2850; €4250) to $20 115 for each finding of therapeutic significance.11 A check for diabetes, however, is inexpensive and appropriate. Most patients with CTS will be in an age group where undetected hyperglycaemia is common. The value of blood tests to screen for connective tissue disease and thyroid function is uncertain, particularly in the absence of any clinical indication other than CTS.12

Complex investigations are not necessary before starting conservative treatment in clinically obvious cases. However, in cases of diagnostic doubt, and before surgery, nerve conduction studies should be carried out. The American Academy of Neurology's guidelines suggest electrodiagnostic studies and therapeutic trials with non-invasive treatment as the strategies of choice when clinical diagnosis is uncertain. Nerve conduction studies should include sufficient measurements to localise median nerve dysfunction to the carpal tunnel, evaluate its severity, and exclude more widespread neuropathy.13 Neurophysiological severity of CTS can be expressed on the 7 point Canterbury scale (0=no abnormality, 6=no recordable median motor or sensory potentials), which I have shown correlates with surgical prognosis.14

However, nerve conduction studies have a small false negative rate; a precise figure is not available for this because no better test exists for comparison as a gold standard. However, with modern nerve conduction studies, it is probably around 5-10%. In east Kent, 4.3% of 3544 successful carpal tunnel decompressions had normal preoperative nerve conduction studies (unpublished personal data).

Conversely not all patients with a neurophysiologically demonstrated median neuropathy at the wrist necessarily have symptoms related to that. An alternative, or ideally complementary, approach is provided by high resolution ultrasonography of the median nerve. In a blind comparison with nerve conduction studies as a gold standard, ultrasonography achieved 89% sensitivity and 69% specificity.15 However, this study retrospectively optimised the ultrasound measurement cut-off values to achieve the best possible diagnostic performance and is limited in any case by the lack of an absolute diagnostic standard for comparison.

Magnetic resonance imaging can make similar measurements of median nerve dimensions but is more expensive. Ultrasonography is more comfortable than nerve conduction studies for patients but will not detect other nerve problems that may be contributing to the presentation. Ultrasonography may show unsuspected structural abnormalities of relevance, such as bifid median nerves, persistent median arteries, or space occupying lesions in the tunnel, but these are rare and even more rarely do they dictate alternative management.

How is CTS treated?

Many treatments, both conventional and complementary, have been suggested for CTS (box 3). Few are supported by good quality evidence from randomised controlled trials. The available studies have been well summarised in a series of reviews by the Cochrane Collaboration.16-19
The recommendations of the American Academy of Neurology for treatment remain reasonable. The academy suggests splinting, activity modification, and non-steroidal anti-inflammatory drugs—and possibly diuretics if there is limb swelling—as conservative treatment, followed by steroid injection and surgery if these fail or in patients with progressive motor deficit. However, activity modification, diuretics, and non-steroidal anti-inflammatory drugs have no positive support from any randomised trials. Meta-analysis of several randomised trials shows that vitamin B-6 supplementation has a negligible therapeutic effect.19

The purpose of treatment is to alleviate the symptoms and, in some people, prevent worsening of the condition. A few, mostly elderly, patients have thenar wasting but no symptoms. Little is to be gained from surgery in such cases. CTS is not necessarily progressive. The condition in some patients may fluctuate slightly for many years—with more symptoms during periods of heavy hand use or variation with the seasons—without progressing to irreversible median nerve damage. The condition may even remit spontaneously. In one study 23% of participants improved over 12-15 months without active intervention though this was not a randomised trial and the researchers were not able to rigorously control factors such as activity modification instituted by the patients.20

The potential benefits of treatment must be viewed against this background. Only three treatments are supported by a substantial body of experimental evidence: splinting, steroids, and surgery.

### Suggested treatments

**Box 3 | Suggested treatments**

**Treatments supported by high quality evidence**

- **Splinting**
- **Steroids**—oral, local injection, local iontophoresis
- **Surgical decompression**—open (several variations, with or without tenosynovectomy, transverse carpal ligament reconstruction, and external/internal neurolysis; all seem equally effective with no clear evidence to support the use of the more elaborate procedures); endoscopic (one or two portal)

**Other treatments**

- **Diuretics**
- **Non-steroidal anti-inflammatory drugs**
- **Rest or activity modification**
- **Nerve and tendon gliding exercises**
- **Vitamin B-6**
- **Synovectomy only**
- **Chiropractic manipulation of the wrist**

* Recommended by the American Academy of Neurology (diuretics, only possibly)

- **Yoga**
- **Ultrasoundography**
- **Acupuncture**
- **Serratiopeptidase**
- **Magnet therapy**
- **Cognitive behaviour therapy**
- **Lidoderm patches**

Satisfactory symptom relief from this measure alone, and splints have the advantage of being inexpensive (£3.50 each) and without serious adverse effects.

### Steroids

Carpal tunnel syndrome has been shown to respond to both systemic steroids and to local steroids given at (or near) the wrist by either injection or iontophoresis (transdermal delivery driven by an electric field). The side effects of oral steroids preclude their routine use for CTS, but local steroid injection has no discernible systemic effects and a very low incidence of local complications. Although median nerve damage from intraneural injection has been reported in eight cases, pooling the reported trials of steroid injection yields a total of over 3000 injections performed without serious complications, and the risk may be estimated at <0.1% in competent hands.

The initial response rate to a single steroid injection is about 70%, but relapse is common. No adequate long term studies exist to allow precise quantification of the relapse rate beyond the first few months. The most pessimistic estimates suggest that 92% may have relapsed by two years.22 At the other extreme is a series in which half of injected patients remain in remission at seven years. No evidence is available to guide policy on treatment after relapse following a successful first injection, though it is common practice to inject a second or sometimes third time, and there are anecdotal reports of patients maintained long term on repeated injections.

### Surgery

Carpal tunnel decompression, usually performed as a day case under local anaesthesia, is considered the definitive treatment. However, although it provides permanent and complete cure in most cases, it is not without risk. A survey of over 4000 patients having surgery under usual NHS circumstances found that about two years after surgery, only 75% considered the operation an unqualified success and 8% thought that they were worse off.23 Although papers in the literature devoted to “recurrent CTS” are numerous, true recurrence, after successful initial surgery, is rare. It may be more common after endoscopic surgery.24 Most reports in fact relate to primary failure of the operation to relieve symptoms. Such failures are mostly attributable to misdiagnosis (the symptoms actually being due to other causes, whether or not...
CLINICAL REVIEW

SUMMARY POINTS

Carpal tunnel syndrome is the commonest cause of nocturnal hand paraesthesias and should be suspected in any patient with this symptom, whatever age. Initial treatment should be with neutral angle splinting at night; milder cases may be treated with local steroid injection before further investigation. Refer more severe cases—those with thenar weakness, sensory deficit, and daytime symptoms—for nerve conduction studies and possible surgery. Either open or endoscopic surgery may be used depending on availability of local expertise.

neurological signs or delayed motor conduction on nerve conduction systems should be offered the option of surgical decompression. All should be advised of the potential risks of the different treatments.

Contributors: JDPB is the sole contributor.

Competing interests: None declared. Provenance and peer review: Commissioned and externally peer reviewed.

5 Bland JDP. The relationship of obesity, age, and carpal tunnel syndrome: more complex than was thought? Muscle and Nerve 2005;32:527-32.

ADDITIONAL EDUCATIONAL RESOURCES

For health professionals

For patients
Carpal Tunnel Syndrome Fact Sheet from the US National Institute of Neurological Disorders and Stroke (www.ninds.nih.gov/disorders/carpal_tunnel/detail_carpal_tunnel.htm)
RATIONAL IMAGING

Investigation of suspected breast cancer

Peter Britton, Ruchi Sinnatamby

The patient
An 81 year old woman was referred to a multidisciplinary breast clinic with a lump in her right breast. Such patients undergo “triple” assessment—clinical examination, imaging, and, if necessary, needle biopsy. On clinical examination she had a mass in the upper outer quadrant, which was suspected to be an underlying carcinoma.

What tests do I order?
It is usual practice for patients over 35 years with discrete breast lumps to undergo mammography and ultrasound. In patients under 35 years, ultrasound is the first line investigation.

Mammography
Mammography has been evaluated more extensively than any other imaging technique and remains a mainstay of the diagnosis of breast cancer. Reported sensitivity in detecting palpable breast cancer is 80-90%, but it is lower in patients with dense breast parenchyma. A normal mammogram can be seen in the presence of a palpable breast cancer, so national guidance recommends that all breast units should provide triple assessment clinics for symptomatic women rather than an open access imaging service for general practitioners.

LEARNING POINTS

- Modern diagnosis of breast cancer is based upon multidisciplinary team work using triple assessment of clinical examination, imaging (mammography and ultrasound), and needle biopsy
- Breast magnetic resonance imaging can aid local breast cancer staging but its exact role remains to be established
- Axillary staging using ultrasound and needle biopsy may detect patients with lymph node involvement preoperatively and thus reduce unnecessary sentinel lymph node biopsies

Ultrasound
Targeted breast ultrasound is the most useful test when evaluating a breast lump. It can distinguish between “lumpiness” caused by a ridge of normal dense parenchyma, a fluid filled cyst, or a solid mass. In expert hands, it can also help characterise solid lesions—its negative predictive value for correctly classifying benign masses is up to 99.5% and sensitivity for identifying malignancy is up to 98.4%.

Breast needle biopsy
The above tests cannot replace histological confirmation, however, and in the United Kingdom, patients with a clinically suspicious or focal solid lesion routinely have a needle biopsy to establish a diagnosis. Core biopsy, with its higher sensitivity and specificity (96.7% and 98.7%), is replacing fine needle aspiration cytology (sensitivity 83.1%; inadequate rate 12.8%). Ultrasound guidance optimises targeting accuracy.

What other tests could I do?
If a diagnosis of breast cancer is made, definitive treatment (usually surgery) can be planned. In some patients, histopathological analysis of surgical specimens shows that disease is more extensive than first suggested by clinical examination and imaging. Further treatment may then be needed, such as margin re-excision, mastectomy, or additional axillary surgery. Can modern breast radiology provide more accurate information about local staging preoperatively? Two additional imaging and intervention techniques show potential.

Breast magnetic resonance imaging
Dynamic contrast enhanced breast magnetic resonance imaging is the most sensitive examination available...
for determining the extent of invasive breast cancer—it detects additional unsuspected tumour sites in 16% of patients. The information it provides on tumour size and extent can help determine whether breast conservation or mastectomy is the best surgical option. The technique is expensive however. In addition, UK machines are overloaded with work, and we do not know which patients with newly diagnosed breast cancer would benefit most from magnetic resonance imaging. A large UK multicentre trial is currently trying to answer this question.

Axillary ultrasound and biopsy
Sentinel lymph node biopsy, with its high accuracy and low morbidity, is now the surgical method of choice for staging the axilla in patients with invasive breast cancer. The sentinel lymph node is identified at surgery after injecting radiotopoe colloid and blue dye into the breast. Patients with malignancy in the sentinel lymph node will need a second operation to clear their remaining axillary nodes. Ultrasound and needle biopsy of the axilla before surgery can identify 42–63% of patients with involved lymph nodes, who may then have therapeutic surgery of both breast and axilla as a single procedure.

What happened to the patient?
Mammography detected an area of parenchymal deformity corresponding to the palpable lump. A further, impalpable, suspicious mass was also seen in the left breast (fig 1). Ultrasound confirmed that both lesions were solid, with features suggestive of malignancy. Bilateral core biopsies guided by ultrasound confirmed an invasive lobular carcinoma in the right breast and an invasive ductal carcinoma in the left breast. Our policy is to perform magnetic resonance imaging in patients with invasive lobular carcinoma, which may have a permissive growth pattern, as it is difficult to determine the extent of disease with standard imaging techniques. Magnetic resonance imaging confirmed the size and position of both known tumours but also showed extra foci in each breast (fig 2). Bilateral axillary ultrasound and core biopsy found no evidence of malignancy.

On the basis of these investigations the patient had bilateral mastectomies and sentinel lymph node biopsies at a single operation. Histology confirmed multifocal invasive lobular carcinoma in the right breast and invasive ductal carcinoma in the left breast, together with bilateral high grade ductal cancer in situ. One of the two sentinel lymph nodes on the right contained a 0.2 mm diameter micrometastasis; the remainder were free of tumour. After discussion with the patient it was decided that no further axillary surgery was necessary.

Contributors: PB received the commission for the article and selected the patient. The literature was searched by PB and RS. PB wrote the initial draft of the paper RS reviewed and edited it and both authors revised it. PB is guarantor.

Funding: None.

Competing interests: None declared.


Endpiece
The medical profession’s misfortune
It is the peculiar misfortune of the medical profession that its members can rarely dare to confess their ignorance, thinking it more or less necessary—in order to maintain their influence with their patients and with the world—to speak with equal decision, whether they are authorized by their knowledge to do so or not… The real fact is that the prestige of a reputation once attained, whether through the influence of charlatanism, good fortune, or superior merit, is not easily destroyed, and the very eccentricities and extravagances which repel patients of sense and delicacy, tend to confirm the prepossessions of those who are wanting in these qualities, and who are naturally apt to wonder at or admire what they do not understand.

George Peacock. Life of Thomas Young, M.D., FRS. London: John Murray, 1855.

Submitted by Jan Coebergh, assistant neurologist, The Hague, Netherlands

USEFUL READING
Life under liberty

PERSONAL VIEW Robbie Foy

A week after moving into our sunny, seaside, and safe apartment in west Los Angeles, we were stirred at midnight by shouts outside and then three sharp cracks. Sirens and helicopter searchlights followed. After a restless night, I got up early to check for any internet accounts of what might have happened. I wondered how to put a positive spin to my partner about the first story I’d found: “It was just a drive-by shooting; no one will specifically be after us . . . yet.” Fortunately, it turned out that Santa Monica’s finest had shot dead an armed man fleeing past the front of our apartment.

It is in no small way thanks to the rhetoric of individual freedom that there were 16,907 firearm related suicides and 11,920 firearm related homicides in the United States in 2003

The dust eventually settled around this event, just as it seems to have mostly settled around another event last April. I was listening to the car radio when news broke that 32 people had been gunned down at Virginia Tech University shortly before their assailant turned the weapon on himself. News commentaries emerging over the day suggested the revitalisation of a vigorous debate on gun control. Yet within days, three further features of the story had distracted most of the media and politicians from such a debate. Firstly, the 23-year-old killer was South Korean and, as if by magic, an unseen hand subtly shifted attention on to the reaction of the Korean community. Secondly, he had a record of mental illness, further differentiating him from the majority. Thirdly, slack enforcement of regulations had allowed Cho Seung-hui to purchase his gun while falsely declaring that he had no record of being treated for mental illness. The ensuing “how could this happen?” deliberations also focused more on security protocols within the college campus than on why firearms are so widely accessible.

A discussion on National Public Radio the weekend after the killings typified this mass distraction. When asked why this event had occurred, two professors of psychiatry spent over 10 minutes discussing psychological profiling and its poor predictability. This is consistent with the national obsession with medical and technical solutions for social problems. Eventually, one of the eminent men almost apologetically mentioned gun control, allowing the other to declare that he still believed in the “right to bear arms.”

Another reaction reminded me of a comedian I’d once seen at the Edinburgh Fringe. Craig Ferguson (aka Bing Hitler) had suggested that guns should be freely available on all passenger plane flights. Then if a hijacker tried to divert the plane to Tripoli, all of the passengers could pull out their guns and declare: “No way—we’re going to Torremolinos!” Discussions I heard on a right wing talk station, promulgated elsewhere, were disdainful of “ridiculous” bans on taking guns into public buildings. A mother of someone who had committed a previous massacre had suggested that Virginia Tech could have been avoided if it were easier for everyone to carry guns.

It is in no small way thanks to the rhetoric of individual freedom, along with continual prodding from the likes of the National Rifle Association, that there were 16,907 firearm related suicides and 11,920 firearm related homicides in the United States in 2003 (www.cdc.gov/ncipc/osp/charts.htm). Yet this country is packed with paradoxes. For example, the state of California was in the vanguard of restrictions on smoking in public places. I have now been reprimanded twice by the local police for walking across empty roads on a red light.

Such contradictions will not be new to seasoned US observers abroad. Less reported are the knock-on effects of the national obsession with gun liberty. We have had a certain amount of fun instructing our two kids on dealing with dangers less commonly encountered in the UK, like the contrasting procedures to follow if confronted by a rattlesnake, mountain lion, or bear. Recently, they experienced the novelty of a “lock down” drill at their elementary school. They practised taking cover under their desks. Both kids know this is the right thing to do for earthquakes. They were less aware that this might, in theory, increase their odds of surviving an attack with an automatic rifle.

Given that public opinion on gun control has shifted little since Virginia Tech, it is not surprising that few, if any, of the candidates lining up for presidential nominations will feel able to take an assertive stance on gun control. How many more Virginia Techs will it take?

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The author is a returning Harkness fellow in healthcare policy funded by the Commonwealth Fund and Health Foundation. The views expressed here are his own.
Trouble down under

Greetings from Australia’s Northern Territory, where I have been learning the meaning of the word “remote.” Yesterday we drove for three hours before meeting another vehicle. Every 200 km or so we encountered a road sign or a shrivelled lake with a solitary pelican. Otherwise there is just bush—and the red, red earth.

The trip began with a lecture tour. At an interdisciplinary meeting on management of chronic disease in rural and remote communities, one questioner had his hand in the air before I had finished speaking. What, he asked, was my view on the problem of child abuse among the Aborigines?

Apparently a number of incidents have persuaded the authorities that child sexual abuse is “widespread” in some remote Aboriginal communities. The current prime minister, said to be the most right wing premier in living memory, recently decreed that all Aboriginal children below the age of 15 in these areas should be medically examined for the telltale signs of abuse. The issue has also, apparently, been used to justify increased police presence and, in some cases, withdrawal of land rights for the Aborigines.

Depending on whom you ask, all this is either a swift and decisive move to save a generation of innocents from unthinkable trauma or, in a community where teenage marriage has been the norm for centuries, Australia’s worst ever example of culturally incompetent health policy, setting back relations with the indigenous community by 20 years.

In Australia’s coastal cities, where 85% of the white population live, it is not hard to spot Aborigines who are drunk, destitute, and sometimes psychotic. When they get under your feet it’s easy to imagine them behaving shamefully towards their children—and hard to remember that they represent a tiny fraction of the indigenous population. With an election looming much political mileage is to be gained from policies that can demonstrate “containment” of such problems.

I guess it would be too much to invite a serving prime minister to take a briefing on the limited predictive value of so called telltale signs of sexual abuse. But is it unreasonable to ask him to divert from his usual campaign trail and visit the communities that he has accused of moral disintegration? They just might have a story of their own to tell.

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Skippy’s last show

I am laid back about emergencies; the little boy has cried “WOLF!” once too often for me. Fax a photo of the wolf chewing on his scrotum, I say, and I might think about it. But the chains of our solemn office bind tightly; when we are called, we gotta go, no matter how bizarre the circumstances.

One day a little kangaroo hopped into the surgery, making urgent chittering noises. I love wild creatures, so I reached for my gun; stuffed and mounted, I thought, it would make a nice trophy for the waiting room, maybe scare the kids a bit, keep them out in the fresh air and away from the health centre and all those superbugs.

“Wait, doc!” my patient shouted, just before I squeezed the trigger, “He’s trying to tell us something . . . something about a little girl, bottom of a cliff, broken leg, may need a splint, analgesia, and a drip.”

“Thanks a million, Dr Doolittle,” I said.

When we got there the mandatory crowd had gathered, and there was already a festive mood; a few tinnies had been cracked open and the scent of barbecued ribs graced the air. A little blonde-haired girl, unmistakably and adorably Aryan, lay at the bottom of the traditional cliff. I noted, with a fatal satisfaction, that the cliff looked to consummate the melodrama. Someone had inexplicably obtained a park ranger’s uniform, and he called me over, unsuccessfully trying to conceal his enormous enjoyment.

“Her leg’s real crook, doc,” he said, “you better get down there.”

I was in my good clothes, it was muddy; where were all those paramedics in combats when you need them, I thought. Eventually I got down, signing a few autographs and reluctantly dismissing a groupie on my way.

“It’s a sprain,” I shouted up, and a ripple of fascinated horror went through the crowd; “A sprain, a sprain,” they wailed, like a sweaty and inebriated Greek chorus.

“The copter’s on its way, doc,” said the park ranger, “but we’ll have to MacGyver a stretcher from didgeridoos and wombat hides.”

“Actually, a sprain’s not too bad,” I said, professional integrity outweighing the need to consummate the melodrama, “Up you get, girlie.” A little pinch emphasised my authority and she got to her feet reluctantly; the crowd began to drift away, giving me disapproving looks. Diverting from the original script was obviously considered bad taste.

Skippy reappeared: “Something about a cave, a landslide, two kids, a pneumothorax, a chest drain, and…”

A single shot echoed through the eucalyptus groves, and far away a flock of parakeets rose, their wings golden in the sunset as the credits rolled for the last time.

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Where there’s a will

As everyone knows, Francis Bacon, the philosopher, was one of the founders of the empirical method in the sciences. Indeed, he was almost a martyr to it, for one day he alighted from his coach to gather snow with which to stuff a dead chicken to establish whether or not refrigeration preserved animal flesh, and in so doing caught a fatal chill.

What, I wonder, is the empirical evidence that behaving as Bacon behaved predisposes to fatal infections? Certainly as a child I behaved like it all the time, for I obstinately refused to wear a coat in winter or take any notice of the holes in my shoes when walking in the rain. Perhaps it is a question of age.

When it comes to medical matters, Bacon left a list of prescriptions and their uses, and they are not evidence based, to say the least. He was a polypharmacist who didn’t even see proof of efficacy as a problem.

Here is his method of preparing what he called “grains of youth”: “Take of nitre four grains, of ambergease three grains, of orris-powder two grains, of white poppy-seed the fourth part of a grain, of saffron half a grain, with water of orange-flowers, and a little tragacanth; make them all into small grains, four in number. To be taken at four o’clock, or going to bed.

Some of his prescriptions were rather unpleasant and messy. As a “preservative ointment” he suggests “deets seet one ounce, of myrrh six grains, of saffron five grain, of hay-salt twelve grains, of Canary wine, of two years old, a spoonful and a half.” Then comes the nasty bit: “Spread it on the inside of your shirt, and let it dry, and then put it on.”

There is also Methusalem water, “against all asperity and torrefaction of inward parts, and all adustion of the blood, and generally against the dryness of age.” For what he calls “openers,” presumably of the bowels, he recommends no fewer than 69 substances, among them solution of millipedes and man’s urine. As for “astringents,” which “by cherishing the strength of the parts, do comfort and confirm their retentive power,” he suggests a “stomacher of scarlet cloth or whelps, or young healthy boys, applied to the stomach.”

Sometimes even Bacon’s psychology goes amiss: for example, when, in his Essay on Death, he suggests that “death is disagreeable to most citizens, because they commonly die intestate,” not wishing to tempt fate with a will.

But Bacon sometimes speaks sense on medical matters. In his Ornamenta Rationalia, for example, he says “that a sick man does ill for himself who makes his physician his heir.” As it happened, I was on a visit to Eastbourne when I read this, and one of the most celebrated medical men of that town was the late Dr Bodkin Adams. Among his patients were rich old widows who made wills in his favour, and tended not to live long afterwards. They died from, or at least with, large doses of opiates.

Strictly speaking, the career of Bodkin Adams was not illustrative of the truth of Bacon’s dictum, because he was found not guilty, and rightly so: for it was not proved that he did more than he said, “easing the passing.”

Still, it would be a pretty dogmatic empiricist who demanded proof of the wisdom of Bacon’s observation. Theodore Dalrymple is a writer and retired doctor

BETWEEN THE LINES
Theodore Dalrymple

Bacon says “that a sick man does ill for himself who makes his physician his heir”
Cosmetic artistry

Colin Martin is fascinated by an exhibition of pseudomedical devices designed to help an artist overcome what he sees as “undersized Asian male complex.”

The Homo Species
An exhibition by Hyungkoo Lee, Korean pavilion, 52nd international art exhibition, Venice Biennale, until 21 November
Rating: ****

Many people feel that their self image and other people’s perception of them might be transformed if they could enhance their appearance. Their attempted metamorphosis could be as simple as wearing different clothes or as drastic as having cosmetic surgery. Korean artist Hyungkoo Lee (b 1969) tackles the subject in a series of works entitled The Objectuals, which forms part of his solo show in the Korean pavilion at the Venice Biennale.

The series explores the additional dimensions of physical differences between races and feelings of cultural inferiority. Lee created them after he experienced “undersized Asian male complex” while studying at Yale University, where he encountered “bigger and stronger” white men. The works were not the result of any locker room comparisons. “One day, Lee was standing in a subway train next to a white man of roughly similar physique,” says Soyeon Ahn, the Korean pavilion commissioner. “He realised that his hand, holding on to the handle, was significantly smaller than the Westerner’s next to his.”

Back in the studio, his artistic response was to develop a series of pseudomedical devices to enlarge or alter parts of his body visually, via a sort of perceptual cosmetic surgery, which made him feel better about his body image.

Lee created the works after he experienced “undersized Asian male complex” while studying at Yale University, where he encountered “bigger and stronger” white men

Lee’s untitled 2003 ink drawing of a nude man, which echoes Leonardo da Vinci’s often reproduced drawing of an ideal Italian Renaissance man with his outstretched limbs bounded by geometry, summarises his own points of perceptual intervention. The first work in the series, A Device (Gauntlet 1) That Makes My Hand Bigger (1999), was constructed using a water filled polyethylene terephthalate (PET) bottle of the type manufactured for laboratory use, some shot glasses, and steel wire.

HK LAB-CPR (2001-2007), a large installation with mixed media from the series, creates a tableau reminiscent of both Dr Frankenstein’s laboratory and an operating theatre. Tubing suspended from the ceiling feeds into the base of an operating table; and glass shelves on the surrounding walls are stacked with assorted laboratory vessels, surgical instruments, limbs, and heads. “By turning his inferiority complex to humour and making the postures of medical science a laughing stock, Lee questions widespread Western values,” asserts Mr Ahn.

Lee’s inherent interest in human physiognomy stimulated his development of a series of helmets that use simple enlarging and reducing lenses to distort the facial features of the people wearing them. Rather than satisfying what Mr Ahn describes as Asian “longing for the large eyes of Westerners” by merely imitating them, Lee’s optical helmets exaggerate and caricature the desired features. Although some of the helmets transform their wearers into visions of doe eyed cuddliness, Altering Facial Features with H-WR (2007) presents a more disturbing metamorphosis. The helmet distorts its wearer’s smile into a grimace which, along with his enlarged metal-capped teeth, produces a sinister, voracious effect.

Helmut WR (2007), a five minute high-definition video playing within the pavilion, follows the helmet wearing artist around Venice as he walks alone around the city at night or sits among tourists at an outdoor restaurant, drinking coffee in the sunshine. The soundtrack includes rasping breaths, similar to those made by artificial ventilators; however, neither these sounds nor the prosthetic devices worn by Lee seem to elicit much attention from surrounding people. At the Venetian winter carnival, locals and visitors are used to seeing people wearing more elaborate and eye catching disguises.

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OBITUARIES

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Edward Joseph Lister Lowbury

Expert on hospital infection and distinguished poet

In a prolific and distinguished career Edward Lowbury pioneered the study of hospital infection, was a founder and first president of the Hospital Infection Society, and was a fellow of three medical royal colleges (pathologists, physicians, and surgeons) and of the Royal Society for Literature. He was, said his colleague and successor, Graham Ayliffe, a leader in dealing with burns infection, the problems of antibiotic resistance, and skin disinfection. He was awarded the OBE for his medical work when he retired in 1979.

His career and future specialty may have been determined when his general practitioner father and musical mother—she was a member of the Hallé family—gave him the middle names of Joseph Lister. He was educated at St Paul’s School in London, University College, Oxford, and Guy’s Medical School, taking a BSc in physiology on the way and qualifying in 1939. He did his house jobs at The London Hospital, and in 1941 moved to the Emergency Public Health Laboratory Service for two years. He then spent three years as a pathologist in the Royal Army Medical Corps, mainly in Kenya, where he took an interest in folk medicine and witchdoctoring.

After three years at the Common Cold Research Unit in Salisbury, he became, in 1949, head of bacteriology at the Medical Research Council Burns Unit, situated in Birmingham Accident Hospital. He stayed there for the rest of his career. Among his major achievements was a controlled clinical trial confirming the finding of his predecessor Leonard Coleman that closed ventilated burns dressing rooms reduced airborne infection. He showed that topical antibacterials helped to prevent infection.

He was interested in the mechanism and prevention of antibiotic resistance and kept a record of its occurrence in burn and wound infections throughout his 30 years at the burns unit. He reported the emergence of a new plasmid in Pseudomonas aeruginosa that made it resistant to carbenicillin and other antibiotics.

With Harold Lilly he developed laboratory tests for measuring surgical and hygienic hand disinfection and did controlled trials on their efficacy. With Owen Lidwell and others he authored a huge MRC controlled trial of clean-air systems in preventing infection in joint replacement surgery.

He founded Birmingham’s Hospital Infection Research Laboratory and was its first honorary director. With Graham Ayliffe, its first director, his work included the epidemiology of infection in the region’s hospitals, the spread of Gram negative organisms, and testing disinfectants and sterilisers. He chaired an MRC subcommittee that published the evidence based Aseptic Methods in the Operating Suite (1968).

He worked well into his retirement, lecturing around the world and publishing 150 papers and two medical books, Drug Resistance in Antimicrobial Therapy (1974) and Control of Hospital Infection (1975, revised 1998).

Edward Lowbury had a parallel career as a poet. He fell in love with poetry when he was 10 and won the Newdigate prize for poetry as an undergraduate at Oxford. He published many volumes of poetry, and edited Apollo, the anthology of doctor-poets published for the BMA’s 150th anniversary. He always carried a notebook in which he wrote medical ideas at one end and ideas for poems at the other, which met in the middle to, he said, mutual enlightenment. At other times, records Roland John, he took a mischievous pleasure in keeping medicine and poetry separate: “Wearing a plain trilby to the lab and a pork-pie hat with a wavy brim when I went out with my artist and poet friends.”

He published the first of his 14 poetry books in 1936, while still an undergraduate. His collected poems were published in 1993, at the same time as a Festschrift to mark his 80th birthday. Birmingham celebrated its centenary in 1985 with an anthology of Lowbury’s poems, entitled Birmingham! Birmingham!

With his wife, Alison Young, he published a biography of the 16th century poet, composer, and physician Thomas Campion, and a biography of his father in law, the poet Andrew Young. Alison was a professional pianist, and together they helped found the Birmingham Chamber Music Society.

Stephen Lock, a former editor of the BMJ, said that Lowbury was a quiet, soft-spoken man. He was, said his friend Eileen Totten, “quite short and slim, and yet the most well-rounded man I knew.” He was modest about his attainments. In addition to his professional and cultural interests, he had an enduring love of steam engines and could imitate the noises they made.

He became blind from glaucoma and went into a nursing home when his wife died in 2001. He is survived by their three daughters.

Caroline Richmond

Edward Joseph Lister Lowbury, bacteriologist and poet; head of bacteriology, MRC Burns Research Unit; cofounder and first chairman, Society for Hospital Infection (b 6 December 1913; q Oxford/ Guy’s Hospital, London, 1939; OBE, MA, DM, FRCPath, FRCP, FRCS), d 10 July 2007.
MINERVA

Did you know that Babinski’s legacy was two clinical signs? The abnormal plantar reflex is the one we all know and love. The second is seen in patients with hemifacial spasm. It occurs when the orbicularis oculi muscle contracts, closing the eye, with the internal part of the frontalis muscle contracting at the same time so that the eyebrow rises when the eye closes. It’s apparently impossible to reproduce this effect voluntarily, and it’s used to distinguish between hemifacial spasm and blepharospasm (Neurology 2007;69:402-4).

Crime scene investigators look for prints from the palm, foot, ear, and lip as well as the traditional fingerprint. Invisible lip marks are possible to develop given the increasingly common use of protective and permanent lipsticks, and lysochromes such as Sudan Black are good at developing recent but invisible lip marks that contain lipstick on dead skin. Fluorescent dyes are just as useful, and they may also reveal lip marks not created by lipstick (Journal of Forensic and Legal Medicine 2007;14:340-2).

To tackle the problem of faulty research citations and their negative influence on the growth of scientific knowledge, journals should consider including a section on their websites where relevant papers that have been overlooked by authors can be cited and where it can be shown how omitted papers relate to the published one. This is one of the suggestions made in a paper entitled Verification of Citations, Fawlty Towers of Knowledge? http://mpra.ub.uni-muenchen.de/4149/03/MPRA_paper_4149.pdf. It makes depressing reading for anyone interested in the accuracy of what is reported in journals.

The species legionella lives mostly in water, so unsurprisingly more rainfall is associated with more risk of legionnaire’s disease. A sharp rise in the disease in the mid-Atlantic region in 2003 coincided with a period of record breaking rainfall (Epidemiology and Infection 2007;135:811-7). The average increase in rainfall from May to September 2003 rose to 15.7 cm from 10.4 cm, which corresponded to an increased risk of legionnaire’s disease of about 14.6%. Doctors in England might bear this in mind in the next few weeks.

A 12 year old girl of Pakistani origin, who was born and brought up in the United Kingdom, presented with a one month history of an indurated area, which measured 2.5 × 2.5 cm, over the bridge of her nose. She had visited Pakistan in the previous six months. She was treated with two courses of flucloxacillin by her general practitioner, with no clinical improvement. A skin biopsy taken at the time of presentation at hospital showed intracytoplasmic inclusion bodies, which led to a diagnosis of cutaneous leishmaniasis. She was treated with intravenous stibogluconate. Cutaneous leishmaniasis is occasionally seen in the UK and should be considered in patients who present with unusual skin lesions, particularly if they have a history of foreign travel.

Can we synthesise natural products? And if so can we make them even better? Many important drugs are natural substances that require complicated artificial development. Two independent research groups have shown that it is possible to create complex natural products by mixing the naturally found enzymes needed to make them with artificial chemicals in a laboratory (Nature Chemical Biology 2007 Aug 12). The end products have potential antibacterial and anti-tumour activity and may be important in future development of drugs.

Another paper that analyses the quality of scientific research says that even use of the randomised controlled trial—the supposed optimal design of trials—doesn’t ensure high quality research or reporting (Journal of Bone and Joint Surgery Am 2007;89:1693-9). In their review of 54 randomised trials of treatment for tennis elbow, the two reviewers found many areas of deficiency, including poor descriptions of recruitment, poor power calculations, and poor randomisation and blinding as well as inadequate follow-up. Scientists, they say, must adhere to the CONSORT (Consolidated Standards of Reporting Trials) criteria.

The pleasure we get from eating, rather than our need for food, might be explained by the appetite suppressing hormone leptin. Leptin, previously thought to increase satiety, also seems to reduce the pleasure associated with food (Science 2007 Aug 9). Two patients with congenital deficiency in leptin found that they felt full sooner and craved food less after being treated with leptin. Brain imaging indicates that leptin produces the rewarding effects of food by acting on the ventral striatum, which is part of the limbic system.

A traditional Chinese herbal concoction referred to as an “ancestral formula” containing Flos lonicerae, Herba menthae, Coretx moutan, Rhizoma atrocytalis, and Cortex phellodendri was put to the test in a randomised, double blind, placebo controlled study in children with moderate to severe atopic dermatitis (British Journal of Dermatology 2007;157:357-63). Two doses a day were efficacious in improving quality of life and reduced the need for topical steroids and were palatable.

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“Assortative mating” is the non-random mating of individuals because of phenotype and cultural factors. It’s one of the things thought to have contributed to the current epidemic of obesity—obese people have mated with other obese people. Researchers propose in the American Journal of Clinical Nutrition that assortative mating’s influence has come about because the age at which obesity develops has shifted progressively earlier, allowing single people in their teens and early 20s to more easily distinguish partners with obese and lean phenotypes (2007;86:316-23).