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Individuals face poverty in trying to meet the high costs of health care, WHO reports
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**Wilma Elizabeth Gemmell**
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**Michael Gregory Price**
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**John William ("Jack") Strain**
Greg Strain
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The magnetic resonance egg timer
Brian Witcombe
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Elephant neck
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Killing you softly
BMJ 2007;335, doi:10.1136/bmj.39272.619722.AD

Read this week's articles on
Self monitoring of blood glucose in type 2 diabetes
Clinicians should stop patients doing this if it has no benefit

Self monitoring of blood glucose costs the NHS more than £100m (€150m; $200m) each year and the cost is rising.1 For many people with insulin treated diabetes and their families, blood glucose self monitoring is an essential tool, enabling them to confirm hypoglycaemia or high glucose concentrations and to take corrective action. Yet large numbers of patients diligently record the results and then do nothing with them.

In this week’s BMJ Farmer and colleagues report the results of a primary care trial in patients with well controlled type 2 diabetes who were not taking insulin. They found no evidence of an effect of blood glucose self monitoring on glycaemic control, with and without structured education, compared with usual care.2 This study confirms that the contribution of self monitoring is not clear in type 2 diabetes, particularly for those treated with diet alone or oral agents other than sulphonylureas. Furthermore, there is wide geographical variation in the use of self testing by such patients.3

One view is that providing such technology to diabetic patients treated with tablets or diet is a waste of time and money, because there is little an individual can do with the results.4 Others believe that the information provided by blood glucose testing is a powerful motivating factor,5 encouraging self management of diabetes by allowing patients to measure directly the impact of their behaviour, such as the effect of eating on postprandial glucose or the glucose lowering effect of exercise. Some,6 7 but not all,8 observational studies have shown that, even in patients treated by diet alone, those who measure their blood glucose more often have better outcomes, including HbA1c concentration and mortality. Such positive associations may simply show, however, that those who are highly motivated (reflected in the frequency of blood testing) are likely to do well in the long term.

A limited number of prospective studies have randomised patients to blood glucose self monitoring or to no monitoring. A recent meta-analysis reported a modest mean improvement in HbA1c concentration of around 0.3%, but the confidence intervals were so wide that this difference was not significant.9 Importantly, the meta-analysis comparing blood and urine testing found no difference in HbA1c concentrations. This suggests that blood glucose self monitoring has little effect on glycaemic control in patients treated with diet or metformin. Structured education on using the information obtained from self monitoring to adjust insulin dosing, however, leads to sustained improvements in glycaemic control in type 1 diabetes,10 and this might also apply to those with type 2 diabetes.

In the diabetes glycaemic education and monitoring trial (DIGEM), Farmer and colleagues directly test the contribution of blood glucose self monitoring on glycaemic control, with and without structured education, in 450 people in primary care with diabetes treated by tablets or diet, with relatively tight glycaemic control.2 Patients were randomised to receive usual care (and were asked not to test their blood), basic information on self management and limited blood self testing, or training in self management and encouragement to undertake more intensive blood monitoring. At one year, HbA1c concentration was unchanged in the usual care group, and marginally and equally improved in the other two groups, with no significant difference among the three.

The trial was well designed and conducted but had some limitations. Patients who were already testing their blood more than twice a week were excluded (possibly removing those who found glucose monitoring valuable and leaving individuals who had already used and rejected it). Furthermore, only around 15% of those eligible entered the study, thus limiting the generalisability of the findings. In one arm of the trial the authors embedded blood glucose self monitoring within an educational intervention designed to enhance self management, yet glycaemic control did not improve. This may be because patients with relatively tight control were included, in contrast to previous studies, or because the intensive intervention was ineffective. Indeed, fewer patients randomised to the intensive arm ended up using a glucose meter than in the less intensive arm, an unexpected outcome among patients who were trained to monitor more frequently. Finally, patients seem to prefer blood glucose monitoring to urine tests,11 and different conclusions might have been reached if patients’ views had been taken into account.

The DIGEM trial has shown that in patients with established diabetes relatively well controlled by oral drugs who monitor blood glucose infrequently, little is gained in promoting blood glucose testing even in conjunction with an education programme.2 Whether self monitoring is useful in patients at diagnosis and whether it offers advantages over urine testing (which is much cheaper) remains uncertain. None the less, the results of this study should encourage clinicians to discuss the value of glucose testing with their patients and give them the confidence to discontinue it if it is providing no benefit.

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EDITORIALS

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Simon R Heller professor of clinical diabetes School of Medicine and Biosciences, University of Sheffield, Sheffield S10 2RX s.heller@sheffield.ac.uk

Competing interests: SRH is principal investigator in an ongoing randomised controlled trial comparing blood glucose to urine testing in newly diagnosed individuals with type 2 diabetes.

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Depression in adolescents

Adding cognitive behaviour therapy to SSRIs is unlikely to improve outcomes

Around 3-5% of adolescents are affected by clinical depression worldwide.\(^1\)\(^2\)\(^3\) Although specific data on depression are not available, an Australian survey found 26% of adolescents with mental disorders were treated in general or paediatric practice, while only 9% received care from specialist mental health services.\(^3\)

Episodes of depression generally last about seven to nine months. Probability of relapse is 40% within two years and 70% after five years.\(^4\) Depression can be devastating to a young person’s academic and social development and can adversely affect family relationships, especially if the problems are misunderstood.

Optimal treatment for depression in adolescents is unclear. Concern about an increased rate of suicidal behaviours with antidepressants in trials in adolescents has led to safety warnings about their use in Europe, North America, and Australasia.\(^6\) Should adolescents with depression be prescribed antidepressants, and if so, should they be given only with psychotherapy?\(^6\)

In this week’s \textit{BMJ}, a randomised controlled trial (adolescent depression antidepressant and psychotherapy trial; ADAPT) by Goodyer and colleagues compares a selective serotonin reuptake inhibitor (SSRI) alone and with cognitive behaviour therapy in 208 people aged 11-17 years with depression.\(^7\) In these adolescents, depression had not responded to a brief psychosocial intervention or was severe at the outset. The investigators tried hard to reflect “real world” conditions—the participants were heterogeneous for previous treatment exposure, self harm, suicidal thoughts, subtype of depression, and comorbidity. The primary outcome was a change in score on the Health of the Nation outcome scales for children and adolescents from baseline. They conducted assessments at six, 12, and 28 weeks, so that follow-up extended beyond that usually seen in trials of antidepressants. The trial found no significant difference in treatment effect between groups at any time point.

The trial reported a 40% response rate in both groups at 12 weeks, which is somewhat lower than that seen in other treatment studies for depression in adolescents. This may have been due to the exclusion of adolescents who had already responded to the brief psychosocial intervention. By 28 weeks the response rate had increased to nearly 60%.

The improvement in response rate from 12 to 28 weeks is noteworthy, as most treatment trials have been shorter in duration,\(^8\) and they may have underestimated the treatment response. The conclusion challenges the recommendation by the National Institute for Health and Clinical Excellence (NICE) and other bodies that SSRIs should be given to moderate and severely depressed adolescents only, in combination with a psychological therapy.\(^8\)\(^9\)

ADAPT is the fourth study to assess the combination of SSRI and cognitive behaviour therapy over monotherapy for depression in adolescents. The treatment for adolescents with depression study (TADS) found that the combination of fluoxetine and cognitive behaviour therapy was better than fluoxetine or behaviour therapy alone in reducing depressive symptoms. Combined treatment and fluoxetine alone were equally effective in achieving a clinical response and superior to cognitive behaviour therapy alone.\(^10\) The most recent trial found no advantage of sertraline plus cognitive behaviour therapy over monotherapy in rates of remission or moderation of depressive symptoms after 12 weeks of treatment, and at follow-up after nine months.\(^11\) The third trial also found that the addition of cognitive behaviour therapy to SSRIs had no significant effect on symptoms of depression.\(^12\)

The results of the ADAPT trial suggest a further trend away from the positive findings of TADS. Differences in the dose and duration of treatment and in the choice of primary outcome measure may have contributed to the variation in study outcomes, but the data suggest that combining cognitive behaviour therapy with an SSRI had only a modest advantage over an SSRI alone in treating depression in adolescents.

Combining cognitive behaviour therapy with an...
SSRI may have other advantages, such as reducing suicidal thinking and prolonging the benefit of treatment, but evidence for this across the four trials is equivocal. Suicidal thinking was lowest in the group receiving combined treatment in one study, but two studies found no significant difference. Suicidal thinking was not measured in the fourth study, which found higher remission rates after 52 weeks for combined treatment than for SSRI monotherapy. In contrast, the ADAPT study found no significant differences between groups in remission rates after 28 weeks.

What does this mean for clinicians managing adolescents with depression? Contrary to the NICE guidelines, evidence suggests that monotherapy with an SSRI is a reasonable treatment option for moderate to severe depression in adolescents, particularly if access to cognitive behaviour therapy may be delayed. The SSRI must be given at a high enough dose and for an adequate amount of time, as some patients take 12 weeks or longer to respond.

Of note, people randomised to monotherapy with an SSRI in the ADAPT and other trials received a high level of clinical care, with frequent clinical reviews and rigorous monitoring of the benefit of treatment and adverse events. The implication for clinical practice is that good quality pharmacological treatment involves more than simply writing the prescription.

Cardiovascular risk models
Moral implications of models based on absolute risk could be better understood

Risk scores based on the Framingham heart study reflect the higher risks of cardiovascular disease in the 1970s and 1980s and tend to overpredict current risks. They do not include family history, body mass index, use of antihypertensive drugs, or measures of social class. Omitting socioeconomic status as a predictor increases the health gap between rich and poor: the risks in poor people are underestimated and undertreated, and risks in rich people are overestimated and overtreated.

In this week’s BMJ/hippisley-Cox and colleagues derive a new cardiovascular disease risk score (QRISK) for the United Kingdom and validate its performance against the Framingham cardiovascular disease algorithm and a newly developed Scottish score (ASSIGN). They found that QRISK provided more appropriate risk estimates to help identify high risk patients on the basis of age, sex, and social deprivation. The QRISK score indicates that in the United Kingdom about 3.2 million men and women aged 35-74 are likely to be at high risk, compared with 4.7 million predicted by Framingham and 5.1 million with ASSIGN.

In rationing the use of statins for primary prevention, cardiovascular disease risk scores were developed to produce the biggest effect at minimum cost. However, the distribution of risk of cardiovascular disease in healthy populations is determined largely by the age, sex, lifestyle, and socioeconomic class distribution in the population. Treatment decisions and resource allocation based on age, sex, and lifestyle have moral implications, depending on what is included in the model and what is left out. The point made by Hippisley-Cox and colleagues, that omission of socioeconomic class from risk prediction models increases health inequities between poor and rich, is correct. But absolute risk scores also label male sex, old age, and risky lifestyles as diseases to be treated, while denying life extending drugs to women, younger people, and those living healthily. To facilitate more equitable and transparent decisions, these moral implications of cardiovascular disease risk models have to be better understood.

Firstly, all cause mortality is reduced more by moderate consumption of alcohol than by taking statins. A bottle of red wine a week seems to be a health investment that increases quality adjusted life expectancy more. Under a wide range of assumptions, the cost utility of red wine in primary prevention is higher than that of statins—so risk models ought to target selectively reimbursed prescriptions of bottles of inexpensive red wine. On the other hand, evidence of the benefits of statins is stronger than that of nutraceuticals such as phytosterols or omega 3 fatty acids, so why should


LUC BonneauX medical epidemiologist Netherlands Interdisciplinary Demographic Institute (NIDI), PB 11650, 2502 AR Den Haag, Netherlands bonneauX@nidi.nl
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Health for London: showing England the way?

Plans to focus hospital services and build polyclinics will have to overcome inertia and rivalries

The review has been based largely on the views of clinicians, concentrated into six working groups of “clinical innovators” drawn from a range of organisations, including the King’s Fund, to look at clinical pathways. They looked at maternity and newborn care, services for staying healthy, acute care, planned care, long term conditions, and end of life care. Mental health was considered by a seventh group, and the overall analysis also included a public opinion poll and two “deliberative” events involving members of the public.

The resulting report makes a cogent case for change...
in London. It describes a highly mobile, highly diverse population with stark health inequalities. Londoners are less satisfied than the rest of the English population with the health services they receive, and their needs are clearly not being met adequately. Furthermore, the review finds that the current configuration of services is not fit for purpose. It argues for more care at home and in the community, citing, for example, studies that show better outcomes for patients with chronic obstructive pulmonary disease and heart failure when they are offered targeted community services. It also points to powerful evidence that more specialisation in bigger hospitals can save lives, notably in dedicated stroke units, and calls for the urgent reconfiguration of services for stroke and trauma. In addition it calls for rapid work to improve the skills of the London Ambulance Service.

Improved services should be focused on individual needs and choices; they should be local where possible and central where necessary; they should be integrated (bridging the gap between primary and secondary care); they should encourage prevention; and they should focus on health inequalities and diversity. Perhaps inevitably, recommendations on the best location of services—including fewer, more specialist hospitals and, in the next two years, “between five and ten polyclinics” which would bring together general practices with community, diagnostic, and urgent care services—have prompted particularly widespread coverage and debate.

A great deal in this review is to be welcomed: its emphasis on outcomes, the experience of patients, and inequalities, as well as its search for a solid evidence base to drive decisions about health care services. The evidence base is, however, incomplete in some areas (how much evidence is there that polyclinics are the answer for every locality?) or absent in others (there are huge gaps in our knowledge of which interventions deliver best outcomes for such an ethnically diverse population). Nevertheless, this emphasis on evidence should help local NHS commissioners and providers construct and communicate a more robust case for change to a sceptical public.

Finally, the review says little about how the levers of system reform in the NHS can help to realise this vision. Yet it will be crucial to understand how the multiple and sometimes conflicting incentives that have already been built into the system will help or hinder the road to implementation. Payment by results (the mechanism to pay NHS providers a fixed price for each individual case treated), for example, has created powerful incentives for hospitals to pull in patients, but it may undermine collaboration between organisations or create conflicts between NHS trusts and primary care trusts. And the evidence so far on practice based commissioning (where general practices are given control over their commissioning budgets for secondary and community care) indicates that only modest efforts have been made to redesign primary care services to counteract the pull of hospitals.3

If the recommendations on the models of care are translated into diktats about the number and location of facilities, they will be seen as yet another “top down” exercise. This could cause planning blight by alienating clinicians and encouraging local commissioners to look up for instructions instead of working out their own solutions with providers.

London’s health services have not been short of blueprints and plans,1 including some from our institution2 and others such as the Tomlinson report.3 Most of their proposals foundered on the near impossibility of implementing reforms that seemed to offer much to primary care and little to hospitals. This time, there can be no doubting Sir Ara’s determination to let the power of evidence overcome institutional inertia and rivalries. But if this review is to succeed where others have failed it must empower local commissioners and clinicians to use the incentives that have been built into the NHS. And if it is necessary to strengthen, amend, or realign those incentives, that too must be done.

6 Murphy E. London’s healthcare services—again. BMJ 1997;315:140.
A UK global health strategy: the next steps

Is better health the fundamental goal, and will politicians collaborate effectively?

A decade ago the US Institute of Medicine argued compellingly that it was no more than enlightened self interest for countries to invest in global health.1 Such investment would help to protect their own citizens from external threats, strengthen the global economy, and contribute to international security. In the intervening period, support for placing health at the centre of foreign policy has gathered momentum. Earlier this year the Global Health and Foreign Policy Initiative was established by a group of foreign ministers convened by the Norwegian and French governments,2 and in the United Kingdom Sir Liam Donaldson, the UK’s chief medical adviser, has proposed a government-wide strategy for global health.3

The British proposals identify five reasons for promoting global health. These are to improve global security and health protection, enhance sustainable development, improve trade by promoting health as a commodity, maximise global public goods, and encourage a human rights approach to health. An interdepartmental steering group has been established to take this agenda forward across government and has embarked on a wide-ranging consultation to help it fill in the details.

The United Kingdom is in a strong position to provide leadership on this issue. The government has already led in areas such as international debt relief; UK overseas aid is recognised to be extremely effective; and many UK universities and government agencies are already fully engaged in the global health agenda. Yet there are also weaknesses in the UK position. Most obviously, there is the special relationship with the United States, during a period when the Bush administration has made no secret of its contempt for concerted international action to tackle many of the world’s problems.4 Another weakness, although not unique to the United Kingdom, is the inherent contradiction between promotion of health and the pursuit of other policies, such as support for British arms exporters and potential tensions between international trade and pro-poor development. Even in the health arena there are contradictions, with the Crisp report encouraging junior doctors to gain experience abroad5 and the new system of medical education discouraging them.6

Sir Liam’s important proposal captures the spirit of the times but, to promote real change, all those with a potential contribution to make must engage genuinely with it, wherever they are in government. For this to happen, some fundamental issues must be resolved.

Firstly, agreement is needed across government on whether the improvement of health is a fundamental goal in its own right, or whether it is simply an instrument to achieve other goals, such as promoting economic growth. This distinction becomes important when objectives conflict. Health is implicit in many of the government’s stated international priorities,7 but nowhere is there an explicit statement of the importance of improving health to match that of, for example, poverty reduction. Similarly, the millennium development goals, to which the UK government has signed up, include some important aspects of health but exclude others, such as virtually all of the burden of disease among adults.8 As a consequence, the rapidly increasing problem of non-communicable disease in low and middle income countries barely features on the international agenda.9 Linked to this is the immediate need to establish clear criteria on what to include in a global health policy. Otherwise, the UK strategy will seem like a disconnected shopping list, all too easy for government ministries to ignore.

How will this national strategy be taken forward in Europe? The European Union has a common foreign and security policy, so that, with a few exceptions, member states vote as block in international forums. Achieving a European consensus on global health will not be easy, especially given some governments’ preoccupation with current revisions to the European Treaties. It will be important to build alliances with like minded governments, especially those that will hold the rotating presidency in the near future.

The UK global health strategy must be sustained over the long term: short term fixes will not do. The creation of an interdepartmental steering group is a good first step, and the recent appointment as a minister in the Foreign Office of the committed internationalist Mark Malloch Brown bodes well. Commitment by the other political parties and, critically, by the administrations in Scotland, Wales, and Northern Ireland is also essential. The consultation process has already visited Edinburgh and Cardiff. Some mechanism is also needed to include the views of the UK’s remaining overseas territories, many of which are especially vulnerable to global forces.

Bridgewater et al suggest counterintuitively that media reporting of CABG mortality statistics (since 2001) has not caused risk averse behaviour in surgeons. However, data reporting practices changed at this time. CABG mortality fell, as did the number of cases with left ventricular ejection fraction <30% (only 5.5%). Without a “surgical breakthrough” this implies modification of patient selection.

The relative merits of PCI and CABG in complex multivessel disease have been addressed in a trial which recently completed recruitment of 1800 patients. This initiative will provide clear guidance to override the use of selected data in support of one approach over the other. Even so, many less sanguine patients will still choose one or more PCIs first, knowing that CABG is possible if symptoms return.

In summary, PCI and CABG are complementary, not competitive. PCI is preferred for multifocal discrete disease and CABG for diffuse disease with chronic occlusions. Patient choice must now be included in the evidence base.

Stephen Westaby professor, department of cardiac surgery John Radcliffe Hospital, Oxford OX3 9DU swestaby@AHF.org.uk Keith Channon professor of cardiovascular medicine, department of cardiology Adrian Banning consultant, department of cardiology Competing interests: The authors, a cardiac surgeon and two cardiologists, are SYNTAX investigators and benefit from private practice in myocardial revascularisation.

Security protection is needed when using USB sticks

Current working hours for junior staff mean that effective patient handovers are critical. Handwritten sheets have been superseded by electronic storage of patient data available to the clinical team.1

Universal serial bus (USB) sticks have greater security risks than other media due to their size, storage capacity, and convenience. Trust policy states that confidential data should be stored on 128-bit encrypted USB sticks, with “if found” labels on them, and be used solely on the trust’s computers.

Criminals now recognise the value of personal data in the growing identity theft market. Recently confidential patient data held on an unprotected USB stick were stolen. The trust had to inform the patient and face liability for distress or damage caused along with public condemnation (D Terry, personal communication, July 2007). In addition, clinical information is lost permanently, and there is the financial cost of replacing equipment.

I asked 50 junior doctors about their electronic storage of patient data. Thirty six of them stored patient data electronically, 20 using a USB stick, three a floppy disk, and 13 a hospital computer hard drive. None of the 20 USB sticks had 128-bit encryption, and only three had password protection (still insufficient for the trust’s requirements). Four doctors used the same device on their personal computer(s), two of which had patient data stored on them.

Cognisant of the sensitive patient information held electronically, the Caldicott and data protection adviser has recommended enhanced USB stick security protection to the trust, with mandatory password protection. The trust intends to supply 128-bit secured USB sticks for medical firms to use on wards, and an extensive communications programme will seek to raise awareness and promote compliance.

Matthew Daunt F1 doctor, Queen’s Medical Centre, Nottingham University Hospitals Trust, Nottingham NG7 2UH mattdaunt@doctors.org.uk

Competing interests: None declared.

1 Wade D. Ethics of collecting and using healthcare data. BMJ 2007;334:1330-1. (30 June.)

MANAGING SMOKING CESSION

Article skips over weaknesses of nicotine replacement

Aveyard and West state that the Allen Carr Easyway method showed abstinence rates similar to those expected from behavioural support alone, quoting McRobbie et al instead of the two cohort studies mentioned.1 2 They omit two studies which found persistent abstinence in half of the cohort, in some of which nicotine replacement had failed.3 4 Even more serious is the omission of the risks of nicotine replacement to the fetus which were reviewed recently.5

Manfred Neuberger professor Department of Preventive Medicine, Medical University of Vienna, Kinderapitalgasse 15, A-1095 Vienna, Austria manfred.neuberger@medunivwien.ac.at

Competing interests: None declared.

1 Aveyard P, West R. Managing smoking cessation. BMJ 2007;335:37-41. (7 July.)

Sciatica

An archaic term

In their clinical review Koes et al use the entirely non-evidence-based term “sciatica.” From the Greek, it literally means hip pain. In English, the Oxford English Dictionary gives precedent to a quote from Shakespeare’s Timon of Athens (act IV, scene I), where sciatica is a curse placed on the senators. None of this is a good basis for current usage, which is supposed to describe nerve root or radicular pain, as the authors note but do not discuss.

The problem is that patients with back pain may also have referred pain, a phenomenon first pointed out by Kellgren over 60 years ago.2 Clinicians are not good at making this distinction, but they should try. This issue takes on greater importance when studying the evidence base where often this distinction is not made. Persistent use of the archaic word sciatica in the clinical setting is not in the best interests of people with a miserable and disabling condition. It remains an effective cure, but English terms such as nerve root pain or radicular pain better describe the clinical problem.

Jeremy C T Fairbank consultant orthopaedic surgeon Nuffield Orthopaedic Centre, Oxford OX3 7LD jeremy.fairbank@nndox.ox.ac.uk

Competing interests: None declared.


ATTENDING PATIENTS’ FUNERALS

We can always care

When our son died of cancer last year at the age of 25, a number of his doctors and nurses came to his funeral.1 We were not able to talk to them at the time, but we knew that they had been there as they filled in cards which the funeral director provided. We have had contact with one or two of them since, and the shared experience was of tremendous importance. It meant a lot to us that they had taken time out of their busy schedule to come. For us it was an important mark of respect for our son. It showed that they cared and was part of a long healing process.

As a community paediatrician I (RT) have tried wherever possible to attend the funerals of disabled children under my care. I have usually grown to know the families well. The untimely death of a child or young adult is devastating, and families have always seemed to appreciate my presence. We cannot always cure but we can always care. My personal experience has reinforced this feeling a hundredfold.

Ros Thorburn consultant community paediatrician ros.thorburn@doctors.org.uk

Martin Roland professor of general practice Warrington WAS 1TP

Competing interests: None declared.

1 Arnold B, Falloon K. Should doctors go to patients’ funerals? BMJ 2007;334:1322. (23 June.)
Hand hygiene is a key health issue, says CMO

Michael Day LONDON
Liam Donaldson, the chief medical officer for England, has named, in his latest annual report, “unacceptably poor” hand hygiene in hospitals and the chronic lack of organs for transplantation as the two most pressing public health issues.

Despite improvements in some hand hygiene practices, he said, such as more widespread use of alcohol based handrubs, the percentage of healthcare staff complying with hand cleaning protocols seldom exceeded 60%—and was often even lower.

“Patients find it astonishing and alarming that often nurses and doctors do not routinely wash their hands,” said Professor Donaldson. “However, they often don’t feel able to ask doctors or nurses if they’ve washed their hands.”

He said it might be possible to empower patients by providing them with their own alcohol based handrubs, which they would be able to offer to clinical staff. A pilot study to test this was already being organised in an NHS hospital, overseen by the hospital hygiene expert Didier Pittet of the World Health Organization.

Professor Donaldson also renewed calls for the introduction of an opt-out system for organ donation, in which it would be assumed that people were willing to donate their organs unless they specified otherwise.

This was, he said, vital to save lives “among a group of people who are currently dying at a rate of one a day.”

He said: “There is a shortage of organs in this country, as there is in other countries, and the situation is getting worse.”

He acknowledged that parliament had already rejected such an opt-out system, but he added: “Confronted with the worsening situation, people who opposed it in the past may now wish to change their minds.”

The chief medical officer’s annual report for 2006, On the State of Public Health, is available at [www.](http://www.sh.gov.uk/cms/)

Doctors attack Brown’s regulation plans

Michael Day LONDON
Doctors’ leaders and legal experts say that government plans to lower the level of proof needed to convict doctors of professional misconduct are unfair and probably unworkable.

Gordon Brown, the prime minister, last week announced details of a new Health and Social Care Bill, which will be introduced in the next parliament. At the heart of the bill will be a shake-up of the regulation of the medical profession.

The proposed reorganisation was announced by the chief medical officer, Liam Donaldson, a year ago (BMJ 2006;333:163). He said that key aspects of the General Medical Council’s regulatory role would be diminished. The council would no longer act as prosecutor, judge, and jury in cases concerning doctors’ fitness to practise. Instead it would be responsible solely for assessment and investigation; an independent tribunal would determine guilt or innocence.

Most controversial, however, was the proposal that the burden of proof needed should be lowered from the criminal one of beyond all reasonable doubt to the civil standard of balance of probability. This would make it easier to strike off practitioners in some cases.

After Mr Brown announced the forthcoming bill the BMA immediately vowed to fight to retain the criminal burden of proof in misconduct cases. The BMA’s chairman, Hamish Meldrum, said, “The BMA’s members have made it very clear that they are against using an independent tribunal to take away a doctor’s livelihood.

‘Sliding scale’ on the burden of proof, she said: “A higher, criminal standard of proof will be retained for cases where there’s a threat of erasure from the register.”

However, she called on ministers to ensure that the lower, civil standard was required in all professional misconduct cases.

“If it’s about protecting the patient, then if there’s any reasonable doubt and you think on the balance of probabilities that that person has done what he or she has been accused of, then that person should not be allowed to practise,” she said.
Former US surgeon general reveals extent of political pressure

Janice Hopkins Tanne NEW YORK

A former US surgeon general told a Congressional committee last week that while he was in office he had been forced by the Bush administration to speak on topics such as stem cell research, emergency contraception, sex education, health of prisoners, mental health, secondhand smoking, and global health issues.

Richard Carmona, the last surgeon general, told the House of Representatives Committee on Oversight and Government Reform that he had been instructed to mention President Bush three times on each page of his speeches, which were vetted by officials at the parent agency, the Department of Health and Human Services. Travel to conferences was prevented, and he was told not to attend the special Olympic games for disabled athletes, which were supported by the Kennedies.

When he wanted to issue information about mental health after the 11 September 2001 terrorist attacks on the United States he was told by his bosses at the Department of Health and Human Services: “You don’t write anything unless we approve it.”

Six previous surgeons general told him they’d also faced political pressure, but not to the extent that Dr Carmona had.

The office of the surgeon general dates from 1798. Nowadays the holder has little power and no budget but is considered “the nation’s doctor,” charged with giving truthful scientific information to the public.

Previous surgeons general have warned about smoking, HIV and AIDS, obesity, sexual behaviour, drink driving, among other issues, and have recommended needle exchange to prevent HIV transmission.

Dr Carmona’s testimony was the lead story in the New York Times on 11 July [www.nytimes.con](http://www.nytimes.con) (“Surgeon general sees 4-year term as compromised”).

Dr Carmona said he was naive when he came to Washington, although he had served as a US army special forces doctor and weapons specialist, a registered nurse, and a police officer before becoming a doctor and trauma surgeon, chief executive officer of a public hospital and health system, and a university professor.

German doctors accused of boosting pay by offering patients “unnecessary extras”

Annette Tuffs HEIDELBERG

Some health experts and patients in Germany are becoming concerned about the increasing frequency with which doctors offer patients inessential diagnostic tests and unproved treatments. They say that these extra services are being offered more to boost doctors’ incomes than to help patients.

“These offers put the doctor-patient relationship at risk,” said Jürgen Klauber, director of the Wissenschaftliche Institut der Ortskrankenkassen (Scientific Institute of General Health Insurance).

A survey published last week by the institute, which provides scientific expertise to Germany’s largest health insurance company, AOK, has shown that last year about 18 million patients were offered these “Individuelle Gesundheitsleistungen” (“individual health benefits”), commonly shortened to IGeL.

German doctors earned an extra €1bn (£0.7bn; $1.4bn) by selling IGeL, equivalent to almost 5% of the state health insurance budget paid for outpatient care each year in Germany.

The benefits were introduced in the mid-1990s by the National Association of Statutory Health Insurance Physicians as a way of circumventing their tight budgets. Initially there were 79 items, including counselling and vaccination before holidays abroad, as well as some forms of complementary medicine.

However, since then the number of items has increased to more than 300, and because no clear scientific evidence exists for most of them, patients cannot have their cost refunded by the statutory health insurance companies, which cover 90% of Germany’s population. Private health insurance companies do cover many of the tests and procedures.

The recent survey, which involved telephone interviews with 3000 AOK customers, showed that specialists were more likely than GPs to offer IGeL. The most common test for sale was extra ultrasound examination in prenatal care, sometimes known as “baby TV.” Health insurance companies will pay only for three such examinations, and expectant mothers wanting more have to pay for them themselves.

Companies offering statutory health insurance will also pay for eye pressure measurements, if glaucoma runs in the patient’s family, and some cancer detection tests at certain intervals for women, but they will not pay for a wide range of other tests and procedures.

Neurosurgeons told to watch for signs of “twiddler’s” syndrome

Roger Dobson ABERGAVENNY

Neurosurgeons need to watch out for signs of “twiddler’s syndrome” in their patients, a new report warns.

With the increasing use of implanted stimulation devices, there have been a number of reports where patients have consciously, subconsciously, or unintentionally moved wires attached to the device.

“With the advent of implanted pulse generators in the treatment of epilepsy, Parkinson’s disease, essential tremor, and pain those caring for patients with such a device should be aware of this potential complication,” says the report in Surgical Neurology (doi: 10.1016/j.surneu.2006.10.062).

It says, “Experience with similar placement of cardiac pacemakers and defibrillators had revealed the possibility of generator migration and subsequent lead fracture either spontaneously or, more often, through a patient’s conscious or subconscious manipulation of the device through the skin. This phenomenon has been termed twiddler’s syndrome.”

Power for such stimulation devices comes from an implanted pulse generator, usually located in a pocket in the chest underneath the skin.

In the latest case, twiddler’s syndrome, defined as the...
Neurosurgeons told to watch for signs of “twiddler’s syndrome” in patients with implanted devices

Implanted devices leading to a brain stimulator

spontaneous, subconscious, inadvertent, or deliberate rotation of the generator, occurred in a 65 year old woman with a history of disabling essential tremor. A deep brain stimulator was implanted, which initially resulted in almost complete resolution of her symptoms, and she was able to carry out activities involving repetitive movements that she had previously avoided, including housework and gardening. But after six months she developed a pain behind her left ear and uncontrolled tremor of her right hand. Tests showed a lack of current getting through to the implant, and it was later found that the wires to the generator had several twists, reducing power supply and putting stress on tissue, causing the ear pain.

“The patient adamantly denied manipulation of the IPG [implanted pulse generator] in a twisting or twirling fashion,” says the report, which states that the device apparently moved within the pocket spontaneously. “This case suggests that twiddler’s syndrome can occur in patients with no known history of manipulating their IPGs.”

Two other case reports, in Der Chirurg (doi: 10.1007/s00104-007-1319-3) and Cardiology (2007;17:220-2), described movement in pacemaker wires.

Overseas health workers look set to escape Libyan death sentence in HIV case

Owen Dyer LONDON

Death sentences pronounced by a Libyan court on five Bulgarian nurses and a Palestinian intern accused of deliberately infecting Libyan children with HIV looked to be on the point of being overturned as the BMJ went to press.

Relatives of the infected children agreed to drop calls for capital punishment in return for compensation of $1m (£0.5m, €0.7m) for each family, the Bulgarian television channel BTV said.

A hearing before Libya’s Supreme Judicial Council concerning the fate of the foreign workers had been set for 16 July, but it has been postponed twice. The Libyan government gave no reason for the delay, but the Bulgarian news programme attributed the delay to the need to collect more signatures from the children’s families, waiving the demand for the death penalty.

The families’ spokesman, Idriss Lagha, told Agence France Presse that relatives were to sign the agreement only at the moment they cashed their cheques. Banks were kept open in Benghazi overnight in an effort to hasten the process, he said. About 270 of the families (60%) had signed waivers by Tuesday morning.

The deal emerged after a visit to Libya last week by Cécilia Sarkozy, wife of the French president. She met with Libya’s president, Muammar Gaddafi, and with infected children. An aide to President Sarkozy, Claude Gueant, said that the meeting between Mrs Sarkozy and Colonel Gaddafi had been a key breakthrough. The Libyan leader seemed to have been swayed by Mrs Sarkozy’s argument that the case was holding up the normalisation of relations between Libya and Europe, said Mr Gueant.

It remains unclear who is paying the compensation to the families. The Bulgarian foreign minister, Ivailo Kalfin, speaking after the deal was reached last weekend, reiterated the longstanding Bulgarian position that his government would not pay compensation, as to do so would imply that the six health workers were guilty.

Colonel Gaddafi’s son, who is director of the Gaddafi Institute which helped broker the deal, told Le Figaro that the compensation was financed by debt remission, but Bulgaria flatly denies this.

The six health workers have been in prison since 1999, when 426 children at Benghazi’s El-Fath Children’s Hospital were infected with HIV. About 50 of the children have since died. The six foreigners were convicted of deliberately spreading infection and were sentenced to death by firing squad in May 2004 (BMJ 2004;328:1153).

The defence counsel blamed poor hygiene standards.

A prosecution report by Libyan scientists suggested deliberate infection.

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BMA backs police campaign against genital mutilation

Peter Moszynski LONDON
A crackdown on female genital mutilation has been launched by the Metropolitan Police in an attempt to protect the estimated 6500 girls it believes undergo the procedure each year in the United Kingdom.

The BMA-backed campaign, dubbed Operation Azure, has been launched at the start of the summer holidays, because that is the time when girls from certain ethnic groups—mainly African communities—are thought to be at most risk. The extended holiday period allows time to recover from the physical effects of the operation. Most girls are sent abroad, but female genital mutilation is also thought to be conducted in the UK, although no one has ever been prosecuted.

A £20 000 ($30 000; €40 000) reward has been offered in an attempt to break the wall of silence surrounding the issue. The Metropolitan Police emphasises: “This is not an attack on culture or faith. It is to raise awareness that this is extreme child abuse, is illegal and will not be tolerated. FGM [female genital mutilation] is both a violation of human rights and a criminal offence, and to administer [it], or arrange for it to be administered, could lead to imprisonment of up to 14 years.”

All female genital mutilation procedures are unlawful in the UK under the Female Genital Mutilation Act 2003. It is also an offence for UK nationals or permanent residents to carry out the procedures abroad or to “aid, abet, counsel or procure the carrying out of FGM abroad,” even in countries where the practice is legal.

Carol Hamilton of Operation Azure said that signs that a child is being prepared for genital mutilation to take place abroad include “knowing that the family belongs to a community in which FGM is practised and are making preparations for the child to take a holiday, arranging vaccinations or planning absence from school” and the child talking about a “special procedure” taking place.

Detective Inspector Hamilton said that doctors had a key role and that involvement was “a matter of child protection, not patient confidentiality.” Addressing doctors, she said: “If you suspect that any girl is at risk of being subjected to any form of FGM, take action to report it immediately.

Time counts, so please act as soon as you suspect that a girl may be at risk . . . If a girl has already undergone FGM, do not think there is nothing you can do. She will be in need of specialist care and support, and if she has sisters they will be in need of protection.”

The Operation Azure team covering the London area can be contacted on 020 7230 8392.

BMA guidelines on female genital mutilation are at www.bma.org.uk/ap.nsf/content/FGM

Scotland considers screening on admission to hospital

Bryan Christie EDINBURGH
Scotland is considering screening patients for methicillin resistant Staphylococcus aureus (MRSA) when they are admitted to hospital, to help reduce the incidence of healthcare associated infections.

The move comes after the completion of a comprehensive study of the prevalence of such infections in Scotland, which found that 9.5% of patients contract an infection while in Scottish hospitals. The annual cost is calculated to be £183m (€270m; $370m).

The study, carried out by Health Protection Scotland, was based on a survey of almost 14000 patients—the entire acute hospital population at the time of the survey visits. The highest prevalence of healthcare associated infections was found in geriatric wards (12%), followed by surgery (11.2%), medicine (9.6%), and orthopaedics (9.2%). Obstetrics had the lowest rate (0.9%). The most common infections were urinary tract (18%),

IN BRIEF

Chinese drug agency chief is executed: The disgraced former head of the Chinese State Food and Drug Administration, Zheng Xiaoyu, was executed on 10 July, after the failure of his appeal against the death sentence for bribery and dereliction of duty. On 29 May Mr Zheng was found guilty of taking ¥6.5m (£0.4m; €0.6m; $0.8m) in bribes and failing to ensure drug safety. On 6 July his former aide, Cao Wenzhuang, was sentenced to death with a two year reprieve.

HRT prescribing for menopause falls: The number of prescriptions of hormone replacement therapy (HRT) for menopause has halved in the UK since 2002, a new study has found. But the study, which was based on prescribing by GPs between 1991 and 2005 to women aged 40 or over, also found that prescribing of bisphosphonates for osteoporosis had risen. This increase “reinforces the need for research into the long term risks and associated infections.”

A £20 000 (€30 000; $40 000) reward has been offered in an attempt to break the wall of silence surrounding the issue. The Metropolitan Police emphasises: “This is not an attack on culture or faith. It is to raise awareness that this is extreme child abuse, is illegal and will not be tolerated. FGM [female genital mutilation] is both a violation of human rights and a criminal offence, and to administer [it], or arrange for it to be administered, could lead to imprisonment of up to 14 years.”

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Hospital consultants’ NHS salaries top £110 000

<table>
<thead>
<tr>
<th>Grade</th>
<th>Mean basic salary (full time equivalent)</th>
<th>Mean total earnings (including pay for overtime, redundancy, location payments, etc)</th>
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<tr>
<td>Foundation year 1 or house officer</td>
<td>£20 900</td>
<td>£31 900</td>
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<tr>
<td>Foundation year 2 or senior house officer</td>
<td>£29 600</td>
<td>£45 900</td>
</tr>
<tr>
<td>Registrar</td>
<td>£38 300</td>
<td>£60 000</td>
</tr>
<tr>
<td>Associate specialist and staff grade</td>
<td>£59 200</td>
<td>£63 800</td>
</tr>
<tr>
<td>Consultant (old contract)</td>
<td>£80 800</td>
<td>£93 900</td>
</tr>
<tr>
<td>Consultant (new contract)</td>
<td>£83 200</td>
<td>£111 800</td>
</tr>
</tbody>
</table>

*Figures based on data collected January to March 2007 from the NHS electronic staff record.

Source: NHS Information Centre

Hospital to cut infections

surgical (16%), and gastrointestinal (15.4%) infections.

Previous prevalence studies have found a prevalence of healthcare associated infections of 8.2% in England, 6.3% in Wales.

A programme is already in force at the Golden Jubilee Hospital outside Glasgow, which has not had a single case of MRSA infection in the past two years.


GPs’ income rose by 23%, not 30%, under new contract

**Zosia Kmietowicz LONDON**

Hospital consultants in England earned on average the full time equivalent of £111 800 (€165 300; $228 050) a year for their NHS work in the first quarter of 2007, new data show.

This figure, which excludes any income from private work, represents a 16% increase in NHS earnings for hospital consultants since 2004.

The figures, from the NHS’s Information Centre, are the first to be collected since Agenda for Change, the new system of pay and conditions, was introduced in the NHS in 2004. They are also the first to be collected from the electronic staff record, a new payroll system being rolled out across the NHS and currently used by 49% of NHS organisations in England. The figures are based on pay data collected between January and March 2007.

The data highlight the disparity between consultants’ pay and that of associate specialist and staff grade specialists, who earned an average yearly salary of £63 800 over the same period.

The data shows that trainee doctors in foundation year 1 received a basic annual salary of £20 900, but additional payments (such as overtime pay) bring their total earnings to £31 900. Qualified nurses earned a basic annual salary of £26 100, which, with an additional 15% from extra payments, brings their total earnings to £31 900.


GPs earned an average net income of £100 170 in 2004-5

The data are based on the tax returns of nearly 18 000 GPs and include income from private as well as NHS work. The Information Centre estimates that in 2004-5 nearly half of all GPs had a net income of more than £100 000. And more GPs are earning the highest incomes. The centre estimates that 629 GPs (1.9%) had a net income of at least £200 000 in 2004-5; in 2003-4 the number was 222 (0.7%).

The average gross earnings for all GPs in 2004-5 were £230 097, and average expenses were £129 926. This gives a proportion of expenses to earnings of 57%, a decrease from the 2003-4 proportion of 60%, reflecting the fact that although expenses have increased in line with previous years, gross earnings have outpaced the increase in expenses.
Hospitals should standardise patient wristband design

Susan Mayor LONDON

Hospitals in England and Wales must standardise the design of patients' wristbands and the information recorded on them to reduce the risk of providing the wrong care, says new guidance from the National Patient Safety Agency.

More than one in 10 reported cases of patients “being mismatched to their care” last year were related to wristbands, the agency warned. Such mismatches occurred in more than 2900 of the total 24,382 reports of patients receiving the wrong care from February 2006 to January 2007.

“Standardising the design of patient wristbands, the information on them, and the processes used to produce and check them, will improve patient safety,” advises the agency.

From July 2008 all NHS organisations in England and Wales that use wristbands will need to ensure that they meet the agency’s design requirements. This means that wristbands should come in a range of sizes to fit all patients, from the smallest newborn babies through to overweight patients and patients with oedema and those with intra- venous lines and bandages. They must be comfortable for patients, easy to keep clean, and secure.

Wristbands must record core patient identifiers, including the patient’s surname, first name, date of birth, and NHS number (a temporary one should be used if their number is not immediately available).

The guidance on wristbands and the review, Design and specification of patient wristbands, are available at [www.npsa.nhs.uk](http://www.npsa.nhs.uk).

Andrew Wakefield is accused of paying children for blood

Owen Dyer LONDON

Andrew Wakefield, whose warnings about a possible link between the measles, mumps, and rubella (MMR) vaccine and autism sparked a public health scare, was accused this week of paying children E5 (€7.40; $10) each to give blood samples at his son’s birthday party.

The accusation was made in the GMC’s case involving three doctors who collaborated on a 1998 *Lancet* paper on developmental disorders in children. Dr Wakefield, John Walker-Smith, and Simon Murch are accused of ignoring limitations placed on them by the research ethics committee of the Royal Free Hampstead NHS Trust and subjecting children to procedures that were not clinically indicated, including lumbar punctures, barium meals, general anaesthesia, and colonoscopy.

Dr Wakefield is also accused of misleading the *Lancet* in failing to disclose his involvement in an application for a patent for a new type of MMR vaccine and his receiving funding from the Legal Aid Board to investigate patients involved in litigation over alleged reactions to the vaccine.

The disclosure that legal aid funding had paid for some of the clinical investigations in the *Lancet* paper led the journal to

Most training posts filled, but 2000 doctors may be jobless

Lynn Eaton LONDON

By the end of the first round of this year’s controversial training application process, 85% of doctors’ training posts in England handled through the computerised medical training application service (MTAS) were filled.

The Department of Health has published the numbers of applicants competing for posts and of posts filled. It has collated data from individual deaneries after its national computerised system was scrapped halfway through the application process.

Deaneries have filled 13,168 posts so far. Of these, 10,804 are run-through training posts (entailing several years of training after the foundation programme and in which doctors train to specialise in either general practice or a specialty), 2,262 are fixed term service training appointments (FTSTAs) (year long posts that must be applied for separately), and 102 are academic posts. Altogether, 2,386 jobs remained to be filled at the end of round one.

However, the situation is changing daily, because someone who has accepted an FTSTA post on round one but is then offered a run-through post (which is more likely to lead eventually to a consultant post) in round two can forgo the FTSTA post and opt for the run-through one instead.

It looks as though as many as 2000 doctors currently at foundation year 2 (F2) or senior house officer level may still be jobless at the end of the second round. However, the health department says it is planning to make around 1000 FTSTA posts available at the end of round two for those applicants who have still not secured a job. The exact number of additional posts has yet to be finalised.

The Modernising Medical Careers team has confirmed that of the 32,649 eligible applicants for posts in the United Kingdom 16,670 were UK graduates (69% of whom have accepted a post) and 15,979 were UK based applicants who had obtained their medical degree outside the UK (29% of whom have accepted a post).
formally retract the study in 2004, citing a “fatal conflict of interest.”

The GMC accuses Dr Wakefield of misleading the Legal Aid Board about how he used £55 000 of their research funding. His costing proposal asked for £13 750 for hospital beds and investigations that were actually covered by the NHS, the charges say.

The GMC charges that Dr Wakefield and Dr Walker-Smith gave an experimental drug called “oral measles virus-specific dialyzable lymphocyte extract transfer factor” to one patient named as Child 10. It says they began administering the drug a year before receiving ethics committee approval and before obtaining information on its safety in children, the charges allege.

Dr Wakefield submitted a proposal to the Royal Free Hospital School of Medicine “to set up a company called Immunospecifics Biotechnologies Ltd to specialise in the production, formulation and sale of Transfer Factor.” The proposal stated that Child 10’s father, known as Mr 10, would be managing director of the company, while Dr Wakefield would be research director.

Andrew Wakefield outside the GMC hearing, which is due to continue until October

The statistics for England alone show that of the 27 849 eligible applicants, 5000 were already in foundation year 2 (F2) posts. Seventy per cent of these (3500) have already accepted posts, leaving 1500 without jobs at the moment. About 900 of the 2320 vacant posts in England are at the second year of specialty training (ST1) level, suggesting that some 600 F2 doctors may not be able to find an ST1 post in round two.

The number of senior house officer applicants is 9700, of whom 5820 (60%) have already accepted posts, leaving 3880 who may not have a job from August. Although there are still 1420 vacancies at more senior levels (ST2, 3, and 4), more than 1600 senior house officers could be jobless when round two ends.

A further 10 750 applicants who were neither senior house officers nor in F2 but who are currently working in the NHS also applied. These applicants could be in staff or associate specialist posts. Of these, 3225 (30%) have accepted jobs.

The health department has said that the highest numbers of unfilled posts are in anaesthetics, obstetrics and gynaecology, paediatrics, psychiatry, and geriatric medicine.

In England, 380 anaesthesia posts had not been filled, including 120 at ST1 level and 252 at ST2 level. Psychiatry has 280 unfilled vacancies.

But there is unlikely to be a problem filling these posts. In round one there were nearly 700 applicants for anaesthesia and more than 3000 applicants for psychiatry.

The BMA has pointed out that the proportion of academic trainee posts filled, at 57%, was rather lower than the other types of post. And some deaneries have achieved much lower fill rates than others, such as Trent, which has filled only 64% of posts.

Jo Hilborne, chairwoman of the BMA’s Junior Doctors Committee, warned that it was still “alarmingly unclear” what would happen at the end of the month when junior doctors’ contracts end.

For further information on vacancies see: www.mmc.nhs.uk

Doctor ordered to pay £300 000 libel damages to company

Clare Dyer BMJ

A company that investigates research fraud on behalf of the drug industry as well as its chief executive and former medical adviser have been awarded libel damages of £300 000 (£445 000; $615 000) against a doctor who is currently facing serious charges before the General Medical Council of research misconduct and dishonesty.

Tomnoy Sharma, a former senior lecturer at the Institute of Psychiatry in London, was ordered by the High Court in London to pay the damages, together with costs, to MedicoLegal Investigations (MLI), its chief executive, Peter Jay, and the retired medical adviser Frank Wells.

Dr Sharma conducted a number of trials for major drug companies in the late 1990s and built up an international reputation before MLI was called in to investigate after several sponsors grew suspicious about his work. The material gathered by MLI led to the GMC proceedings.

The GMC accuses him of having falsely claimed to have sought and received approval by telephone without informing his carers; offering financial inducements to research participants; breaching agreed research protocols; lying in a job application; posing as a professor; falsely claiming to have a doctorate; and threatening a patient with withdrawal of treatment if she left a study.
NEWS

WHAT’S NEW IN THE OTHER GENERAL JOURNALS

Alison Tonks, associate editor, BMJ atonks@bmj.com

Breast cancer genes don’t affect prognosis in breast cancer

Several teams of researchers have already tried to find out, with limited success, whether mutations in the BRCA1 and BRCA2 genes affect prognosis in women with breast cancer. The inconsistency of previous studies led researchers from Israel to look again, this time in a cohort of Jewish women who were diagnosed and treated in the 1980s—before testing for these mutations was routine. Women with either mutation survived just as long as women without. Ten-year survival was around 50% for all groups. Nor were there any discernible differences in breast cancer related mortality. Adjusted hazard ratios for death were 0.76 (95% CI 0.45 to 1.30, P=0.31) for women carrying the BRCA1 mutation and 1.31 (0.80 to 2.15; P=0.28) for women carrying BRCA2. Overall, 135 of the 1748 (8%) Jewish women in the cohort had one or the other. Although this and previous studies are too small to be conclusive, together they suggest that the prognosis is no different for women with these mutations than for those without, says a linked editorial (p 175). Testing for BRCA1 and BRCA2 probably doesn’t help doctors plan treatment or predict outcome. N Engl J Med 2007;357:115-23

Neural tube defects fall by almost a half in Canada after folate added to flour

In November 1998, the Canadian authorities introduced mandatory fortification of many cereal products with folic acid. They aimed to increase intake of folic acid by 30-70% in women of childbearing age and reduce the incidence of neural tube defects. It worked.

A close look at all live births, still births, and terminations for fetal anomaly in seven Canadian provinces found that the incidence of all neural tube defects fell from 1.58 per 1000 births before the legislation to 0.86 per 1000 births by 2002, a reduction of 46% (95% CI 40% to 51%). The effect was biggest in spina bifida (53% reduction), but fewer cases of anencephaly (38% reduction) and encephalocele (31%) were also seen. The Eastern provinces—which had the highest incidence to start with—benefited most. By 2002, fortification had wiped out this well documented east-west gradient.

Currently, Canadian millers add 0.15 mg of folate to each 100 g of flour or cornmeal and 0.20-0.27 mg to each 100 g of pasta. Experts estimate this gives everyone around 0.4 to 2.0 µg of extra folic acid a day. American cereals were also fortified in 1998, say the researchers. But the incidence of anencephaly and spina bifida combined fell by 30-70% in women of childbearing age and reduce the incidence of neural tube defects. It worked.

In 611 children aged 6 or less presenting with a first urinary tract infection, prophylaxis was not associated with a reduced risk of a recurrent infection (hazard ratio 1.01, 95% CI 0.5 to 2.02). In 83 children who did develop recurrent infections, prophylaxis was associated with an increased likelihood of antibiotic resistance (odds ratio 7.5, 1.60 to 35.17).

US guidelines recommend prophylaxis for children with a first urinary tract infection and vesico-ureteral reflux, despite mixed results from previous trials. These authors found no link between recurrence and grade 1-3 reflux, but their results for more severe disease were inconclusive. They suggest that doctors discuss the risks and benefits with families before prescribing prophylaxis. The alternative is close surveillance without antibiotics.

These authors found a lower rate of recurrent urinary tract infection (12% per year after a first infection) than previous studies in other populations. But they are confident that their estimate accurately reflects the incidence of symptomatic recurrent infection in primary care. JAMA 2007;298:179-86

Diaphragms “disappointing” against HIV

African women at the epicentre of the HIV pandemic urgently need a way to protect themselves from infection. They have inadequate control over the only two preventive interventions that work—condoms and male circumcision—and a disappointing trial has just reported that cervical diaphragms don’t give extra protection when added to a comprehensive package including condoms.

All 4948 HIV negative women were given intensive counselling, treatment of sexually transmitted diseases, and condoms. Half were also given diaphragms and told how to use them. They developed HIV at the same rate as control women without the diaphragms (4.1 per 100 women years v 3.9 per 100 women years, relative hazard 1.05, 95% CI 0.84 to 1.32).

Perhaps worse, women with diaphragms used condoms significantly less often than other women, although this did not affect their risk of infection in this study.

HIV prevention trials are notoriously
Hydroxychloroquine may help prevent diabetes

Hydroxychloroquine is an antimalarial and a safe and effective treatment for rheumatoid arthritis. It may also help prevent diabetes, according to a large cohort study of nearly 5000 adults. All had rheumatoid arthritis, and patients who took hydroxychloroquine were significantly less likely to develop diabetes than those who didn’t, during a follow-up of more than 20 years. After adjusting for obvious confounding factors such as body mass index and use of steroids, the hazard ratio for incident diabetes in patients who had ever taken the drug was 0.62 (95% CI 0.42 to 0.92). The longer the duration of treatment, the lower the risk.

Researchers have known for years about the antidiabetic properties of hydroxychloroquine, but these authors say this is the first study to suggest a prophylactic effect in people without diabetes. In patients taking the drug for more than four years, the risk of diabetes was reduced by 77% (adjusted relative risk 0.23, 0.11 to 0.50).

The participants in this cohort reported their own diagnoses, and the authors were unable to distinguish between type 1 and type 2 diabetes. Even so, they think their findings are strong enough to proceed to prospective trials of hydroxychloroquine in high risk patients with and without rheumatoid arthritis.

JAMA 2007;298:187-93

Pay for performance linked to better care for some primary care patients in UK

UK patients with type 2 diabetes or asthma have had better quality primary care since the government introduced pay for performance incentives in 2004, a study has found. Their care was improving before the new contract, but the trend accelerated significantly soon afterwards in 42 representative practices. Care of patients with coronary heart disease has also improved recently, but the authors found no sharp increase in quality after pay for performance was introduced.

It is hard to know for certain whether particular events are responsible for trends in care, but the authors think that UK general practitioners probably did respond to the financial incentives introduced in 2004. Even before the change, quality of care was highest for patients with coronary heart disease, leaving less room for improvement. In 2001 and 2002, 98% of primary care trusts already had quality initiatives for coronary heart disease in place.

If the new contract did improve general practitioners’ performance, the effect was only modest and the government accepts it paid a high price, say the authors. Officials are currently busy amending the details. Doctors may soon have to work harder for their rewards.


The pros and cons of new treatments for type 2 diabetes

Incretins are gut peptides that help regulate glucose metabolism by augmenting the release of insulin. Since 2005, the US Food and Drug Administration has licensed two new classes of drug exploiting this pathway for treating adults with type 2 diabetes. Glucagon-like peptide 1 (GLP-1) analogues, which mimic the action of one of the incretin peptides, were moderately effective in a recent meta-analysis, reducing concentrations of glycated haemoglobin by about 1% compared with placebo (−0.97%, 95% CI −1.13% to −0.81%). But they made up to 57% of patients feel sick. Patients lost an average of 1.4 kg in weight.

The dipeptidyl peptidase 4 (DPP4) inhibitors, sitagliptin and vildagliptin, which prolong the action of incretin peptides, also worked moderately well compared with placebo, but they seemed to increase risk of infection (risk ratio 1.5, 1.0 to 2.2 for urinary tract infections).

Both new classes of agent looked as effective as other treatments for diabetes in the small number of head to head trials. But the evidence has plenty of gaps, and other trials with active comparators have yet to report. It is still unclear where the new drugs fit into the treatment of most adults with type 2 diabetes, say the authors.

JAMA 2007;298:194-206

Genomics starts to deliver on its promises

Scientists are closer than ever to understanding the genetic basis of common diseases, thanks to the accelerating pace of genomics research, say experts from California. In 2007 alone, researchers found DNA markers for obesity, type 2 diabetes, coronary heart disease, and acute lymphoblastic leukaemia—one of the most important childhood cancers.

But it hasn’t been easy or cheap. Studies looking for associations between diseases and variations in the human genome require thousands of patients and fast genotyping technology. For each study, the reagents alone cost $500 000 (£245 000; €363 000) to $1 000 000. Statistics are another problem, as traditional techniques aren’t robust enough to cope with the half a million or so comparisons in genome-wide research.

One ultimate goal is to assemble panels of DNA markers to use as screening tools for common diseases, they say. Another is to use the markers to guide drug development, preferably prophylactic agents for people with variants that cause disease. Both are still some way off. Finding associations is one thing, but discovering how a particular arrangement of DNA causes disease is quite another. We still expect. This trial was powered to detect a probability of developing diabetes of 0.02 and we have much less room for improvement. In 2001 and 2002, 98% of primary care trusts already had quality initiatives, but the authors think that UK general practitioners probably did respond to the financial incentives introduced in 2004. Even before the change, quality of care was highest for patients with coronary heart disease, leaving less room for improvement. In 2001 and 2002, 98% of primary care trusts already had quality initiatives for coronary heart disease in place.

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The UK’s medicines watchdog caused a stir last month when it announced a groundbreaking payment by results plan with the drug company Janssen-Cilag. In draft proposals on which final guidance is due in October, Janssen-Cilag will charge the NHS for bortezomib (Velcade), its new drug for multiple myeloma, only if the patients show a complete or partial response.

It will rebate the full £25 000 (€37 000; $50 000) cost of bortezomib for those who do not respond when treated in line with the drug’s indication—progressive multiple myeloma in patients who have received at least one previous drug and had, or are unsuitable for, bone marrow transplantation. This risk sharing approach is part of a broader effort by healthcare systems around the world to introduce value based pricing, in an attempt to clamp down on rising medicine costs.

Unveiling the proposal, Andrew Dillon, chief executive of the National Institute for Health and Clinical Excellence (NICE), said: “If the drug’s manufacturer accepts the proposals . . . it will mean that when the drug works well the NHS pays but when it doesn’t the manufacturer should bear the cost. All patients suitable for treatment will get the chance to see if the drug works well for them.”

The announcement was a sobering reminder that most medicines do not work in all patients. If that is the case in carefully controlled clinical trials, it is even truer in the real world, where complications and poor compliance in taking drugs correctly lower efficacy still further.

The deal was one of the most striking examples of a tougher attitude to reimbursement around the world. NICE, set up to scrutinise cost and clinical effectiveness of treatments for England and Wales in 1999, is in the vanguard of the movement. Janssen-Cilag had originally sought blanket approval for the NHS to reimburse bortezomib. When that was rejected on grounds of excessive cost relative to the benefits, it appealed unsuccessfully before proposing conditional payment as a last resort. Even then, the company suggested offering a rebate in vouchers for other Janssen-Cilag drugs. NICE held out for straight cash reimbursement.

Other countries are using similar approaches in the face of rising prices for new medicines. Iqwig (the Institute for Quality and Efficiency in Healthcare), NICE’s counterpart in Germany, ruled in 2005 that Pfizer’s anticholesterol drug atorvastatin offered insignificant clinical benefits compared with its off-patent rivals. It ordered reimbursement only at the cost of generic statins, effectively killing the drug in Germany.

Since the early 1990s, Australia’s Pharmaceutical Benefits Advisory Committee has taken a similarly tough approach, with the result that its medicine prices are lower than those in much of the rest of the developed world. Other countries are also considering introducing systems to assess health technology—an idea taken up by the European Union’s High Level Pharmaceutical Forum, convened last year between patients, payers, regulators, and companies to discuss issues including drug pricing.

In the US, the drug companies have lobbied hard against price negotiations by government funded medicine purchasing schemes. But private insurers are becoming tougher. United Healthcare, for instance, last year removed AstraZeneca’s esomeprazole, a proton pump inhibitor, from its formulary, effectively rejecting claims that the drug offered better value for money than the cheaper alternatives. The tensions are only likely to grow, with drug companies charging ever more for medicines—notably those to treat rare “orphan” diseases in small patient groups and in cancer, where the costs can easily exceed $50 000 a year for each patient.

**Market forces**

In theory, a free market for drugs ought to provide value based pricing automatically: the more medicines that exist with similar therapeutic effect, the greater the competition and the lower the price. If a new drug provides additional efficacy and saves health costs overall (such as by providing an alternative to expensive surgery), the more its manufacturer can justifiably charge.

In practice, the relation between value and cost is far less clear, partly because drug pricing is not freely determined but set by government. The UK and Germany come closest to free pricing in Europe, but even in these countries after an initial price has been set—and later scrutinised by NICE or Iqwig—it cannot rise and rarely falls until the patent expires and competition drives down the cost.
Many countries’ governments regularly impose crude price cuts after launch, with little regard to the efficacy of particular drugs. The most recent renegotiation of the UK’s long running pharmaceutical price regulation scheme in 2005 demanded an average reduction of 7% across all drugs, for example.

In a report published earlier this year, the Office of Fair Trading highlighted important weaknesses with the system and called for reforms in order to introduce value based pricing for medicines in the UK.

One idea it endorsed was a risk sharing scheme that GlaxoSmithKline recently began discussing with several European healthcare systems. The company argues that it should be allowed to set an initial price at launch but then be able to raise or lower the price after 1-2 years once meaningful data on its true benefits and costs have been collected.

The Office of Fair Trading also highlighted the possibility of price-volume agreements—a way to deal with the fact that companies launching a drug at a high price for a small group do not then cut the price when it is approved for other indications and used by far larger numbers of patients.

Finally, the office recommended introducing a cap on the price of new drugs that offer only a marginal benefit over existing treatments. However, that raises one of the drug companies’ greatest concerns with value based pricing. They argue that most innovative medicines are developed in stages, with each new drug providing modest improvements that lead to breakthrough medicines over time. Removing the financial incentives for incremental research risks killing off long term progress.

More generally, Arthur Higgins, head of Bayer HealthCare and the newly elected president of the European Federation of Pharmaceutical Industries and Associations, the trade body, says he is open to discussing value based pricing but the industry fears that the approach is being used as a pretext by politicians simply to add additional hurdles to the approval of medicines and save costs.

Value based pricing is a tempting objective for policy makers but far from a universal cure

The industry also argues that many countries that have rejected or aggressively pushed down the price of new medicines have also failed to build—or undermined—a domestic drug industry. Their health systems are free-riding on research funded by more generous payers elsewhere.

There are certainly few research based drug companies in lower priced markets such as Australia or southern Europe, and many more in the US, the UK, and Switzerland, which have paid higher prices and launched other policies to encourage research.

Furthermore, in many European countries the price of generic drugs is only slightly below the patent price. The US, by contrast, stimulates more aggressive competition and much lower generic prices, saving costs and allowing healthcare providers to reward newer patented drugs with higher prices.

Value based pricing offers a separate set of challenges for regulators and advisory bodies such as NICE. Health economics remains a relatively undeveloped and poorly resourced discipline, and there are fierce intellectual debates over how to measure the additional efficacy and cost savings of new drugs. NICE’s own resources would need to be significantly increased to undertake such scrutiny.

Tracking the true costs and benefits of drugs after launch is also likely to be expensive and not always easy to do. It may be feasible for bortezomib, given the infrastructure already in place to monitor patients with myeloma closely. It will prove more difficult for many other treatments.

After NICE rejected NHS reimbursement of interferon beta and glatiramer acetate to treat multiple sclerosis in 2002 as not cost effective, the Department of Health approved the medicines in any case. In a model for bortezomib, it established a pioneering risk sharing system with the manufacturers, who could face price cuts if the treatment results are disappointing.

So far an estimated 10 000 patients are being treated at annual cost of £50m,1 of whom half are being regularly monitored over a decade by researchers. The Multiple Sclerosis Trust, which helps administer the schemes, estimates the system is likely to cost a further £5m. The first assessment is due to be completed this summer, so no price changes have yet been introduced.

Risk sharing offers advantages to companies that can show their medicines provide important extra value to patients. But they will need to be able to prove it with data, and any price reductions implemented in one country are likely to be rapidly imposed in other countries.

More broadly, value based pricing is a tempting objective for policy makers but far from a universal cure. They have to trade price reductions against the need to continue to stimulate future medical innovation.

Above all, drugs typically represent 10-15% of total healthcare expenses in most countries. Value based pricing will probably make only a marginal difference to that proportion. If healthcare providers’ real concern is capping a growth in health spending, they will also need to tackle the more difficult task of limiting salaries, infrastructure, and other far greater drains on their budgets.

Andrew Jack is pharmaceuticals correspondent, Financial Times, London. Andrew.Jack@ft.com

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The proposal by the University and Colleges Union congress to discuss whether it should boycott Israeli academic institutions has caused a furor. The House of Lords set aside time for a debate, and the UK government dispatched a minister to reassure its Israeli counterparts. Full page advertisements appeared in newspapers condemning the decision. The great and the good were mobilised. Irrational, one sided, anti-semitic, and counterproductive were some of the accusations levelled against us for deciding to debate.

As the motion’s mover, I have been subjected to sustained vilification. Supporters of Israel have threatened to destroy the careers of any union members who support a boycott.

The conflation of a boycott proposal and a proposal to debate the appropriateness of a boycott serves the purpose of those who wish to deflect attention from the key issue: the plight of people suffering under occupation.

So why has the union brought this condemnation down on its head? Delegates decided that we could not ignore what is being done in the Occupied Territories, or the denial of educational opportunities and academic freedom to Palestinian students and scholars. Some BMA members have also expressed concern about the complicity of the Israeli Medical Association in the occupation.

The territories, occupied since 1967, have been colonised by Israeli settlements built on illegally confiscated land. The area has been disaggregated and rendered ungovernable by road networks for Israeli use only. Houses are demolished as collective punishments. Farmers are separated from their land, and the supply of water discriminates between the needs of Palestinians and those of Israeli settlers.

In these circumstances, there can be no normal educational provision. Tutors and students face delays and harassment at checkpoints, visa and travel restrictions, and problems of infrastructural decay and underfunding. Work for most inhabitants is all but non-existent, and 46% of the population is suffering from or vulnerable to food insecurity.

In all of this, there is strong evidence of the complicity of Israeli academic institutions. No Israeli college or university has publicly condemned what is being done in the name of every Israeli citizen. Some Israeli educational institutions have established campuses for settlers on illegally confiscated land; others conduct archaeological digs on land from which Palestinian farmers have been expelled.

Some Israeli colleagues have spoken out against the occupation. But these are the heroic few—they risk their careers.

Our boycott debate is accused of infringing academic freedom. It does so, and that is to be regretted. The pursuit of scientific and artistic advance without hindrance is indeed crucial for human improvement. But academic freedom is not an absolute value taking precedence over all else. The values of human life and dignity are the ultimate objectives, and sometimes these may not be entirely compatible with untrammeled academic freedom.

We are also accused of interfering with free speech. But it is our opponents who are trying to prevent such a debate from taking place.

Unfair to Israel?

We are accused of singling out Israel—the Jewish state—and of being anti-semites. We are asked why we do not propose a boycott of other states whose policies are barbaric, such as China, Saudi Arabia, Iran, or Zimbabwe.

But whether a boycott is appropriate in such places depends on the merits of each individual case. In the case of Israel, we are speaking about a society whose dominant self image is one of a bastion of civilisation in a sea of medieval reaction. And we are speaking of a culture, both in Israel and in the long history of the Jewish diaspora, in which education and scholarship are held in high regard. That is why an academic boycott might have a desirable political effect in Israel, an effect that might not be expected elsewhere.

Anti-semitism?

The accusation of anti-semitism is absurd and offensive. Accusing those who criticise Israel of being anti-semites presumes an identity of interests between Israel and all Jewish people. This is contrary to the facts. Most people who spoke in favour of the motion at our congress are Jewish, as are the members of the British Committee for the Universities of Palestine. The response of Israel’s defenders is to say that such people are not proper Jews—that they are “self-hating Jews.” Jewishness thus is transformed from a cultural or religious identity into an ideological position.

The result of the debate may not be a decision to boycott. If that is so, it will not be because most members are unconcerned about the plight of the Palestinians. It would be because an alternative proposal for their aid and support, and for opposing the policies of the Israeli state, had emerged.

The boycott would be of Israeli academic institutions only. We would not sever links with Israeli colleagues. This would be counterproductive. Individual and group collaboration on joint projects could continue, as long as such projects were not formally sponsored by Israeli institutions.

The fundamental issue is how to raise the current outrages to national and international prominence. Whether an institutional boycott is the most appropriate tactic will remain an open question. What is not, and cannot be, open is whether it is appropriate to debate and discuss the pros and cons of the tactic.

If Israeli academic institutions are complicit in the inhuman treatment of the Palestinians, doing nothing would also make us complicit, if only by default. We cannot turn away and say, “Business as usual.”

Competing interests: None declared.
Tony Blair’s appointment as Middle East peace envoy is intended to invigorate the peace process. **Tom Hickey** thinks boycotting universities might encourage the Israeli government to reach a settlement, but **Michael Baum** believes collaboration is a more effective way forward

Michael Baum: professor emeritus of surgery, University College London, London WC1E 6AU. michael@baum freeserve.co.uk

First of all I should declare a conflict of interest. I am a Jew and a Zionist. I consider myself a secular Jew who abhors the fanaticism among West Bank settlers. I support a two state solution. The Palestinians must have self-determination; 60 years of statelessness after the British mandate is enough. This position is held by all my Israeli academic friends and colleagues. These academics are the very constituency the boycotters are targeting and are disproportionately represented in the peace camp. How can alienating this group enhance the peace process?

The Israeli universities and research institutes are no more agents of Israel than Oxford or Cambridge are of the United Kingdom. And they are not responsible for repression of Palestinians in the Occupied Territories—a policy which is universally unpopular. Furthermore, it is nonsense to suggest that you can target the institution without damaging the individual.

**Multicultural society**

Let me also dismiss the big lie that Israel is an apartheid state. Israel is a multicultural mosaic with Jews, Muslims, Christians, and other faiths. Druze, Bahá’í, and Armenian Christians chose to live there after persecution in Muslim countries. Only malign commentators can be blind to the Arabs who form 20% of Israeli citizens. They are free to vote and express their views (including the right to campaign against the state itself) and serve in the cabinet. Arab judges hold high office and newspapers argue the Palestinian cause.

My first hand experience of Israel started as a young surgeon in 1963-4. I worked in northern Israel in a hospital serving Arab villages, kibbutzim, new immigrant townships, and ancient communities of Arabs and Jews in Nazareth, Afula, and Tiberias. A fifth of the doctors and nurses were Arabs, trained at the expense of the Israeli government. Arab and Jewish patients were treated with the same respect in adjacent beds. This is still true in all Israeli hospitals. It is also a lie to suggest that the Israel Medical Association is complicit in the ill treatment of prisoners.1 I would go even further and state that Israel provides more academic freedom for Arab scholars than anywhere else in the Middle East.

There are numerous examples of Palestinian and Israeli collaborations. For example, the Israel Cancer Association funds initiatives that benefit both Israeli and Palestinian patients and their families. These include the Breast Care Centre at the Holy Family Hospital in Nazareth, which holds joint sessions with Israeli Jewish and Arab women and Palestinians who share common experience as survivors of breast cancer. Hadassah Hospital and the Hebrew University in Jerusalem provide outreach programmes for the Occupied Palestinian Territory. Poor children from the territory get free, state of the art treatment, often supported by the Peres Foundation. Ben Gurion University of the Negev has launched the joint Israel-Jordan-Palestine project for improvement of motor skills in children with cerebral palsy and also funds the work of Ohad Birk (Israeli Jewish), Izzedulin Abuelaish (Gaza Palestinian), and Khalil Elbedour (Israeli Bedouin), who have unravelled rare genetic disorders among Negev Bedouin.

Universities must encourage a spirit of inquiry, where members join in dialogue, with freedom of expression, learning from each other’s narratives. As Malcolm Grant, provost of University College London, put it: the boycott “betrays a misunderstanding of the academic mission which is founded squarely on academic freedom of inquiry and freedom of speech” Lord Adonis went further in the House of Lords:

“Not only would a boycott be inconsistent with the spirit of openness and tolerance that should inform public life. It would also be counter-productive. Education plays a vital role in developing and aiding understanding between different people. It is therefore all the more important to keep open channels of communication with academic and educational institutions in the Middle East during these difficult times.”

Finally, we shouldn’t lose sight of the fact that this call for a boycott damages the reputation of British academia in the eyes of the wider world.3

**Balance and cooperation**

There are two narratives concerning the tragic history of the Israeli-Palestinian conflict. Both have verity, yet they are recounted as if one had the monopoly of truth. To accept one side only and delegitimise Israel shows either ignorance or malice. For a balanced account I commend *City of Oranges*, which tries to look at the history of Jaffa, a microcosm of the wider conflict, from both sides.1

Instead of boycott, might I suggest a more constructive approach, emulating my late brother, David? David died eight years ago while president of the Royal College of Paediatrics and Child Health. His last act was to establish a sick children’s clinic in Gaza. His family continue this legacy through the David Baum International Foundation at the college. I believe passionately that we can all do our bit for peace by building bridges between British, Israeli, and Palestinian academics and physicians. Through this collaboration and dialogue the health and welfare of all will improve, leading to increasing mutual respect and trust; sowing seeds for a peaceful solution ahead of any “road map.”

**Competing interests:** As stated at the start of this article. References are in the full version on bmj.com.

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MMR: the scare stories are back

A UK newspaper has once again linked autism with MMR and sparked a spate of media scaremongering. But the original story was wrong on every count, writes Ben Goldacre

It was inevitable that the media would re-ignite the MMR (measles, mumps, rubella) autism scare during Andrew Wakefield’s General Medical Council hearing (see p 118). In the past two weeks, however, one front page splash in the broadsheet Sunday newspaper the Observer (8 July) has drawn widespread attention: the newspaper effectively claimed to know the views of named academics better than those academics themselves, and to know the results of research better than the people who did it. Smelling a rat—as one might—for once, I decided to pursue every detail.

The Observer’s story made three key points: that new research had found an increase in the prevalence of autism, to 1 in 58; that the lead academic on this study was so concerned he suggested raising the finding with public health officials; and that two “leading researchers” on the team believed that the rise was due to the MMR vaccine. By the time the week was out, this story had been recycled in several other national newspapers, and the 1 in 58 figure had even been faithfully reproduced in a BMJ news article (doi:10.1136/bmj.39272.468044.4E).

On every one of these three key points the Observer story was simply wrong.

The newspaper claimed that an “unpublished” study from the Autism Research Centre in Cambridge had found a prevalence for autism of 1 in 58. I contacted the centre: the study that the Observer reported is not finished and is not published. The data have been collected, but they have not been analysed.

Unpublished data is a recurring theme in MMR scares, and it is the antithesis of what science is about: transparency, where anyone can read the details of this study illustrate just how important this transparency is. The study was specifically designed to look at how different methods of assessing prevalence affected the final figure. One of the results from the early analyses is “1 in 58.” The other figures were less dramatic, and similar to current estimates. In fact the Observer now admits it knew of these figures and that these should have been included in the article. It seems it simply cherry picked the single most extreme number—from an incomplete analysis—and made it a front page splash story.

And why was that one figure so high anyway? The answer is simple. If you cast your net as widely as possible, and use screening tools and many other methods of assessment, and combine them all, then inevitably you will find a higher prevalence than if—for example—you simply trawl through local school records and count your cases of autism from there.

This is not advanced epidemiology, impenetrable to journalists—this is basic common sense. It would not mean that there is a rise in autism over time, compared with previous prevalence estimates, but merely that you had found a way of assessing prevalence that gave a higher figure. More than that, of course, when you start doing a large scale prevalence study, you run into all kinds of interesting new methodological considerations: is my screening tool suitable for use in a mainstream school environment? how does its positive predictive value change in a different population with a different baseline rate? and so on.

These are fascinating questions, and to answer them statisticians and epidemiologists were invented. As Professor Baron-Cohen, lead author on the study, says: “This paper has been sitting around for a year and a half specifically because we’ve brought in a new expert on epidemiology and statistics, who needs to get to grips with this new dataset, and the numbers are changing. If we’d thought the figures were final in 2005, then we’d have submitted the paper then.”

The Observer, however, is unrepentant: it has the “final report.” And what is this document? I can’t get the paper to show it to me (and what kind of a claim about scientific evidence involves secret data?), but grant giving agencies expect the figures were final in 2005, then we’d have submitted the paper then.”

The Observer has is simply the last of those: “That might have been titled ‘final report,’” said Professor Baron-Cohen. “It just means the funding ended, it’s the final quarterly report to the funders. But the research is still ongoing. We are still analysing.”

But these are just nerdy methodological questions about prevalence (if you skip to the end, there is some quite good swearing). How did the Observer manage to crowbar MMR into this story? Firstly, it cranked up the anxiety. According to the Observer, Baron-Cohen “was so concerned by the 1 in 58 figure that last year he proposed informing public health officials in the county.”

But Professor Baron-Cohen is clear: he did no such thing, and this was simply scaremongering. I put this to the Observer, which said it had an email in which Baron-Cohen did as the paper claimed. Observer staff gave me the date. I went back to the professor, who went through his emails. We believe that I too now have the email to which the Observer refers. It is one sentence long, and it is Professor Baron-Cohen asking if he can share his and the other researchers’ progress with a clinical colleague in the next door office. This dramatic smoking gun reads: “can i share this with ayla and with the committee planning services for AS [autism services] in cambridgeshire if they treat it as strictly confidential?”

Professor Baron-Cohen told me, “That’s not saying I'm concerned, or that we should notify anybody; these are just the people who run the
apparently the

The media have diligently avoided writing anything on the negative findings in autism research. Instead they have chosen repeatedly to concoct huge stories from the “concerns” of “experts” and research that is unpublished and inaccessible.
Getting America to take the shame

Film maker Michael Moore is to be thanked for holding up mirrors to the US healthcare system.

Can anyone in Canada, Europe, or Cuba imagine a hospital that calmly quotes a patient showing up with two sawn off fingertips a price of $60,000 to repair one of the two fingers and a “bargain price” of only $12,000 to repair the other, and then to ask this hapless, bleeding, and uninsured patient to make on the spot a rational consumer choice between three options: no service, repair of the “low cost” finger only, or repair of both the low cost and high cost fingers? (The “consumer” in the vignette chose the second option.)

To some dyed in the wool libertarian American economists, this scenario may be the ultimate dream of “consumer driven health care,” based on the theory that patients can be retrained to act as smart, well informed consumers of health care. Elsewhere in the United States, this vignette is apt to be viewed as a source of national shame. No well balanced scholarly paper and no equally balanced testimony before Congress could ever kindle that sense of shame among Americans as well as Michael Moore does in Sicko.

Moore’s vignettes should not be seen as rare and isolated instances. Several years ago the Wall Street Journal featured on its front pages a series of investigations by staff reporter Lucette Lagnado chronicling the plight of uninsured Americans in need of hospital care. One low income American, whose wife had been treated for cancer at a non-profit academic health centre, had incurred a hospital bill of some $20,000. In the five years after her death, her husband—an unskilled, low paid worker—was mercilessly hounded by the hospital for payment of that bill. Although over the years he did pay installments adding up to nearly the original $20,000, interest charges and legal costs had puffed up the amount owed to the hospital to over $50,000. In another vignette, an uninsured waitress working at a pizza parlour had incurred a hospital bill of several thousand dollars as the result of a miscarriage. Fearful that a judge might force her to agree to an unaffordable payment schedule, she had failed to show up at a court hearing, whereupon she was arrested and briefly jailed.

To Canadians and Europeans it will be incomprehensible that in for-profit and non-profit hospitals alike, along with community pharmacies, bills for uninsured patients, who typically are from the lower income strata, are routinely twice or three times higher than the prices paid by private insurance companies. Jailing a mother of two over an unpaid hospital bill caused by a miscarriage would be even more incomprehensible. Surely it can fairly be asked, as Moore does, why these harsh edges are necessary in a system that spends almost twice as much per capita on health care as does neighbouring Canada and many times more than comparable European countries. Indeed, it can be asked what Canada’s or Europe’s health systems could offer their citizens if, like the United States, they chose to allocate 16% of their gross domestic product to health care, rather than the 9% to 10% these countries actually spend.

It remains to be seen what impact Moore’s Sicko ultimately will have on the forthcoming debate over health reform in the United States, and on the plight of underprivileged people in America on obtaining health care. Meanwhile, Americans should be thankful that Moore uses his talent and his financial resources to hold up mirrors in which they can behold the blemishes in their complexion. It is one necessary step on the way to a better countenance.

Uwe E Reinhardt is James Madison professor of political economy, Princeton University, Princeton, NJ, United States reinhard@princeton.edu
Uncertainty in classification of repeat sudden unexpected infant deaths in Care of the Next Infant programme

It is misleading to classify every unexplained infant death as natural if no unnatural cause has been established, argue CJ Bacon and EN Hey

Sudden unexpected infant death (cot death) has become much less common in recent years, and it is rare for a family to experience two such deaths. Carpenter and colleagues recently published valuable data on the repeat deaths that occurred among 5229 families in the Care of the Next Infant programme.1 This voluntary scheme funded by the Foundation for the Study of Infant Deaths provides extra support to families in England and Wales who have had a cot death and now have a new baby. There were 48 sudden unexpected deaths among babies on the programme between 1988 and 1999, including two third deaths. After examining all the circumstances and postmortem findings of the 46 second deaths, the authors concluded that all but six of the babies died from natural causes. This contrasts with earlier studies by Emery2 and Wolkind and colleagues,3 which concluded that a much higher proportion of repeat cot deaths were probably homicides.

Apart from two short letters,4 5 Carpenter and colleagues’ report was initially unchallenged. It has proved very influential, being accepted by bodies such as the American Academy of Pediatrics.9 More recently, however, Gornall published a wide ranging critique of how the authors presented their data.7 The authors defended their classification,8 but we believe their dichotomy of the deaths into natural or unnatural is particularly open to criticism. Experience in child protection teaches that it is often impossible to determine whether the parents have been in some way and to some degree responsible for the unexplained death of their baby.

In this article we show how many of the second deaths might be more appropriately categorised as “undetermined” rather than “natural.” This approach is now favoured by many pathologists when reporting on unexplained infant deaths.9

Analysis
Carpenter and colleagues divided families into groups with similar patterns of first and second deaths (table). We have not attempted to examine the first deaths because the published details are insufficient. From the information given in the paper we have reassessed the 46 second deaths to see how many might reasonably be regarded as undetermined. We take “natural deaths” to be deaths arising from disease or a wholly accidental event, “unnatural deaths” to be deaths due to homicide (murder, infanticide, or manslaughter), and “covert homicide” to be an unnatural death that was not initially recognised as such.

Classification
Second death homicide
In six families the authors classified the second death as unnatural. This was obvious in four cases: in one there was a serious head injury and a criminal conviction; in the other three there was inflicted injury but nobody was prosecuted, either because it was unclear who was responsible or because the perpetrator was a juvenile. In the other two cases homicide was not initially recognised, despite the presence of fractured ribs. A family court later decided one death was homicide. The other was initially attributed to sudden infant death syndrome but was reclassified as homicide after the father confessed to suffocating another child and was convicted of the murder of all three babies. Thus in all the six deaths that the authors classified as unnatural, either a court pronounced the death to be homicide or the evidence of homicide was extremely strong.

Original and alternative assessment of 46 second sudden unexpected infant deaths

<table>
<thead>
<tr>
<th>Group of cases</th>
<th>Original assessment</th>
<th>Alternative assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Natural</td>
<td>Unnatural</td>
</tr>
<tr>
<td>Both deaths explained</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>One explained and one unexplained death</td>
<td>6</td>
<td>6*</td>
</tr>
<tr>
<td>Both deaths unexplained</td>
<td>18</td>
<td>12*</td>
</tr>
<tr>
<td>Information incomplete because:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Further review was declined</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Mother was murdered</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Case was under legal review</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total (%)</td>
<td>40 (87%)</td>
<td>6 (13%)</td>
</tr>
</tbody>
</table>

*Re-assessment not possible because the original paper provides no information on these cases.†Numbers allotted to each category are arbitrary (for explanation see text).
Both deaths explained
In three families both deaths were attributed to specific natural causes: a familial metabolic defect in both babies, long QT syndrome in both babies, and pneumonia in the first baby followed by endomyocardial fibroelastosis in the second. Postmortem examination of the second baby whose death was ascribed to metabolic defect showed rib fractures, which were attributed to resuscitation. This was one of four cases in the study in which, despite the presence of fractured ribs, death was initially thought to be natural (although two of these, not including the metabolic defect case, were later reclassified as unnatural). A recent literature review shows that resuscitation very rarely breaks children’s ribs and when it does the site is always anterior.10 Most rib fractures in babies are posterior and indicate abuse, as may some anterior fractures. This suggests that when rib fractures are found in addition to a natural disorder, the natural disorder cannot be assumed to be the cause of death. However, in the absence of details of the site of the fractures this particular case must remain categorised as natural. As regards the second baby whose death was attributed to long QT syndrome, at the inquest into the child’s death the coroner recorded an open verdict, which indicates that he did not consider the evidence sufficient to attribute the death to natural causes.11 On this basis, we have recategorised this death as undetermined.

One explained and one unexplained death
In six families one death was attributed to a specific natural cause and the other to sudden infant death syndrome. The authors gave no additional information so we cannot review the categorisation of these cases.

Both deaths unexplained
In 18 families both deaths were attributed to sudden infant death syndrome. The authors state that all these families were at high risk of cot death and that the second deaths exhibited many untoward features: violent family relationships (9 cases), pathology findings suggestive of asphyxia (9), parental mental health problems (6), concern about the welfare of a subsequent baby (4), imprisonment of the father (3), previous apparent life threatening events (3), deafness of both parents (2), open coroner’s verdict (2), failure to thrive (1), and abuse of a previous child (1).

One of the difficulties in distinguishing between sudden infant death syndrome and covert homicide is that both tend to occur against a background of social disadvantage.12 13 The features reported in these families could have been associated with either. We do not suggest that violence in the family, for example, necessarily implies that a baby’s death was unnatural; but we think that when the family has two unexplained deaths this possibility at least has to be considered and may sometimes be true. To most observers the number of untoward features in these 18 cases would seem disproportionate. Since the available information does not allow individual assessment of each case, we have resorted to the arbitrary estimate that a third of them might be classed as undetermined.

Many of the deaths in this group had features of asphyxia. This raises the questions of whether some should have been attributed to unintentional harm rather than to sudden infant death syndrome, and whether in some the circumstances were such that they might have been regarded as unnatural—as two of the authors had previously suggested.14 Another unusual finding was successive unexplained deaths of babies in two families in which both parents were profoundly deaf. Such a concurrence of extremely rare events is unlikely to have resulted from chance alone and raises the question of whether the deaths were in some way related to the deafness or an associated disorder.15 16 One of these, long QT syndrome, was considered but discounted by Carpenter and colleagues and is not supported by a recent genetic study.17 Whatever the explanation, this finding is important and suggests that babies of profoundly deaf parents should receive extra surveillance.

Information incomplete
Information on the second death was incomplete for 13 families. In one of these the mother was murdered. In five families further inquiry was not attempted because the police had become involved. In two of these a parent faced prosecution (though neither finally resulted in conviction), and in three the other children were taken into care. The authors classified these five deaths as natural, apparently because they regarded judicial decisions or decisions not to prosecute as equivalent to medical diagnoses. We do not think this is justified. In criminal trials the jury must be persuaded beyond reasonable doubt that the defendant is guilty, and the Crown Prosecution Service recommends prosecution only when it considers that a court “is more likely than not to convict” and that prosecution is in the public interest.18 Failure to reach the high level of proof required in criminal proceedings does not mean that a possible cause of death has been excluded by the normal standards of medical diagnosis. We therefore categorise these five cases as undetermined.
In another seven families further inquiry was declined. The second baby to die in one family had two fractured ribs and a healing fracture of the clavicle, and a third death in another family resulted in all the remaining children being taken into care. Four of the babies in these families died while sleeping with a parent on a sofa. In the absence of more complete information, classification of all these deaths as natural seems unwarranted. The authors, however, acknowledge the information was insufficient to enable them to distinguish between sudden infant death syndrome and a specific natural cause. Since distinction between sudden infant death syndrome and covert homicide can be equally difficult, it seems illogical to exclude covert homicide when there is not enough information to exclude a specific natural cause.

**Discussion**

The table summarises how an alternative analysis of these second deaths might categorise 13% as probably unnatural, 43% as probably natural (although this includes the six cases we could not review), and 43% as undetermined. This contrasts with the assessment by Carpenter and colleagues that 87% of the deaths were natural. But it is closer to the findings of Emery and colleagues, who thought that about two fifths of the unselected repeat deaths they studied probably resulted from homicide.

Our purpose is not to second guess the original authors, who, being directly involved in the cases and having access to additional information, were much better placed than we are to assess them. However, we hope we have shown how a comparatively small change of perspective can result in a large change in the conclusions reached. We think the perspective we have taken is no less reasonable than that of the paper’s authors and would be shared by most paediatricians. Most, for example, would not designate as “natural” so-called accidents that are entirely foreseeable and preventable.

We acknowledge that our assessments may be wrong, which is why in the table we prefix the categories natural and unnatural with probably, as well as introducing the third category of undetermined. We think using a dichotomy of natural or unnatural is unhelpful. It glosses over complexities and uncertainties and fosters polarisation. It is also more likely to be erroneous, as shown by the case where two deaths that were classified natural had to be reclassified after a third baby was murdered. Uncertainty may be uncomfortable, but it is truer to reality, more conducive to scientific inquiry, and safer for children than a dogmatic stance at either pole.

It is unfortunate that the summary that headed the paper was much more categorical than the text, which is not easy to follow and will have been less widely read. We do not think the summary’s unqualified assertion that 40 out of 46 repeat unexplained infant deaths were natural is justified by the data presented. Furthermore, quoting precise confidence intervals for numbers derived from subjective judgment imparts a false veneer of precision.

The paper will help avert unjustified suspicion of parents, which is important, but we are concerned that it may also lead to mistakes in child protection. Following a recent decision in the Court of Appeal, the Crown Prosecution Service is less likely to embark on the prosecution of a mother suspected of causing the death of her baby. This will be generally welcomed. The process of child protection, however, has to be uncoupled from decisions about criminal proceedings. We would encourage professionals to keep an open mind in assessing unexplained infant deaths, to be aware of the difficulties in diagnosis, and to try to keep a balance between the need to support parents and the need to protect children.

**Contributors and sources:** CJB has long had an interest in cot death and has been a leading participant in regional and national studies, while ENH has conducted and reported on many studies relating to neonatal and infant deaths. This article, first submitted in October 2006, arose from discussions with other paediatricians who were concerned about the conclusions and possible effects of the paper in question. Both authors contributed equally to this article. CJB is guarantor.

**Competing interests:** Both authors have worked for the Foundation for the Study of Infant Deaths. CJB as trustee then as medical adviser, ENH as an honorary scientific adviser. CJB has written court reports in cases involving unexpected infant death, for which he received the standard fee.

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

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Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial

Andrew Farmer, lecturer,1 Alisha Wade, resident,2 Elizabeth Goyder, reader,3 Patricia Yudkin, reader,1 David French, reader,4 Anthea Craven, trial manager,1 Rury Holman, professor,5 Ann-Louise Kinmonth, professor,6 Andrew Neil, professor,7 on behalf of the Diabetes Glycaemic Education and Monitoring Trial Group

ABSTRACT
Objective To determine whether self monitoring, alone or with instruction in incorporating the results into self care, is more effective than usual care in improving glycaemic control in non-insulin treated patients with type 2 diabetes.

Design Three arm, open, parallel group randomised trial.
Setting 48 general practices in Oxfordshire and South Yorkshire.
Participants 453 patients with non-insulin treated type 2 diabetes (mean age 65.7 years) for a median duration of three years and a mean haemoglobin A1c level of 7.5%.

Interventions Standardised usual care with measurements of HbA1c every three months as the control group (n=152), blood glucose self monitoring with advice for patients to contact their doctor for interpretation of results, in addition to usual care (n=150), and blood glucose self monitoring with additional training of patients in interpretation and application of the results to enhance motivation and maintain adherence to a healthy lifestyle (n=151).

Main outcome measure HbA1c level measured at 12 months.

Results At 12 months the differences in HbA1c level between the three groups (adjusted for baseline HbA1c level) were not statistically significant (P=0.12). The difference in unadjusted mean change in HbA1c level from baseline to 12 months between the control and less intensive self monitoring groups was −0.14% (95% confidence interval −0.35% to 0.07%) and between the control and more intensive self monitoring groups was −0.17% (−0.37% to 0.03%).

Conclusions Evidence is not convincing of an effect of self monitoring of blood glucose, with or without instruction in incorporating findings into self care, compared with standardised usual care can improve glycaemic control in patients with non-insulin treated diabetes.

METHODS
The diabetes glycaemic education and monitoring (DiGEM) study was a four year open, randomised, three arm, parallel group trial with sequential recruitment of patients from general practices in Oxfordshire and South Yorkshire. The trial was managed from the coordinating centre at the Department of Primary Health Care, University of Oxford.3

Our primary aim was to determine whether haemoglobin A1c (HbA1c) levels at 12 months were significantly different between patients with non-insulin treated type 2 diabetes receiving one of three allocated interventions: standardised usual care with measurements of HbA1c levels by health professionals every three months (control group); use of a blood glucose meter, with advice for participants to contact their doctor for interpretation of results (less intensive self monitoring); and use of a blood glucose meter with training in self interpretation and application of the results to diet, physical activity, and drug adherence (more intensive self monitoring).
Patients were eligible for randomisation if they had type 2 diabetes, were aged 25 years or more at diagnosis, were managed with diet or oral hypoglycaemic agents alone, had an HbA1c level ≥6.2% at the assessment visit, and were independent in activities of daily living. Exclusion criteria were the use of a blood glucose monitor twice a week or more often over the previous three months, serious disease or limited life expectancy that would make intensive glycaemic control inappropriate, or inability to follow trial procedures.

Outcome measures

The primary outcome was the HbA1c level at 12 months. Secondary outcomes were blood pressure, weight, total cholesterol level, ratio of total cholesterol to high density lipoprotein cholesterol, and body mass index. HbA1c was measured using a Variant II Hemoglobin Testing System (Bio-Rad Laboratories, Hercules, CA) certified by the US glycohaemoglobin standardisation programme and comparable to the diabetes control and complications trial standard, with an interassay coefficient of variation across the range of the assay of less than 2%. Cholesterol was assayed in local laboratories and the results aligned with results of a sample of paired specimens analysed with an automated chemistry analyser (Olympus AU400; Olympus, Tokyo), with interassay coefficients of variation across the range of less than 2%. Blood pressure was measured twice in the right arm, with the participant seated, using a UA-779 electronic blood pressure monitor (A&D instruments, Abingdon), and the mean of these values was analysed.

We transcribed the frequency of blood glucose testing from patient held diaries. Episodes of hypoglycaemia were categorised as grade 2 (mild symptoms requiring minor intervention), grade 3 (moderate symptoms requiring immediate third party intervention), or grade 4 (unconscious). Increases in hypoglycaemic drugs were defined as an increase in the dose or frequency prescribed, progression from use of a single oral agent to combination oral therapy, or addition of insulin to the treatment regimen.

To characterise the groups and identify subgroups for predefined analysis at 12 months we collected additional personal and clinical data on duration of diabetes, drug treatment, diabetes related complications, and EuroQol (EQ-5D) score.10

Randomisation

We used computerised randomisation (Minim, www.sghms.ac.uk/depts/phs/guide/randser.htm) incorporating a partial minimisation procedure to adjust the randomisation probabilities between groups to balance three important covariates collected at baseline: duration of diabetes, HbA1c level, and current treatment (diet, oral monotherapy, or oral combination therapy). The minimisation procedure to assign patients to their allocated intervention was conducted independently of the research nurses who managed recruitment and carried out the assessment visit. The allocation was also concealed from laboratory staff.

Procedures

We identified patients suitable for trial inclusion from lists held on computer by their general practitioners. Those eligible were sent an invitation to participate signed by their general practitioner accompanied by an information sheet and a reply paid envelope. One further letter was sent if no response was received within one month.

Eligibility for the trial and willingness to be randomised to self testing of blood glucose was confirmed by a preassessment phone call and at the visit for assessment. At the assessment visit, after obtaining informed consent, beliefs about diabetes were elicited using a standard approach to help patients understand how diabetes might present a threat to their health.11 The roles of diet, physical activity, and drugs were discussed within the framework of the commonsense model of illness representation,12 in which we set out to optimise the use of feedback on glucose levels to
facilitate behaviour change through influencing beliefs. The behaviour change techniques were selected on the basis of evidence for effectiveness and included goal setting and review of physical activity and eating patterns to help patients with lifestyle change.12 13 The goal setting and review approach was continued in subsequent visits. Baseline blood tests and clinical measurements were taken and questionnaires completed at the assessment visit.

Interventions

After the assessment visit and confirmation of eligibility, patients were allocated to receive one of the three interventions. The rationale behind these interventions is described in more detail elsewhere.9 The intervention was initiated at the first visit after randomisation and continued at the scheduled visits at one, three, six, and nine months. Each of the three interventions included a series of standardised components.

Patients allocated to the control intervention received standardised usual care, including the use of goal setting and review. They were asked not to use a blood glucose meter unless their doctor considered it essential for their clinical management. A diary was used to record self care goals and strategies for achieving them.

Patients allocated to the less intensive self monitoring intervention continued to use the goal setting and review techniques introduced at the assessment visit. In addition they were given a blood glucose meter. They were asked to record three values daily on two days during the week (one after fasting and the other two before meals or two hours after meals) and to aim for glucose levels of 4-6 mmol/l after fasting and before meals and levels of 6-8 mmol/l two hours after meals. They were advised by the nurse to consider contacting their doctor if readings were consistently high (>15 mmol/l) or low (<4 mmol/l). They were not given information about how to interpret their blood glucose readings. Separate diaries were used to record identified goals and activity and to record blood glucose results.

Follow-up visits differed in content according to the allocated intervention in line with usual practice. Patients allocated to the control intervention had a blood test to measure HbA1c level two weeks before their scheduled visit, the result of which was fed back to them as an indication of the impact of their self care activities on their glycaemic control. Blood glucose values were reviewed at the scheduled visit for those allocated to self monitoring, and patients were told to seek advice from their doctor if fasting values were persistently greater than 6 mmol/l. Patients in each arm of the trial received feedback on glycaemic control, which was used to explore success of goals and to set new ones. The patient’s doctor was notified of all HbA1c results and asked to consider changes in drugs in line with the National Institute for Clinical Excellence diabetes guidelines for all patients.14 The doctor was also notified if blood glucose readings were consistently greater than 15 mmol/l.

The meters were calibrated to provide plasma equivalent results (Optium, Abbott Diabetes Care, Maidenhead, UK). Calibration of the meters was

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control group* (n=152)</th>
<th>Meter group; less intensive self monitoring (n=150)</th>
<th>Meter group; more intensive self monitoring (n=151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>66.3 (10.2)</td>
<td>65.2 (10.6)</td>
<td>65.5 (9.9)</td>
</tr>
<tr>
<td>Men</td>
<td>85 (55.9)</td>
<td>88 (58.7)</td>
<td>87 (57.6)</td>
</tr>
<tr>
<td>Occupational group:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Professional, managerial, and clerical</td>
<td>80 (52.6)</td>
<td>81 (54.0)</td>
<td>84 (55.6)</td>
</tr>
<tr>
<td>Skilled manual or manual</td>
<td>69 (45.4)</td>
<td>68 (45.3)</td>
<td>66 (43.7)</td>
</tr>
<tr>
<td>No occupation stated</td>
<td>3 (2.0)</td>
<td>1 (0.7)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Age (years) at leaving full time education:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;17</td>
<td>109 (71.7)</td>
<td>114 (76.0)</td>
<td>121 (80.1)</td>
</tr>
<tr>
<td>17 or 18</td>
<td>20 (13.2)</td>
<td>14 (9.3)</td>
<td>13 (8.6)</td>
</tr>
<tr>
<td>&gt;18</td>
<td>23 (15.1)</td>
<td>22 (14.7)</td>
<td>17 (11.3)</td>
</tr>
<tr>
<td>Cigarette consumption:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>58 (38.2)</td>
<td>54 (36.2)</td>
<td>54 (35.8)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>80 (52.6)</td>
<td>74 (49.7)</td>
<td>77 (51.0)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>14 (9.2)</td>
<td>21 (14.1)</td>
<td>20 (13.2)</td>
</tr>
<tr>
<td>Duration of diabetes and treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range) duration (years) of diabetes</td>
<td>3(2-6)</td>
<td>3(2-7)</td>
<td>3(2-6)</td>
</tr>
<tr>
<td>Treatment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet only</td>
<td>44 (28.9)</td>
<td>39 (26.0)</td>
<td>41 (27.2)</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>57 (37.5)</td>
<td>58 (38.7)</td>
<td>58 (38.4)</td>
</tr>
<tr>
<td>Combined oral therapy</td>
<td>51 (33.6)</td>
<td>53 (35.3)</td>
<td>52 (34.4)</td>
</tr>
<tr>
<td>Presence of diabetes related complications</td>
<td>32 (21.1)</td>
<td>32 (21.3)</td>
<td>39 (25.8)</td>
</tr>
<tr>
<td>Use of blood glucose meter:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not using</td>
<td>104 (68.4)</td>
<td>110 (73.3)</td>
<td>102 (67.5)</td>
</tr>
<tr>
<td>Using once weekly or less</td>
<td>48 (31.6)</td>
<td>40 (26.7)</td>
<td>49 (32.5)</td>
</tr>
<tr>
<td>Physical and laboratory findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) haemoglobin A1c (%)</td>
<td>7.49 (1.09)</td>
<td>7.41 (1.02)</td>
<td>7.53 (1.12)</td>
</tr>
<tr>
<td>Mean (SD) total cholesterol level (mmol/l)</td>
<td>4.7 (1.1)</td>
<td>4.6 (1.1)</td>
<td>4.7 (1.1)</td>
</tr>
<tr>
<td>Mean (SD) blood pressure (mm Hgl):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>140 (18)</td>
<td>141 (17)</td>
<td>137 (18)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80 (10)</td>
<td>80 (10)</td>
<td>78 (10)</td>
</tr>
<tr>
<td>Mean (SD) body mass index</td>
<td>30.9 (6.1)</td>
<td>31.9 (6.2)</td>
<td>31.0 (5.3)</td>
</tr>
</tbody>
</table>

*No use of blood glucose meter.
Table 2: Changes in haemoglobin A1c levels, weight, and body mass index between baseline and one year in patients with non-insulin treated type 2 diabetes, by randomisation group. Values are means (standard deviations) unless stated otherwise.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group* (n=152)</th>
<th>Meter group, less intensive self monitoring (n=150)</th>
<th>Meter group, more intensive self monitoring (n=151)</th>
<th>P value for difference between groups†</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>Baseline</td>
<td>7.49 (1.09)</td>
<td>7.41 (1.02)</td>
<td>7.53 (1.12)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>7.49 (1.20)</td>
<td>7.28 (0.88)</td>
<td>7.36 (1.05)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−0.00 (1.02)</td>
<td>−0.14 (0.82)</td>
<td>−0.17 (0.73)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>Baseline</td>
<td>140 (18)</td>
<td>141 (17)</td>
<td>137 (18)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>136 (18)</td>
<td>137 (17)</td>
<td>134 (17)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−4 (14)</td>
<td>−3 (16)</td>
<td>−3 (14)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>Baseline</td>
<td>80 (10)</td>
<td>80 (10)</td>
<td>78 (10)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>77 (10)</td>
<td>78 (10)</td>
<td>76 (10)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−3 (9)</td>
<td>−2 (9)</td>
<td>−2 (8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>Baseline</td>
<td>86.7 (18.9)</td>
<td>90.4 (18.9)</td>
<td>86.9 (16.4)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>86.4 (19.4)</td>
<td>89.9 (19.0)</td>
<td>86.1 (15.7)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−0.3 (2.7)</td>
<td>−0.5 (2.6)</td>
<td>−0.8 (3.3)</td>
</tr>
<tr>
<td>Total cholesterol level (mmol/l)</td>
<td>Baseline</td>
<td>4.73 (1.02)</td>
<td>4.64 (1.11)</td>
<td>4.67 (1.07)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>4.56 (1.03)</td>
<td>4.42 (0.95)</td>
<td>4.28 (0.84)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−0.16 (0.84)</td>
<td>−0.22 (0.93)</td>
<td>−0.40 (0.90)</td>
</tr>
<tr>
<td>Ratio of total cholesterol to high density lipoprotein cholesterol:</td>
<td>Baseline</td>
<td>4.33 (1.12)</td>
<td>4.40 (1.33)</td>
<td>4.48 (1.35)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>4.18 (1.12)</td>
<td>4.11 (1.17)</td>
<td>4.02 (1.17)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−0.15 (0.72)</td>
<td>−0.29 (0.86)</td>
<td>−0.46 (0.91)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>Baseline</td>
<td>30.9 (6.1)</td>
<td>31.9 (6.2)</td>
<td>31.0 (5.3)</td>
</tr>
<tr>
<td></td>
<td>Follow-up</td>
<td>30.8 (6.3)</td>
<td>31.8 (6.3)</td>
<td>30.7 (5.0)</td>
</tr>
<tr>
<td></td>
<td>Change</td>
<td>−0.1 (1.0)</td>
<td>−0.2 (0.9)</td>
<td>−0.3 (1.2)</td>
</tr>
</tbody>
</table>

Change is measured as one year follow-up minus baseline values.

*No use of blood glucose meter.
†Adjustment for baseline values.
‡Based on 414 participants with paired values (137/152, 136/150, 141/151).

checked by the research nurses using a test aliquot at baseline and at six months.

Data on adverse reactions or complications were collected at each study visit, together with information on the use of drugs.

Delivery of intervention

Training and support for the research nurses delivering the intervention was designed to ensure adherence to the study protocol. The nurses were taught psychological theory and trained in behaviour change techniques and skills in delivering the intervention (six days of case based training over five weeks). Intervention protocols included self review of taped consultations by the research nurses and external review by a sociologist. Prompts were also built into the patient diaries to help patients adhere to their allocated intervention.

Statistical analysis

The trial was designed to have a 90% power to detect a difference of 0.5% in HbA1c levels as the primary end point at a two sided significance level of P<0.05. We estimated the standard deviation of HbA1c levels to be 1.5% based on a previous trial of patients with type 2 diabetes, and assumed a 10% loss to follow-up. We required a total of 630 patients to achieve the specified statistical power. Subsequently we revised the estimated standard deviation for HbA1c levels to 1.25% when it became clear that it had been overestimated. We retained a 10% dropout rate and 90% power and revised the recruitment target to 450 patients.

We carried out a single intention to treat analysis of the main trial end points at the end of the study using analysis of covariance to compare mean levels of HbA1c at follow-up between the three allocated groups, with the baseline level of HbA1c as a covariate. If no follow-up data were available we imputed values by carrying forward the last available measurement. We specified that in the event of a statistically significant overall result, comparisons of the two self monitoring groups independently with the control group would be carried out using t tests. Levels of HbA1c over the course of the trial were compared between groups using repeated measures analysis of variance. We also estimated the intervention effect in prespecified subgroups defined at baseline as duration of diabetes (above or below median), current management (oral hypoglycaemic drugs or dietary management only), health status (above or below the median EQ-5D score), and presence or absence of diabetes related complications. We tested for effect modification using analysis of covariation.

A Kaplan-Meier plot was used to explore adherence to a minimal level of self monitoring, defined as at least 26 tests over three months (equivalent to two tests each week); significance was assessed with a log rank test. The mean numbers of tests by patients carrying out at least 26 tests in each quarter are also reported, with differences between the less intensive and more
intensive intervention groups compared with a repeated measures analysis of variance.

**RESULTS**

Between January 2003 and December 2005, 453 patients with non-insulin treated type 2 diabetes from 48 practices in Oxfordshire and South Yorkshire were randomised to one of three interventions (fig 1): usual care (n=152), less intensive self monitoring, using a blood glucose meter and advice to contact doctor for interpretation of the results (n=150), and more intensive self monitoring, with a blood glucose meter and training in interpreting the results (n=151). The median (range) number of patients per practice recruited in 24 Oxfordshire practices was 9 (2-24) and in 24 South Yorkshire practices was 8 (3-16).

Baseline personal and clinical characteristics were well balanced between the groups (table 1). The median (interquartile) duration of diabetes was 3.0 years (1.8-6.4 years), mean (SD) age was 65.7 (10.2) years, and mean (SD) level of haemoglobin A1c was 7.5% (1.1). Only 57 (12.6%) patients were lost to follow-up, which did not differ between groups (fig 1). Measurements for high density lipoprotein cholesterol levels were not obtained for 39 patients at baseline. At follow-up, HbA1c measurements were not collected for two patients, blood pressure for five, cholesterol levels for 10, and high density lipoprotein cholesterol levels for 15.

**Primary outcome**

Table 2 shows the main results. At 12 months no difference was found in HbA1c levels between the groups after adjustment for baseline HbA1c levels (P=0.12).

The mean difference in change in HbA1c levels from baseline to 12 months between the control group and less intensive intervention group (not adjusted for baseline) was −0.14% (95% confidence interval −0.35% to 0.07%) and between the control group and more intensive intervention group was −0.17% (−0.37% to 0.03%). Figure 2 shows the change in HbA1c levels over the 12 months of follow-up, with no evidence of differences in levels between groups over the period of follow-up (P=0.38).

**Secondary outcomes**

A significant difference was found in the change in total cholesterol levels between the three groups (P=0.010).

The mean difference in change in total cholesterol levels from baseline to 12 months between the control group and less intensive intervention group (not adjusted for baseline) was −0.06 mmol/l (−0.26 to 0.14) and between the control group and more intensive intervention group was −0.23 (−0.43 to −0.04). No differences were found in the other secondary outcome measures (table 2). Within the prespecified subgroups no significant interactions were found with allocated group (table 3).

**Hypoglycaemia**

During the trial one or more grade 2 hypoglycaemic episodes were experienced by 14 patients in the control group, 33 in the less intensive intervention group, and 43 in the more intensive intervention group (χ²=18.3, P<0.001). Only one patient in the control group experienced a grade 3 hypoglycaemic episode.

**Use of meter**

Patients allocated to less intensive self monitoring were significantly more likely to persist with use of the meter than those allocated to more intensive self monitoring. Ninety nine (67%) of those receiving the less intensive intervention and 79 (52%) of those receiving the more intensive intervention continued to use the meter at least twice a week for the 12 months of the study (P=0.012; fig 3). Among those who continued to use a
Changes in hypoglycaemic and lipid lowering drugs
No differences were found between the groups in the proportions of patients prescribed an increase in hypoglycaemic drugs between baseline and 12 months. In the control group 45 (30%) patients had increased drugs compared with 43 (29%) in the less intensive intervention group and 48 (32%) in the more intensive intervention group. One patient in the control group, four in the less intensive intervention group, and five in the more intensive intervention group were using insulin therapy by 12 months. No differences were found between groups in the proportions of patients where hydroxymethyl glutaryl coenzyme A reductase inhibitor (statin) treatment was increased or added to therapy. Overall, 17 (11%) patients in the control group, 11 (7%) in the less intensive intervention group, and 19 (13%) in the more intensive intervention group who were not taking a statin at baseline were taking a statin by 12 months.

Further analyses
Later papers will report on quality of life, cost effectiveness, and subgroup and more detailed multivariate analyses.

DISCUSSION
No significant improvement in glycaemic control was found after 12 months in patients with non-insulin treated type 2 diabetes using self monitoring of blood glucose levels when compared to those not self monitoring. No evidence was found of a significantly different impact of self monitoring on glycaemic control when comparing subgroups of patients defined by duration of diabetes, therapy, diabetes related complications, and EQ-5D score. Also no evidence was found that more intensive compared with less intensive monitoring led to differences in glycaemic control.

Strengths and weaknesses of the study
In this study patients were independently randomised, with concealed allocation of measurement of the main outcome and a low loss to follow-up. Participants were drawn from a well defined sampling frame and the reasons for exclusion were fully recorded. Recruitment targets were revised after baseline data on haemoglobin A1c levels in the first 245 randomised patients indicated that the standard deviation had been overestimated in the original power calculations. We did not, however, change the proposed power or significance levels. Participants’ diabetes was reasonably well controlled and although most were not using a meter a minority had had experience of their use. Both these factors may have limited scope for further improvement in glycaemic control. However, the participants were representative of well controlled non-insulin treated patients with type 2 diabetes in the community who are the target group for current recommendations.

Designing a trial to evaluate self monitoring of blood glucose levels is complex because it must include an educational component on the use and interpretation of testing for the intervention group, whereas advice on improving self care must be offered to the comparison group. We tackled these issues by providing a common structure for interventions, incorporating standardised good care in all three arms of the trial within which nurses discussed issues of glycaemic control, assessed either by HbA1c levels or self monitoring of blood glucose, and its role in setting and monitoring self care goals. The stepwise approach to the interventions across the three arms of the trial allowed examination of what aspects of the intervention, if any, were responsible for improved outcomes. Recent consensus guidelines have based recommendations for self monitoring of blood glucose levels on a theoretical potential to better self manage glycaemic control. We incorporated self monitoring of blood glucose into a framework that, based on psychological theory, should have optimised its effect. Careful specification, training, and monitoring of consultations ensured that the allocated interventions were delivered as

Fig 3 | Adherence to minimal level of self monitoring of blood glucose levels using a meter

Fig 4 | Frequency of self monitoring of blood glucose levels using a meter, by randomisation group
planned, although some patients in the less intensive intervention group may themselves have adopted a more intensive monitoring approach. Despite an intervention based on standards of best clinical practice and underpinned by appropriate psychological theory, we found no convincing evidence of an effect on glycaemic control.

Strengths and weaknesses in relation to other studies

Comparisons with early trials of blood glucose monitoring are of limited relevance because of their small size, the large quantity of blood required to be read by older meters, and the skill required for their use. However, more recent trials have been carried out with meters utilising technologies that require smaller amounts of blood and simplified procedures for testing. Our findings support those of a recent small trial using standardised counselling for both intervention and control groups. The trial reported a non-significant reduction in HbA1c levels of 0.2% in the intervention group compared with the control group. Our findings, however, conflict with the findings of two of the largest trials of self monitoring of blood glucose to date. One of these trials reported a significant decrease in HbA1c level of 0.3% in the intervention group compared with the control group. However, over 30% of those randomised were lost to follow-up and missing values were not imputed, which might lead to bias. In addition, initial specific training in use of a blood glucose meter was not matched by additional training for the control group, although all patients received dietary advice regardless of randomisation. A second trial reported a reduction in HbA1c level of 0.46% in the intervention group compared with the control group. This type of educational support for self management in itself has been estimated as improving HbA1c levels by 0.26%. The meaning of the study

Fewer people in our trial allocated to more intensive self monitoring compared with less intensive self monitoring continued testing; previous studies have found that trying to understand blood glucose measurements may lead to frustration when results do not fall into a pattern, or cease to be of interest when they are entirely predictable. Patients with reasonably well controlled diabetes do not need active encouragement to use a meter. The increased recording of hypoglycaemia in the self monitoring arms may be a result of an increased awareness of low blood glucose levels from using the meter rather than a true biochemical difference between groups. Although no improvement in glycaemic control was observed, a small but significant improvement was found in total cholesterol levels with the self monitoring intervention. This finding is consistent with an increased intensity of self management in these groups, possibly mediated through increased dietary adherence or through taking lipid lowering drugs more regularly.

Unanswered questions and future research

Recent systematic reviews have estimated a benefit of 0.4% from self monitoring, and on this basis a previous study has estimated an incremental cost of £4500 (€6050; $8880) to £15 515 per quality of life year gained. Our estimates of the size of effect on HbA1c levels suggest that it is probable that the previous study underestimated the cost per quality of life year gained. A comprehensive economic evaluation with cost effectiveness estimates will be detailed in a future report.

Evidence of benefit from self monitoring of blood glucose for other patient groups is stronger. Large trials of management of patients with type 1 diabetes have incorporated self monitoring of blood glucose as an essential part of self management. Self monitoring for insulin treated patients with type 2 diabetes is accepted practice, although the evidence base requires further work and optimisation of its use may be possible. However, routine self monitoring of blood glucose for patients with reasonably well controlled non-insulin treated type 2 diabetes seems to offer, at best, small advantages; is not well accepted; and the cost, effort, and time involved in the procedures may be better directed to supporting other health related behaviours. Current guidelines for the use of self monitoring of blood glucose among patients with reasonably well controlled non-insulin treated type 2 diabetes should be reviewed.

We thank the patients who took part in this study and their doctors for support and help. W Hardeman and J Hobbis contributed to the development of the intervention protocols and prepared and led some of the training sessions for the nurses. M McKinnon and J Donnelly helped train the nurses and L Rossmovitz carried out external review of interventions.

Contributors: AF, A-LK, and AN had the original idea for the study and wrote the trial protocol with PY, DF, and RH. AF, AW, DF, and A-LK developed the trial measures and intervention. PY was trial statistician and analysed the data. AW, AF, AC, and EG managed the trial. AF wrote the first draft of the manuscript with AN and A-LK and all members of the writing group reviewed and commented on the final manuscript. AF is guarantor of this paper. The DIGEM Trial Group. Writing committee: AF, AW, EG, PY, DF, AC, RH, A-LK, and AN. Investigators: AF, AN, A-LK, D Mart, S Ziebland, DF, A Gray, PY, and RH. Steering committee: N Stott (chair), AF, AN (to 2005), S Sutton, H Tewson, D Chapman, H Hearnshaw, E Goyder (from 2005), P Glasziou (from 2005), M Iwa (2004 to 2005), and M Gordon (from 2005). Intervention development: AW, AF, DF, A-LK, and MP Selwood. Coordinating Centres: (Oxford) AW (to 2005, trial coordinator), AC (trial manager), PY (trial statistician), J Simon (health economist), and A Fuller (data manager). (Sheffield) Vivienne Walker (local trial administrator). Data monitoring committee: C Baigent (chair), J Levy, and K Wheale. Research nurses (Oxford) MP Selwood, H Kilkow, M Chapman, and S Turner. (Sheffield) A Casbott, K Dobson, A Willert, A Roberts, and H Wood. Central laboratory: K Islam.

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Competing interests: None declared.

Ethical approval: This study was approved by the Oxfordshire Research Ethics Committee B (002.059).


It is not necessary to routinely recommend self monitoring of blood glucose in reasonably well controlled patients with non-insulin treated type 2 diabetes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Self monitoring of glucose for non-insulin treated patients with diabetes is costly but may improve glycaemic control. Although some observational studies have suggested benefits, the results of randomised trials have been inconclusive.

WHAT THIS STUDY ADDS

It is not necessary to routinely recommend self monitoring of blood glucose in reasonably well controlled patients with non-insulin treated type 2 diabetes.
ABSTRACT

Objective To derive a new cardiovascular disease risk score (QRISK) for the United Kingdom and to validate its performance against the established Framingham cardiovascular disease algorithm and a newly developed Scottish score (ASSIGN).

Design Prospective open cohort study using routinely collected data from general practice.

Setting UK practices contributing to the QRESEARCH database.

Participants The derivation cohort consisted of 1.28 million patients, aged 35-74 years, registered at 318 practices between 1 January 1995 and 1 April 2007 and who were free of diabetes and existing cardiovascular disease. The validation cohort consisted of 0.61 million patients from 160 practices.

Main outcome measures First recorded diagnosis of cardiovascular disease (incident diagnosis between 1 January 1995 and 1 April 2007): myocardial infarction, coronary heart disease, stroke, and transient ischaemic attacks. Risk factors were age, sex, smoking status, systolic blood pressure, ratio of total serum cholesterol to high density lipoprotein, body mass index, family history of coronary heart disease in first degree relative aged less than 60, area measure of deprivation, and existing treatment with antihypertensive agent.

Results A cardiovascular disease risk algorithm (QRISK) was developed in the derivation cohort. In the validation cohort the observed 10 year risk of a cardiovascular event was 6.60% (95% confidence interval 6.48% to 6.72%) in women and 9.28% (9.14% to 9.43%) in men. Overall the Framingham algorithm over-predicted cardiovascular disease risk at 10 years by 35%, ASSIGN by 36%, and QRISK by 0.4%. Measures of discrimination tended to be higher for QRISK than for the Framingham algorithm and it was therefore calibrated to the UK population than either the Framingham model or ASSIGN. QRISK is likely to provide more appropriate risk estimates to help identify high risk patients on the basis of age, sex, and social deprivation. It is therefore likely to be a more equitable tool to inform management decisions and help ensure treatments are directed towards those most likely to benefit. It includes additional variables which improve risk estimates for patients with a positive family history or those on antihypertensive treatment. However, since the validation was performed in a similar population to the population from which the algorithm was derived, it potentially has a “home advantage.” Further validation in other populations is therefore required.

INTRODUCTION

Cardiovascular disease is the leading cause of premature death and a major cause of disability in the United Kingdom. Asymptomatic patients thought to be at high risk of cardiovascular disease need to be identified so they can be offered advice about lifestyle changes, such as smoking cessation, physical activity, and diet, about treatment to lower blood pressure and modify cholesterol levels, and about use of aspirin when appropriate.

Many guidelines recommend that the risk of cardiovascular disease is estimated by combining different risk factors into a numeric estimate of risk. A variety of risk calculators are available, as charts, tables, computer programs, and web based tools. Equations derived from the American Framingham cohort study are the most widely used in the United Kingdom.
Although the Framingham risk equations have been the most used method for many years they have major limitations. The Framingham cohort is almost entirely white and recalibration may be needed in more ethnically diverse populations.6 The Framingham risk equations were developed during the peak incidence of cardiovascular disease in America. They perform well in similar populations but may over-estimate risk by up to 50% in contemporary northern European populations where the incidence of cardiovascular disease is lower.7 The confidence intervals for estimates produced from the Framingham algorithm have been difficult to quantify and any estimate is uncertain for estimation of an individual’s risk. The equations may also underestimate risk in some high risk subgroups, such as patients from deprived areas, potentially exacerbating health inequalities.8,9 Lastly, the Framingham algorithm does not include factors such as social deprivation, body mass index, family history of cardiovascular disease, and current treatment with antihypertensives. The evidence supporting the utility of cardiovascular risk scores for primary prevention in the United Kingdom is scarce.10

In a major initiative to improve public health in the United Kingdom the National Institute for Health and Clinical Excellence has lowered the threshold for primary prevention with statins from a 10 year cardiovascular disease risk of 40% to that of 20%.11,12 We refer to a 10 year cardiovascular disease risk of 20% or more as high risk. Any systematic over-estimation of risk results in an excessive number of people being identified for treatment. Not only would this have a major impact on prescribing costs and NHS resources supporting lifelong treatment, it potentially also exposes patients to unnecessary treatments and hence possible side effects. It is important that this new public health programme includes social deprivation to reduce rather than to exacerbate existing social inequalities in cardiovascular disease and to target those at greatest risk.13 In recognition of these problems Scotland has adopted ASSIGN equations that include social deprivation.14 For these reasons the underlying methods of risk prediction should be fit for purpose, targeting those likely to benefit most and avoiding inappropriate treatment of those at lower risk. The equation underpinning the estimate of cardiovascular disease risk needs to be revised and calibrated for the contemporary UK population, with an appropriate weighting for social deprivation and current treatment with antihypertensives. We therefore carried out a study to derive and validate a new cardiovascular disease risk score and compared this with the Framingham5 and the new ASSIGN equations.15

Table 1 | Computer recorded incidence of cardiovascular disease per 1000 person years with 95% confidence intervals in derivation and validation cohorts by age, sex, and deprivation fifth

<table>
<thead>
<tr>
<th>Age group:</th>
<th>Derivation cohort</th>
<th>Validation cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Townsend fifth:</td>
<td>No of incident cases of cardiovascular disease</td>
<td>Incidence rate per 1000 person years (95% CI)</td>
</tr>
<tr>
<td>Townsend fifth:</td>
<td></td>
<td>Person years</td>
</tr>
<tr>
<td>First</td>
<td>4851</td>
<td>931 167</td>
</tr>
<tr>
<td>Second</td>
<td>5134</td>
<td>921 744</td>
</tr>
<tr>
<td>Third</td>
<td>5698</td>
<td>865 316</td>
</tr>
<tr>
<td>Fourth</td>
<td>6187</td>
<td>804 175</td>
</tr>
<tr>
<td>Fifth</td>
<td>5958</td>
<td>715 907</td>
</tr>
<tr>
<td>No of men</td>
<td>37 843</td>
<td>4 001 632</td>
</tr>
</tbody>
</table>

| Townsend fifth: | | |
| Townsend fifth: | | |
| First | 3851 | 1 521 521 | 2.53 (2.45 to 2.61) | 1865 | 738 492 | 2.53 (2.41 to 2.64) |
| Second | 9197 | 1 237 808 | 7.43 (7.28 to 7.58) | 4238 | 584 812 | 7.25 (7.03 to 7.47) |
| Third | 12 591 | 777 769 | 16.19 (15.91 to 16.47) | 5877 | 365 856 | 16.06 (15.66 to 16.48) |
| Fourth | 12 204 | 464 535 | 26.27 (25.81 to 26.74) | 5725 | 220 831 | 25.92 (25.26 to 26.61) |
| Fifth | 7208 | 724 013 | 9.96 (9.73 to 10.19) | 3513 | 354 477 | 9.91 (9.59 to 10.24) |
METHODOLOGY

Our prospective cohort study was carried out within a large UK primary care population. We used version 14 of the QRESEARCH database (www.qresearch.org). This is a large, validated electronic database representative of primary care and containing the health records of 10 million patients over a 17 year period from 529 general practices using the EMIS computer system. It covers about 7% of the current UK population and the contributing practices are similar to over 8000 practices nationally for a wide variety of measures. It has been used for a wide range of health service analyses and research studies, including studies of the incidence, risk, and treatment of cardiovascular disease. The database contains area measures of ethnicity and deprivation evaluated at output area on the basis of the 2001 census and linked to every patient’s record. The Townsend score is a good area measure of material deprivation based on four variables (unemployment, overcrowding, non-car ownership, and non-home ownership) and has been widely used in medical research. It is available at output area, about 125 households. Most recently QRESEARCH has been linked to cause of death data from the Office for National Statistics enabling sensitivity analyses including certified cause of death. QRESEARCH is sufficiently large to allow modelling on two thirds of the database, with validation using the remaining third.

Practices and cohorts

We included all the contributing practices in the United Kingdom once they had been using their EMIS system for at least a year. We randomly allocated two thirds of eligible practices to the derivation dataset, saving the remaining third for the validation dataset. The derivation dataset was used to derive a new risk equation for estimating cardiovascular risk, validated using the validation dataset.

We identified an open cohort of patients aged 35-74 at the date of study entry, drawn from patients registered with eligible practices from 1 January 1995 to 1 April 2007. We excluded those with a diagnosis of cardiovascular disease or diabetes before their entry date. We also excluded temporary residents and patients with interrupted periods of registration with the practice. We also excluded 4% of patients who did not have a valid postcode related Townsend score.

For each patient we determined an entry date to the cohort analysis, which was the latest of the following dates: 35th birthday, date of registration with the practice, date on which the practice computer system was installed, and the beginning of the study period (1 January 1995). In addition we only included patients in the analysis once they had a minimum of one year’s complete data in their medical record.

For each patient we determined the right censor date, which was the earliest date of the dates on which they developed the outcome of interest, the study period ended (1 April 2007), date of death, date of deregistration with the practice, or date of last upload of computerised data. We determined the person years at risk—the difference between the entry date and the right censor date. We used person years at risk as the denominator term for the incidence rates.

Cardiovascular disease outcomes

The primary outcome was the first recorded diagnosis of cardiovascular disease on the general practice’s clinical computer system either before or at death occurring between 1 January 1995 and 1 April 2007. Our definition included myocardial infarction, coronary heart disease, stroke, and transient ischaemic attack.

Table 2 | Baseline clinical characteristics for men and women aged 35-74 initially free from cardiovascular disease and diabetes in derivation and validation datasets. Values are means (standard deviations) unless stated otherwise

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Derivation cohort</th>
<th>Validation cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (n=636 753)</td>
<td>Women (n=646 421)</td>
</tr>
<tr>
<td>Median (interquartile range) age (years)</td>
<td>48 (40-57)</td>
<td>49 (41-59)</td>
</tr>
<tr>
<td>Median (interquartile range) Townsend score</td>
<td>-1.1 (-3.1-2.3)</td>
<td>-1.2 (-3.1-2.1)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.5 (4.0)</td>
<td>26 (4.8)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>135.7 (19.6)</td>
<td>132.6 (21.5)</td>
</tr>
<tr>
<td>Total serum cholesterol level (mmol/l)</td>
<td>5.7 (1.1)</td>
<td>5.9 (1.2)</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol level (mmol/l)</td>
<td>1.3 (0.4)</td>
<td>1.6 (0.4)</td>
</tr>
<tr>
<td>Ratio of total serum cholesterol to high density lipoprotein</td>
<td>4.6 (1.3)</td>
<td>4.0 (1.3)</td>
</tr>
<tr>
<td>No (%) of current smokers</td>
<td>179 144 (28.1)</td>
<td>149 089 (23.1)</td>
</tr>
<tr>
<td>No (%) with family history of cardiovascular disease*</td>
<td>57 708 (9.1)</td>
<td>78 442 (12.1)</td>
</tr>
</tbody>
</table>

Current treatment:

- **Antihypertensives†** | 53 742 (8.4) | 80 066 (12.4) | 26 080 (8.5) | 38 868 (12.6) |
- **Angiotensin converting enzyme inhibitors†** | 15 969 (2.5) | 16 101 (2.5) | 7714 (2.5) | 7787 (2.5) |
- **β blockers†** | 25 084 (3.9) | 38 536 (6.0) | 12 109 (4.0) | 18 720 (6.1) |
- **Calcium channel blockers†** | 16 566 (2.6) | 18 618 (2.9) | 8019 (2.6) | 9107 (2.9) |
- **Thiazides†** | 15 476 (2.4) | 31 919 (4.9) | 7389 (2.4) | 15 331 (5.0) |

*In first degree relative aged less than 60.
†At entry to cohort.
We used nationally agreed definitions—that is, computer recorded Read codes—from the General Medical Services contract quality and outcomes framework.

We have used the general practitioner’s clinical diagnosis of cardiovascular disease for our main analysis. At the time of writing, however, patient level data for cause of death were available from the Office for National Statistics for the five years between 2002 and 2007. We were able to link these data at patient level within the general practices’ clinical computer systems and extract the resulting data onto the QRESEARCH database. We were therefore able to identify patients who had a primary or underlying certified cause of death as either coronary heart disease (codes I20-I25, international classification of diseases, 10th revision), stroke, or transient ischaemic attack and to use these data to examine the completeness of outcome data on QRESEARCH.

Risk factors for cardiovascular disease
We included the following risk factors in our analysis, using the value closest to the entry date to the cohort for each patient and imputing missing values when necessary: age (in single years); sex (men vs women); smoking status (current smoker, non-smoker—including former smoker); systolic blood pressure (continuous); ratio of total serum cholesterol to high density lipoprotein levels (continuous); left ventricular hypertrophy recorded in clinical records (yes or no); body mass index (continuous); family history of cardiovascular disease in a first degree relative aged less than 60 (yes or no); Townsend deprivation score (2001 census data at output area level evaluated as a continuous variable); percentage of South Asian residents at output areas (2001 census data evaluated at output areas as a continuous variable); current prescription of at least one anti-hypertensive—thiazide, β blocker, calcium channel blocker, or angiotensin converting enzyme inhibitor (yes or no).

Model derivation and development
We used the Cox proportional hazards model in the derivation dataset to estimate the coefficients associated with each potential risk factor for the first ever recorded diagnosis of cardiovascular disease for men and women separately. A priori we specified the variables we intended to include in the model on the basis of traditional risk scores (for example, Framingham...
We compared models using the Bayes information criterion. This is a likelihood measure in which lower values indicate better fit and in which a penalty is paid for increasing the number of variables. We examined the strength of the association between one unit increases in each continuous variable and we compared categories for other variables—for example, current smoking compared with non-smoking. Continuous variables were centred for analysis. We checked the assumptions of the proportional hazards model for each variable and tested for any non-linear relation between continuous independent variables and the outcome. We used fractional polynomials to model non-linear risk relations with continuous variables when appropriate. Modelling using fractional polynomials is a flexible approach for modelling non-linear risk relations with continuous variables. We tested for interactions between systolic blood pressure and antihypertensive treatment and between smoking and deprivation.

Initially our models were fitted using patients without any missing data (complete case analysis), and the fractional polynomial terms were obtained from the complete case analysis using a multivariable approach. However, because patients with complete data might have a different health status and risk of cardiovascular disease compared with those with missing data, we fitted our principal models on the basis of multiple imputed datasets using Rubin’s rules to combine effect estimates and estimate standard errors. We tested for interactions between systolic blood pressure and antihypertensive treatment and between smoking and deprivation.

We took the log of the hazard ratio for each of the risk factors (that is, the coefficients from the Cox regression) from the final model and used these as weights for the new cardiovascular disease risk equation. We then estimated each patient’s probability of experiencing a cardiovascular event within 10 years by combining these weights with the characteristics of the patient and also using the baseline survivor function for all participants, as in other studies.

Table 3 | Adjusted hazard ratios with 95% confidence intervals for preferred QRISK model for men and women aged 35-74

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted hazard ratio</th>
<th>Lower 95% confidence limit</th>
<th>Upper 95% confidence limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log (age/10)</td>
<td>87.75</td>
<td>81.34</td>
<td>94.66</td>
</tr>
<tr>
<td>Ratio of total serum cholesterol to high density lipoprotein cholesterol levels</td>
<td>1.001</td>
<td>0.999</td>
<td>1.002</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>1.015</td>
<td>1.013</td>
<td>1.018</td>
</tr>
<tr>
<td>Family history of premature cardiovascular disease</td>
<td>1.229</td>
<td>1.187</td>
<td>1.273</td>
</tr>
<tr>
<td>Smoking status (current smoker)</td>
<td>1.530</td>
<td>1.487</td>
<td>1.574</td>
</tr>
<tr>
<td>Townsend score of output area</td>
<td>1.035</td>
<td>1.031</td>
<td>1.038</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>1.050</td>
<td>1.004</td>
<td>1.005</td>
</tr>
<tr>
<td>Receiving treatment for blood pressure at baseline</td>
<td>1.734</td>
<td>1.674</td>
<td>1.796</td>
</tr>
<tr>
<td>Interaction terms for systolic blood pressure*blood pressure treatment</td>
<td>0.996</td>
<td>0.995</td>
<td>0.997</td>
</tr>
<tr>
<td>Men:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log (age/10)</td>
<td>50.634</td>
<td>47.792</td>
<td>53.646</td>
</tr>
<tr>
<td>Ratio of total serum cholesterol to high density lipoprotein cholesterol levels</td>
<td>1.001</td>
<td>0.999</td>
<td>1.003</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>1.022</td>
<td>1.019</td>
<td>1.025</td>
</tr>
<tr>
<td>Family history of premature cardiovascular disease</td>
<td>1.300</td>
<td>1.257</td>
<td>1.344</td>
</tr>
<tr>
<td>Smoking status (current smoker)</td>
<td>1.417</td>
<td>1.385</td>
<td>1.449</td>
</tr>
<tr>
<td>Townsend score of output area</td>
<td>1.017</td>
<td>1.014</td>
<td>1.020</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>1.004</td>
<td>1.004</td>
<td>1.005</td>
</tr>
<tr>
<td>Receiving treatment for blood pressure at baseline</td>
<td>1.847</td>
<td>1.788</td>
<td>1.908</td>
</tr>
<tr>
<td>Interaction terms for systolic blood pressure*blood pressure treatment</td>
<td>0.993</td>
<td>0.992</td>
<td>0.995</td>
</tr>
</tbody>
</table>

Variables simultaneously adjusted for other variables in table. Continuous variables were centred. Hazard ratios correspond to increase of 1 unit for log (age/10), 1 mm Hg for systolic blood pressure, 1 kg/m² for body mass index, 1 unit for Townsend score, and 1 unit for ratio of total serum cholesterol to high density lipoprotein cholesterol levels.

Validation of the new cardiovascular disease risk equation
Having obtained the risk equation in the derivation dataset (the QRISK score) we tested its performance (calibration and discrimination) in the validation dataset. We calculated the 10 year estimated cardiovascular disease risk for each patient in the validation dataset, replacing missing values for continuous variables with mean values obtained from the derivation dataset by five year age-sex bands and assuming patients were non-smokers when smoking status was not recorded.

To assess calibration (the degree of similarity between observed and predicted risks) we calculated the mean predicted risk of cardiovascular disease at 10 years and the observed risk at 10 years obtained using the 10 year Kaplan-Meier estimate. We then compared the ratio of the predicted to the observed cardiovascular disease risk for patients in the validation cohort in each tenth of predicted risk. We also
compared predicted and observed risks overall for men and women by age band and by fifth of Townsend score. We calculated the area under the receiver operating curve to assess discrimination—that is, the ability of a risk prediction equation to distinguish between those who do and those who do not have a cardiovascular event during the follow-up period. We also calculated the D statistic and an $R^2$ statistic, which are measures of discrimination and explained variation for survival models.

Comparison with the Framingham and ASSIGN equations

We compared the performance of QRISK against the risk estimates derived from Framingham equations. We used an equation for cardiovascular disease risk that was computed by summing the coronary risk (including myocardial infarction and coronary heart disease death plus angina plus coronary insufficiency) and stroke risk (including transient ischaemic attack) as these outcomes are closest to those used in randomised trials of drug effectiveness. They are also the outcomes used to define cardiovascular disease in the current Joint British Society Guidelines.

We calculated the area under the receiver operating curve and the D statistic for the Framingham estimates in the validation dataset and compared them with the corresponding QRISK values. We also compared the performance of QRISK against the ASSIGN equation. ASSIGN contains similar variables to QRISK except it uses the number of cigarettes smoked per day instead of a categorical variable for smoking and the index of multiple deprivation as the measure of deprivation.

Finally, we calculated the proportion of patients in the validation sample who have a 20% or more risk of cardiovascular disease at 10 years, by age, sex, and deprivation according to QRISK and the Framingham and ASSIGN equations. We determined the proportion of patients who would be reclassified into a higher or lower risk category using the new risk equations. We estimated the number of people in the United Kingdom with a 10 year cardiovascular disease risk of 20% or more for each score, using UK population estimates for 2005. Stata (version 9.2) was used for all analyses.

RESULTS

Overall, 478 UK practices met our inclusion criteria of which 318 were randomly assigned to the derivation dataset and 160 to the validation dataset.

In the derivation cohort 3 374 617 patients of all ages were registered with 318 practices at some point during the study period. Of these, 1 283 174 were aged 35-74 years and were free of cardiovascular disease.

<table>
<thead>
<tr>
<th>Tenth*</th>
<th>QRISK</th>
<th>Framingham</th>
<th>ASSIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Predicted risk (%)</td>
<td>Observed risk (%)</td>
<td>Ratio</td>
</tr>
<tr>
<td>Women:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>0.71</td>
<td>0.44</td>
<td>1.61</td>
</tr>
<tr>
<td>Second</td>
<td>1.06</td>
<td>0.95</td>
<td>1.12</td>
</tr>
<tr>
<td>Third</td>
<td>1.49</td>
<td>1.45</td>
<td>1.03</td>
</tr>
<tr>
<td>Fourth</td>
<td>2.11</td>
<td>2.11</td>
<td>1</td>
</tr>
<tr>
<td>Fifth</td>
<td>2.97</td>
<td>3.06</td>
<td>0.97</td>
</tr>
<tr>
<td>Sixth</td>
<td>4.22</td>
<td>4.5</td>
<td>0.94</td>
</tr>
<tr>
<td>Seventh</td>
<td>6.06</td>
<td>6.16</td>
<td>0.99</td>
</tr>
<tr>
<td>Eighth</td>
<td>8.9</td>
<td>9.65</td>
<td>0.92</td>
</tr>
<tr>
<td>Ninth</td>
<td>13.36</td>
<td>13.95</td>
<td>0.96</td>
</tr>
<tr>
<td>Tenth</td>
<td>22.52</td>
<td>20.19</td>
<td>1.12</td>
</tr>
<tr>
<td>Overall</td>
<td>6.34</td>
<td>6.25</td>
<td>1.02</td>
</tr>
<tr>
<td>Men:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>1.64</td>
<td>0.93</td>
<td>1.77</td>
</tr>
<tr>
<td>Second</td>
<td>2.24</td>
<td>1.6</td>
<td>1.39</td>
</tr>
<tr>
<td>Third</td>
<td>2.92</td>
<td>2.6</td>
<td>1.12</td>
</tr>
<tr>
<td>Fourth</td>
<td>3.81</td>
<td>3.86</td>
<td>0.99</td>
</tr>
<tr>
<td>Fifth</td>
<td>5</td>
<td>4.86</td>
<td>1.03</td>
</tr>
<tr>
<td>Sixth</td>
<td>6.61</td>
<td>6.67</td>
<td>0.99</td>
</tr>
<tr>
<td>Seventh</td>
<td>8.88</td>
<td>9.88</td>
<td>0.9</td>
</tr>
<tr>
<td>Eighth</td>
<td>12.24</td>
<td>14.24</td>
<td>0.86</td>
</tr>
<tr>
<td>Ninth</td>
<td>17.4</td>
<td>18.46</td>
<td>0.94</td>
</tr>
<tr>
<td>Tenth</td>
<td>27.86</td>
<td>25.72</td>
<td>1.08</td>
</tr>
<tr>
<td>Overall</td>
<td>8.86</td>
<td>8.88</td>
<td>1.00</td>
</tr>
<tr>
<td>All patients</td>
<td>7.59</td>
<td>7.56</td>
<td>1.004</td>
</tr>
</tbody>
</table>

Comparison between QRISK, Framingham, and ASSIGN in validation cohort in patients aged 35-74.

*First tenth is lowest tenth of risk.
and diabetes at baseline. These patients were included in the study. Of these, 50.4% were women. During the study period 65,671 incident cases of cardiovascular disease from 8.2 million person years of observation occurred giving a crude incidence rate for cardiovascular disease of 7.96 per 1000 person years. Incidence rates were higher in men than in women and increased steeply with age (table 1). The computer recorded incidence of cardiovascular disease was also significantly higher among men and women from deprived areas, the effect being more noticeable for women. The median follow-up was 6.5 years (range 0-12 years) and 306,259 patients were followed-up for at least 10 years. The 10 year observed risk of a cardiovascular event in women aged 35-74 was 6.69% (95% confidence interval 6.61% to 6.78%) and in men was 9.46% (9.36% to 9.56%).

In the validation dataset 614,553 eligible patients were aged 35-74 and of these 50.3% were women. Incidence rates among patients in the validation cohort were similar to those in the derivation cohort (table 1). The 10 year observed risk of a cardiovascular event in women aged 35-74 was 6.60% (6.48% to 6.72%) and in men was 9.28% (9.14% to 9.43%).

Table 2 compares the characteristics of eligible patients in the cohorts. Although the validation cohort was drawn from an independent group of practices, the baseline characteristics were similar to those for the derivation cohort.

Outcome comparison with data from the Office for National Statistics

A subgroup analysis was undertaken in the period 2002-7 for practices with linked data on death to determine the degree of under-ascertainment of deaths from cardiovascular disease on the general practice’s clinical computer record—that is, patients with a cardiovascular disease death recorded on Office for National Statistics data who had not been identified through the general practice’s clinical record. Of the 39,057 patients with a cardiovascular disease outcome on either record between 2002 and 2007, 37,074 (93.8%) had already been identified on the basis of their general practice record alone—that is, an additional 6.2% of patients were identified by virtue of their Office for National Statistics cause of death linked record.

Baseline characteristics of derivation cohort

At baseline 8.4% of men and 12.4% of women were receiving treatment for blood pressure. A family history of premature coronary heart disease in a first degree relative aged less than 60 was recorded in 9.1% of men and 12.1% of women and 0.4% had a recorded diagnosis of left ventricular hypertrophy.

The figure shows the percentage of patients with recorded values. It also shows mean values for body mass index, systolic blood pressure, total serum cholesterol and high density lipoprotein, and the proportion of smokers at baseline compared with data from the health survey for England for the year closest to 1996 that included measurement of the risk factor. Values by age for most variables were similar to those in the health survey suggesting that the study cohort is representative of the general population. The exception was smoking where the survey rates were slightly higher than the study rates for women but lower than the study rates for men.

We compared characteristics of patients with and without recorded values. Women with missing data on smoking status were less likely to be taking blood pressure treatment or to have a family history of premature coronary heart disease. Women with missing values for body mass index were less likely to be receiving treatment for blood pressure, less likely to smoke, and less likely to have a family history of premature coronary heart disease. Women with missing blood pressure measurements were less likely to be receiving treatment for blood pressure, less likely to smoke, less likely to have a family history of premature coronary heart disease, and were slightly younger. Women with missing data on the ratio of total serum cholesterol to high density lipoprotein were less likely to be receiving treatment for blood pressure or to have a family history of premature coronary heart disease, were more likely to be smokers, were younger, had lower systolic blood pressure, and had a slightly lower body mass index. A similar pattern was observed for men. In general patients with missing data had significantly different survival rates—for example, women with a cholesterol ratio recorded had a 10 year observed risk of a cardiovascular event of 4.0% compared with 7.9% for those with missing values. For men the values were 4.9% and 10.9%.

Model derivation

Table 3 shows the results of the Cox regression analysis for the final model. A log transformation was used for age but otherwise variables were fitted as linear terms as this best fitted the data according to the fractional polynomial analysis. Three main models were compared for fit and interpretability. The final model included the logarithm of age, ratio of serum

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### Table 5: Summary statistics comparing QRISK equation for 10 year risk of cardiovascular disease to predictions based on Framingham and ASSIGN equations applied to validation cohort in patients aged 35-74

<table>
<thead>
<tr>
<th>Summary statistics</th>
<th>QRISK</th>
<th>Framingham</th>
<th>ASSIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receiver operating curve statistic*</td>
<td>0.7879</td>
<td>0.7744</td>
<td>0.7841</td>
</tr>
<tr>
<td>D statistic (SE)</td>
<td>1.549 (0.014)</td>
<td>1.393 (0.014)</td>
<td>1.472 (0.014)</td>
</tr>
<tr>
<td>R² statistic† (SE)</td>
<td>36.4% (0.43)</td>
<td>31.7% (0.44)</td>
<td>34.1% (0.43)</td>
</tr>
<tr>
<td>Men:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receiver operating curve statistic*</td>
<td>0.7674</td>
<td>0.7598</td>
<td>0.7644</td>
</tr>
<tr>
<td>D statistic (SE)</td>
<td>1.647 (0.013)</td>
<td>1.31 (0.012)</td>
<td>1.357 (0.012)</td>
</tr>
<tr>
<td>R² statistic† (SE)</td>
<td>33.3% (0.39)</td>
<td>29.1% (0.38)</td>
<td>30.5% (0.38)</td>
</tr>
</tbody>
</table>

Although QRISK validation sample was drawn from independent practices all use same clinical computer system (EMIS) therefore score needs to be validated in practices using other clinical systems.

*Higher scores indicate better discrimination.
†Indicates percentage of variation explained.
cholesterol to high density lipoprotein levels, systolic blood pressure, body mass index, family history of premature cardiovascular disease, smoking status, Townsend deprivation score, and use of at least one blood pressure treatment. The final model also included an interaction term between systolic blood pressure and blood pressure treatment. Left ventricular hypertrophy was omitted from the final model as the prevalence of recording was low and its inclusion made little difference to the overall model. The area measure of ethnicity was also omitted from the final model since it did not improve the model fit over and above the inclusion of the area measure of deprivation and interpretation of the results was difficult. Overall the final model was superior to the other models according to the Bayes information criterion statistic. 

Hazard ratios for the final model show that the risk of a cardiovascular disease event increased with increasing age, body mass index, and Townsend deprivation score. The risk was higher in patients who smoked, had a family history of premature cardiovascular disease, and were receiving blood pressure treatment at baseline. Risk increased more steeply with systolic blood pressure in those not receiving treatment for blood pressure. The hazard ratio associated with the ratio for total serum cholesterol to high density lipoprotein level was just above and close to one for both sexes. However, we decided a priori to include this risk factor in the model. The model was repeated omitting the cholesterol ratio term and a small change was found to the coefficients for some of the other variables.

Calibration and discrimination of QRISK v Framingham v ASSIGN

Table 4 compares predicted and observed risks of a cardiovascular disease event at 10 years across each tenth of risk (the first tenth representing the lowest risk) for the Framingham, ASSIGN, and QRISK equations. Overall, the Framingham equation over-predicted risk at 10 years by 35%, ASSIGN by 36%, and QRISK by 0.4%. All three equations tended to over predict risk in the lowest three tenths for men and women. The most noticeable over-prediction occurred with ASSIGN, followed by the Framingham equation and then QRISK. The Framingham equation, however, consistently over-predicted risk in men across every tenth, with a 51% over-prediction in the top tenth compared with 36% for ASSIGN and 8% for QRISK

Table 5 shows the validation statistics for QRISK compared with the Framingham and ASSIGN equations. The receiver operating curve statistic indicates that the final QRISK score has at least as good as, if not slightly better, discrimination than the Framingham and ASSIGN equations. The R² statistic (standard error) for QRISK in women was 36.4% (0.43%), which is higher than the corresponding value for the Framingham equation which was 31.7% (0.44%). Similarly, the R² statistic for the model for men was higher for QRISK than for the Framingham equation. The D statistic for QRISK was 1.45 for men and 1.55 for women, both higher than the corresponding values for the Framingham equations which were 1.31 and 1.39 respectively, indicating better discrimination for QRISK.

Predictions with age, sex, and social deprivation

Table 6 shows the proportion of patients with a cardiovascular disease risk score ≥20% by sex and Townsend fifth in patients aged 35-74, estimated using three risk scores.
equation are 6.3% (most deprived) and 4.6% (most affluent).

QRISK predicts 12.6% of men from the most deprived areas to be at high risk compared with 9.6% of those from the most affluent areas. The corresponding values for the Framingham equation were 19.5% (most deprived) compared with 20.5% (most affluent).

Overall QRISK predicted 8.5% of patients aged 35-74 to be at high risk compared with 12.8% for the Framingham equation. The corresponding values for the Framingham equation were 19.5% (most deprived) compared with 20.5% (most affluent).

Overall QRISK predicted 8.5% of patients aged 35-74 to be at high risk compared with 12.8% for the Framingham equation and 14.0% for ASSIGN (table 7). Using QRISK 34.5% of women and 72.9% of men aged 64-75 would be at high risk compared with 24.1% and 86.0% using the Framingham equation. Estimates based on QRISK give 3.2 million patients aged 35-74 at high risk in the United Kingdom for 2005, with the Framingham equation predicting 4.7 million and ASSIGN 5.1 million.

DISCUSSION

We derived and validated a new cardiovascular disease risk equation (QRISK) in the United Kingdom in readiness for a major change in national policy on the identification of patients at high risk of cardiovascular disease. It is the largest such study to have ever been undertaken and the first time that routine data in a UK general practice population have been used rather than an observational study in a predefined cohort. The study was validated on an independent sample of practices (although data capture methods are uniform in the derivation and validation sample) and performs as well if not better than the Framingham algorithm in the UK population. However, since the validation was carried out in a similar population to the population from which the algorithm was derived, it potentially has a “home advantage.” Further validation in other populations is therefore required.

QRISK includes standard as well as additional risk factors for cardiovascular disease, such as deprivation, family history of premature coronary heart disease, body mass index, and the effect of existing antihypertensive treatment. Inclusion of antihypertensive treatment at baseline is of relevance to 1 in 10 of the population and failure to take this into account would lead to a significant underestimation of cardiovascular disease risk in the population. The positive associations with antihypertensive treatment and cardiovascular disease risk were expected as these patients might have several factors as well as blood pressure associated with increased risk. Also these patients might have subclinical disease.

Unlike the existing Framingham equations and the European SCORE equation, QRISK identifies and includes deprivation in the estimation of cardiovascular disease risk. This will be an important step in supporting national initiatives to reduce health inequalities in cardiovascular disease and is likely to be an improvement on the Framingham algorithm, which tends to overestimate risk in affluent areas and underestimate risk in deprived areas. Also, a weighting for social deprivation might help to minimise health inequalities, which may increase when new interventions are introduced because of the inverse equity hypothesis. The inclusion of a family history of premature coronary heart disease is important because observational studies indicate that such disease in a first degree relative increases risk by 50% or more, although our estimates were lower. Further work is needed to identify the utility of using self reported ethnicity rather than an area based measure,

<table>
<thead>
<tr>
<th>Age band</th>
<th>Total No in validation cohort</th>
<th>QRISK at high risk in validation cohort</th>
<th>Proportion at high risk (%)</th>
<th>Estimated No at high risk in UK, 2005</th>
<th>Framingham at high risk in validation cohort</th>
<th>Proportion at high risk (%)</th>
<th>Estimated No at high risk in UK, 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
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<td>35-44</td>
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<tr>
<td>55-64</td>
<td>61 729</td>
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<td>74 008</td>
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<tr>
<td>65-74</td>
<td>48 021</td>
<td>16 563</td>
<td>34.49</td>
<td>917 189</td>
<td>11 568</td>
<td>24.09</td>
<td>640 587</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
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<tr>
<td>Age group:</td>
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<td>439 660</td>
<td>23 164</td>
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<tr>
<td>65-74</td>
<td>36 483</td>
<td>26 596</td>
<td>72.9</td>
<td>1 741 720</td>
<td>31 385</td>
<td>86.03</td>
<td>2 055 342</td>
</tr>
<tr>
<td>All patients</td>
<td>614 553</td>
<td>51 908</td>
<td>8.45</td>
<td>3 183 291</td>
<td>78 588</td>
<td>12.79</td>
<td>4 714 860</td>
</tr>
</tbody>
</table>
because the inclusion of area measures of ethnicity in QRISK did not improve the utility of the score possibly as a result of the correlation with the area based measure of deprivation. QRISK tackles components not included in SCORE, which was designed for European use. SCORE does not include cardiovascular disease morbidity, which is an integral part of both trial data (non-fatal myocardial infarction and stroke) and cost effectiveness reviews. The health technology assessment of statins in the United Kingdom has identified a cardiovascular disease event of 20% in 10 years as the threshold for treatment, of which most are non-fatal events.36

Although QRISK includes more variables than the Framingham algorithm and therefore seems more complex, QRISK has been derived from routinely collected clinical data from general practice. Not only is QRISK likely to have a face validity in the setting where it is likely to be applied, but software can be developed within the general practice clinical system to automatically calculate scores. Therefore this could be implemented simply in clinical practice to flag high risk patients for further assessment. Furthermore, the case for inclusion of antihypertensive treatment has already been made with respect to Framingham equations for risk prediction of stroke, a component of this new equation.37

This study is based on a large, representative and contemporary UK population with data obtained from a validated research database. We used an open cohort study design, which allowed patients to enter the study population throughout the study period. This was done so that patients who had more recent data could be included in the estimation of the model coefficients. The disadvantage of this approach is that not all our patients had the opportunity to contribute 10 years of follow-up data although we did have over 300 000 patients with at least 10 years of follow-up data. The median follow-up time was therefore relatively short compared with the long established Framingham cohort and the more recent cohort used for ASSIGN. This could introduce some imprecision in the estimate of survival at 10 years. To assess this we restricted the analysis to the closed cohort and found minimal difference in the baseline survivor function. As incidence of cardiovascular disease is changing over time it is important to update this algorithm periodically as planned. The cohort is socially, ethnically, and geographically diverse and over 250 times the size of the original Framingham cohorts from 30-50 years ago. It includes both men and women.

The utility of any tool for risk prediction depends on the quality of the data used to derive it; both risk factors and outcome measure. Although levels of completeness for some risk factors were good (notably body mass index, smoking, and blood pressure), recording levels were low for serum cholesterol. This is a likely source of bias and may have contributed to the attenuation of the hazard ratio of the cholesterol ratio term towards one. However, comparison with the mean values for systolic blood pressure, cholesterol, and body mass index from the health survey for England shows that this population is likely to be representative of the population in England. This means our results should be generalisable. The exception was smoking where the survey rates were higher than the study rates for women but lower than the study rates for men. This could reflect a differential bias in self reported smoking status either within the survey, within the patients’ electronic health record, or within both. A strength of our study, however, is the use of multiple imputation of missing values, a technique that is designed to increase the power of the analysis and produce models that are more statistically reliable and applicable within clinical practice.24 25 The pattern of missing values, including differences in survival for patients with and without missing data, supported the use of this approach as compared with a complete case analysis. We used a single baseline measure for systolic blood pressure, which might lead to underestimation of its association with cardiovascular disease risk owing to large variation within individuals. Also we included a relatively crude measure of blood pressure treatment rather than undertaking a more complex time varying approach.

The outcome measures in our study were not formally adjudicated—that is, some patients with a diagnosis of cardiovascular disease may have been misdiagnosed. Validation studies of similar general practice databases show that false positive diagnoses occur in fewer than 10% of cases.38 Similarly, the information for some patients with cardiovascular disease may not be recorded on the clinical records. Such misclassification of outcomes, if present and if non-differential for risk factors, will result in hazard ratios tending towards one, which would reduce the discriminatory power of a risk score. Our subgroup analysis between 2002 and 2007, however, showed a 94% ascertainment rate for cardiovascular disease outcomes based on the general practice clinical record alone compared with outcomes including death certification data.

Under-ascertainment is more likely to affect patients from the most deprived areas and so it is possible that our algorithm will underestimate risk in these patients. This underlines the need to include measures of deprivation in both the development and the application of risk prediction scores as well as the need for more and better data linkage across the health service. It is worth noting that this is the first time that cause of death data from the Office for National Statistics have been linked to general practice data across 60% of the United Kingdom. Only a five year subset of data were ready in time for this analysis, data back to 1993 will be used to update algorithms for coronary heart disease and stroke.

Lastly, although we have validated QRISK on a separate sample of one third of practices from QRESEARCH (that is, a different population from the population used to develop the algorithm), it could be argued that this is not an entirely independent population because all the practices were using the EMIS clinical system. This potentially gives a “home advantage”
WHAT IS ALREADY KNOWN ON THIS TOPIC
Current cardiovascular risk prediction algorithms based on the Framingham model tend to over-predict risk and are not well calibrated for the UK population.
The Framingham model does not include measures of deprivation, family history, body mass index, or current treatment with antihypertensives.

WHAT THIS STUDY ADDS
A new risk score, QRISK, performed at least as well as the Framingham model for discrimination and was better calibrated to the UK population than either the Framingham model or ASSIGN.
QRISK would identify a different high risk group of patients than the Framingham equation, with one in ten patients being reclassified into high or low risk.
QRISK includes additional variables that allow better tailoring of management to the individual patient and will help to minimise health inequalities.

to QRISK as prediction algorithms tend to perform better in populations similar to the ones in which they were derived. A second validation is therefore under-way using a different general practice database (THIN) derived from practices using a different clinical computer system. This analysis, which will be a more severe test of the performance of QRISK, will be reported separately when complete.

Comparison with Framingham and ASSIGN algorithms
The Framingham cohort is an invaluable resource for epidemiology and aetiology owing to the completeness of data. The weakness is that it was based on exceptionally high rates of cardiovascular disease at the height of an epidemic but is now used as a tool to describe risks in contemporary European populations for the purpose of drug treatment. It has repeatedly been shown to be seriously inaccurate. QRISK explains a higher percentage of the variation than either the Framingham or ASSIGN algorithms in both men and women. Discrimination (the ability to differentiate between high and low risk patients) with QRISK was better than with the Framingham equation. Improved discrimination using QRISK results in a steeper gradient of cardiovascular disease risk for social deprivation compared with estimates using the Framingham equation. QRISK tends to increase cardiovascular disease risk estimates in people living in deprived areas relative to those in more affluent areas. This effect is most noticeable for women from deprived areas. Inclusion of area based deprivation measures within the QRISK prediction algorithm is likely to predict more accurately which patients are at high or low risk and so target interventions more appropriately on the basis of likely clinical need.

Our analysis shows that neither the Framingham nor ASSIGN equations is well calibrated for this UK population, with both scores tending to over-predict risk. If the patient’s absolute risk is lower than predicted, the absolute benefits of an intervention will be smaller and the balance of risks and benefits will be less favourable. Additionally, overestimation of risk prediction will adversely affect direct prescribing costs as well as the costs associated with monitoring for, and managing, side effects. The degree of over-prediction for the Framingham algorithm is consistent with that reported in other validation studies of the Framingham equation in the United Kingdom. We think that the over-prediction is probably the result of a combination of differences in risk factor means and prevalences and baseline survival function. In ASSIGN, for example, 41.5% of patients smoked compared with 26% of the study population; 26% of patients in the ASSIGN cohort had a family history of premature coronary heart disease in a first degree relative compared with 11% recorded in the study population. The mean serum cholesterol level in the ASSIGN cohort was 6.23 mmol/l compared with 5.8 mmol/l in our population. ASSIGN is calibrated to the incidence of cardiovascular disease in Scotland, which is higher than that in England. Although much less noticeable, some over-prediction occurred in the top tenth using QRISK, which might reflect an effect of increasing age when the effect of risk factors diminish and survivors are more resilient. Alternatively it could be due to competing risks of death, such as cancer, which become more important at higher ages.

Conclusion
We have derived and validated a new cardiovascular disease risk prediction score that is better calibrated for the UK population and has better discrimination. Overall in patients aged 35-74, the Framingham algorithm over-predicted cardiovascular disease risk at 10 years by 35%, ASSIGN by 36%, and QRISK by 0.4%. QRISK predicted 9% of patients aged 35-74 to be at high risk compared with 13% for the Framingham equation and 14% for ASSIGN. Using QRISK we estimate that 34% of women and 73% of men aged 64-75 would be at high risk compared with 24% and 86% according to the Framingham equation. UK estimates on the basis of QRISK give 3.2 million patients at high risk in 2005, compared with 4.71 million for the Framingham equation and 5.1 million for ASSIGN. Overall, QRISK would reclassify about 1 in 10 patients from high to low risk or vice versa compared with the Framingham algorithm.

We think that QRISK is likely to provide more appropriate estimates of cardiovascular disease risk in contemporary UK populations and better discriminate those at high risk on the basis of their age, sex, and social deprivation as well as existing antihypertensive treatment. It is likely therefore to be a more equitable tool to inform patient management decisions.

We thank EMIS and the EMIS practices contributing to QRESEARCH; Patrick Royston for advice on multiple imputation, fractional polynomials, and the D statistic; Rod Jackson, Stuart Pocock, Philip Bath, Hugh Tunstall-Pedoe, and Mark Woodward for reviewing the protocol; and the following who enabled the project, contributed to discussions, or facilitated the linkage of cause of deaths data with general practice data—Nirupa Dattani and Sir Peter Goldblatt (Office for National Statistics), Steve Daniels (Connecting for Health), John Fox and Dave Roberts (Information Centre), Andy Whitwam and David Stables (EMIS), Bill Kirkup, Maggie Rae, Michael Soljak, and Roger Boyle (Department of Health).
Contributors: JHC initiated and designed the study, obtained approvals, prepared the data, undertook the analysis and interpretation, and wrote the first draft of the paper. CC, YV, and MM contributed to the development of the protocol, design, analysis and interpretation, and drafting of the paper. CC and YV undertook some of the primary analyses with JHC. JR and PB contributed to the conception, design, analysis, interpretation, and drafting of the article and approved the final version.

Funding: The study received no external funding.

Competing interests: JR, chains, and PB is a member of, the NICE guideline development group on cardiovascular risk assessment "The modification of blood lipids for the primary and secondary prevention of cardiovascular disease." JHC is codirector of QRESEARCH, a not for profit organisation that is a joint partnership between the University of Nottingham and EPS (leading supplier of information technology for 60% of UK general practices). QRESEARCH undertakes analyses for the Department of Health and other government organisations. All research using the database is peer reviewed and published. QRESEARCH is not used for studies for the pharmaceutical industry.

Ethical approval: This study was approved by the Trent multicentre research ethics committee.

16 Hippisley-Cox J, Vinogradova Y, Coupland C, Pingle M. Comparison of key practice characteristics between general practices in England and Wales and general practices in the QRESEARCH data. Report to the Health and Social Care Information Centre; University of Nottingham, 2005.

Accepted: 27 June 2007
Preventing deep vein thrombosis in hospital inpatients

William E Cayley

Most hospital inpatients are at risk of deep vein thrombosis (DVT) and the associated complications of fatal or non-fatal pulmonary embolism and post-thrombotic syndrome. Recognised risk factors for DVT are generally related to one or more elements of Virchow’s triad (stasis, vessel injury, and hypercoagulability), and include surgery, trauma, immobilisation, malignancy, use of oestrogens, heart or respiratory failure, and smoking (box 1). Surveillance studies have found that the absolute risk of DVT is 10%-20% among general medical patients and up to 40%-80% in patients having hip surgery, knee surgery, or major trauma (table). It is difficult to predict which at-risk patients will develop DVT, and fatal pulmonary embolism can occur without warning without prior clinical suspicion. It is therefore important to take appropriate preventive measures for all hospital inpatients and to determine which of them warrant additional prophylaxis. Major guidelines on DVT prophylaxis have been produced by the American College of Chest Physicians, the Institute for Clinical Systems Improvement, the Scottish Intercollegiate Guidelines Network, the American College of Obstetricians and Gynecologists, and the National Institute for Health and Clinical Excellence (NICE).

What are the methods of DVT prophylaxis?
Methods of DVT prophylaxis include general measures: the use of aspirin, mechanical prevention with graduated compression stockings, and intermittent pneumatic compression devices. Anticoagulants often used include unfractionated heparin (UFH) (usually given as 5000 units two or three times daily), low molecular weight heparins (LMWH) (usually enoxaparin or dalteparin), vitamin K antagonists (most often warfarin, but also acenocoumarol, phenindione, and dicoumarol), and fondaparinux (a selective factor Xa inhibitor) (box 2).

How well do the mechanical methods of prophylaxis work?
A Cochrane review found that graduated compression stockings were effective in reducing rates of DVT for general medical and surgical patients whether they were used alone or in addition to other DVT prophylaxis. In nine studies comparing graduated compression stockings with no prophylaxis, rates of DVT were reduced from 27% to 13%, and in seven studies the addition of the stockings to background prophylaxis further reduced DVT rates from 15% to 2%.

Additionally, a recent randomised but non-blinded clinical trial found that the use of graduated compression stockings in patients with DVT reduced the risk of post-thrombotic syndrome from 49% to 26%. A meta-analysis of 57 studies found that intermittent pneumatic compression devices for the thigh and calf were effective in reducing rates of DVT when compared with placebo (from 29% to 11%) and with graduated compression stockings alone (from 15% to 8%). A recent systematic review found that graduated compression stockings, intermittent pneumatic compression devices, and foot pumps reduce the risk of DVT in surgical patients by two thirds when used as monotherapy and by an additional 50% when added to drug prophylaxis. The review also found that mechanical prophylaxis in surgical patients may reduce the risk of pulmonary embolism by about two fifths. Mechanical prophylaxis must be used with caution, however, if a patient has peripheral arterial insufficiency.

Can aspirin be used to reduce the risk of DVT?
Aspirin has been considered as a possible low risk measure for preventing DVT. One large trial has documented a reduction in symptomatic DVT and fatal pulmonary embolism with aspirin prophylaxis, with only a small increased risk of minor bleeding that did not require transfusion. Although the guidelines from the American College of Chest Physicians

SOURCES AND SELECTION CRITERIA
I identified sources for this review by searching Medline (www.ncbi.nlm.nih.gov/entrez/query.fcgi), the Cochrane Collaboration (www.cochrane.org) and the National Guideline Clearinghouse (www.guideline.gov) in November 2005 for references to prevention of deep vein thrombosis. I selected reviews, guidelines, and studies if they discussed prevention of deep vein thrombosis in medical or surgical inpatients.
and the Institute for Clinical Systems Improvement recommend against relying on aspirin for prevention DVT because of the risk of increased bleeding, the guidelines from the Scottish Intercollegiate Guidelines Network advocate aspirin as an effective prophylaxis in surgical patients because of its efficacy in reducing fatal pulmonary embolism.

### How can we reduce risk of DVT in general medical patients?

Medical patients account for up to a quarter of venous thromboembolic events in the general population. UFH and LMWH have been studied for DVT prophylaxis in the general medical population, and a meta-analysis published in 2000 found that both heparin types reduced the rates of DVT and clinical pulmonary embolism by 56%-58%. No differences were found between the two types of heparin in the rates of DVT, clinical pulmonary embolism, or death, but use of LMWH carried a lower risk of major bleeding. Guidelines from the American College of Chest Physicians, the Institute for Clinical Systems Improvement, and the Scottish Intercollegiate Guidelines Network support ambulation for all patients if possible, and recommend LMWH or UFH for medical patients with heart failure or respiratory disease or with substantial immobility plus additional risk factors for DVT. Mechanical prophylaxis may be considered in all immobile patients and should be used for those who cannot receive anticoagulants.

### How can we reduce risk of DVT in surgical patients?

A recent systematic review found that, across all types of surgery, monotherapy with oral anticoagulants halved the risk of DVT. However, oral anticoagulants also doubled the risk of major bleeding and were less effective than heparins at preventing DVT.

### General and other non-orthopaedic surgery

Patients admitted to hospital for general surgery are at moderate risk of DVT, and a 1997 meta-analysis of 33 studies showed that both UFH and LMWH were effective in reducing rates of DVT and pulmonary embolism in general surgery patients. The meta-analysis found no difference in major bleeding between the two treatments, but LMWH showed a 25% relative risk reduction in the risk of minor bleeding.

A more recent meta-analysis based on published randomised controlled trials confirmed that LMWH reduced rates of asymptomatic and symptomatic DVT and rates of pulmonary embolism in general surgery patients compared with placebo; it also found that high quality studies showed no difference between LMWH and UFH in terms of efficacy (reduction of DVT or pulmonary embolism) or safety (risk of bleeding). These findings were confirmed by a second meta-analysis published the same year, based on original patient data, which again found that both types of heparins were equally effective and equally safe for reducing DVT in general surgery patients.

Guidelines from the American College of Chest Physicians, the Institute for Clinical Systems Improvement, and the Scottish Intercollegiate Guidelines Network recommend early mobilisation for general surgery patients at low risk of DVT; UFH or LMWH for patients with risk factors for DVT (including age), and the addition of mechanical prophylaxis to LMWH or UFH for those with multiple risk factors for DVT. The NICE guidelines recommend that all surgical inpatients are offered graduated compression stockings (unless contraindicated) from the time they are admitted and that general surgery patients with one or more risk factors for DVT are also given LMWH or fondaparinux.

Patients having major gynaecological surgery have a 7%-45% risk of DVT, and 1% of those with DVT may have a fatal pulmonary embolism. A Cochrane review of eight trials found evidence that, compared with placebo, 5000 units of subcutaneous UFH when started perioperatively and given two or three times daily for seven days reduced rates of DVT in women with malignancy, and, in one trial, warfarin given 6 mg daily reduced rates of DVT in women without malignancy. The review found no difference in...
DVT rates when UFH was compared with warfarin or with LMWH. None of the studies in the review were able to show a reduction in pulmonary embolism.

Minimal research has been conducted on mechanical methods of DVT prophylaxis for major gynaecological surgery. Guidelines from the American College of Obstetricians and Gynecologists recommend that patients at moderate or high risk of DVT (such as those having major surgery or who have malignancy or other risk factors) should receive prophylaxis with either thigh high graduated compression stockings placed intraoperatively and continued until the patient is ambulatory, or UFH or LMWH started preoperatively and continued until discharge. The American College of Chest Physicians and the Scottish Intercollegiate Guidelines Network also recommend UFH or LMWH, with use of intermittent pneumatic compression devices or graduated compression stockings if anticoagulation is contraindicated. NICE recommends mechanical prophylaxis for all patients, with the addition of LMWH for those with one or more risk factors for DVT.

Colorectal surgery may carry a higher risk of DVT than other general surgery procedures, and a Cochrane review in 2003 found that both LMWH and low dose UFH reduced risk of DVT and pulmonary embolism to the same extent, while the use of graduated compression stockings in addition to a heparin provided additional protection. Patients having major open urological procedures often have multiple risk factors for DVT (including age and immobility). Little high quality evidence relates to this population, but guidelines favour using prophylaxis with UFH, LMWH, graduated compression stockings, or intermittent pneumatic compression devices in urology patients at high risk. Patients having major vascular surgery (such as aortoiliac or aortofemoral surgery or aortic aneurysm resection) usually also have multiple risk factors for DVT, but as these procedures are usually accompanied by antiplatelet therapy, it is difficult to tell whether DVT prophylaxis confers an independent benefit. Guidelines recommend UFH or LMWH for DVT prevention if vascular surgery patients have additional thrombotic risk factors.

Orthopaedic surgery

Patients having major orthopaedic surgery are at particularly high risk of DVT, and methods of prophylaxis have been extensively investigated. Two meta-analyses found that rates of DVT after total knee arthroplasty were much lower with intermittent pneumatic compression devices or LMWH (17%-29%) than with aspirin or warfarin (45%-53%).

A Cochrane review of DVT prophylaxis after hip fracture surgery found that although both UFH and LMWH reduced lower limb DVT, the two heparins did not differ in efficacy; the review found no reduction in rates of pulmonary embolism with either of the heparins. The review found insufficient data to evaluate the efficacy of intermittent pneumatic compression devices. A more recent meta-analysis of multiple vitamin K antagonists in orthopaedic surgery [including warfarin, acenocoumarol, phenindione, and dicoumarol] confirmed their effectiveness in reducing DVT.
and clinical pulmonary embolism compared with placebo and in reducing DVT compared with intermittent pneumatic compression devices but still found they were less effective than LMWH for reducing DVT. The same review found no difference between vitamin K antagonists and LMWH in the rates of wound haematoma. Meta-analyses have been unable to detect significant differences in DVT rates when comparing different currently recommended LMWH dosing regimens, or when comparing preoperative and postoperative initiation of LMWH prophylaxis.

Current guidelines from the American College of Chest Physicians and the Institute for Clinical Systems Improvement recommend LMWH, vitamin K antagonists, or fondaparinux for elective hip or knee arthroplasty. These same methods, plus UFH are also recommended for hip fracture surgery, and either of the heparins should be started after hospital admission if fracture repair is going to be delayed. Prophylaxis should continue at least 10 days after major orthopaedic surgery and preferably up to four to five weeks after hip replacement or hip fracture surgery. The Scottish Intercollegiate Guidelines Network places more emphasis on the use of aspirin for DVT prophylaxis in elective orthopaedic surgery and hip fracture surgery. NICE recommends mechanical prophylaxis plus either LMWH or fondaparinux for elective orthopaedic surgery and hip fracture surgery, with continuation of the heparin or fondaparinux for four weeks after hip fracture surgery and hip replacement in patients with risk factors for DVT.

Trauma patients

Major trauma can place patients at particularly high risk of DVT or pulmonary embolism. The American College of Chest Physicians and the Scottish Intercollegiate Guidelines Network recommend LMWH for prophylaxis, with mechanical prophylaxis if the risk of bleeding precludes using anticoagulants.

Summary

Appropriate use of DVT prophylaxis in hospital inpatients is important for reducing the risk of postthrombotic complications as well as fatal and non-fatal pulmonary embolism. One of the most important steps in ensuring adequate prophylaxis against DVT is encouraging doctors to follow appropriate guidelines. A meta-analysis of interventions to improve compliance with guidelines found that strategies using electronic or paper based audit and feedback, or some other active reminder, were much more successful at improving rates of prophylaxis compared with passive education or dissemination of guidelines.

For patients at low risk of DVT, ambulation is important, and mechanical methods of prophylaxis can provide added protection. Patients at higher risk of DVT should be considered for guideline based anticoagulation with LMWH, UFH, or vitamin K antagonists unless clearly contraindicated. Fondaparinux is a newer agent that may provide additional prophylactic options. The place of aspirin in DVT prophylaxis remains controversial.

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Competing interests: None declared.
Provenance and peer review: Not commissioned; externally peer reviewed.

The magnetic resonance egg timer

Unless something is happening, an x-ray department can seem as uninteresting as an empty garage or aircraft hangar, but it is unethical to let visitors watch patients being examined. Fortunately, when the distinguished members of the Cirencester Science and Technology Society visited us to learn about radiological scanning, one of our secretaries agreed to act as a model, so demonstrating ultrasonography was not a problem. The visitors could see her heart and aorta pulsating, learn how a Doppler signal can be used to assess vascular flow, and witness how abdominal anatomy can be obscured by calcium in the ribs or air in the bowel.

A selection of foods and other items hidden in a cardboard box proved a popular way to demonstrate computed tomography. The visitors enjoyed being quizzed about the contents of the box, and having to distinguish cherries from grapes, a banana from a courgette, and a bruised apple from a sound one. They were also asked to distinguish a length of skating board from a piece of “tongue-and-groove” plank, and the grain of the timber was shown exquisitely. Scans were completed in seconds, sections in all three orthogonal planes were quickly constructed, and post-processing techniques such as surface rendering were demonstrated.

We showed off magnetic resonance imaging (MRI) using a different phantom, a chicken carcasse filled with eggs. The MR images not only revealed the detail of the chicken’s anatomy but also distinguished each egg’s embryo, yolk, and albumen. The differences between a fresh egg, a bad egg, and a chocolate cream egg were discernable, and one egg was made invisible by wrapping it in aluminium foil. The foil acts like a Faraday cage: it is a barrier to the passage of the radio waves which cause the resonance of protons on which MR signal is dependent.

An unforeseen effect, however, was how cooking an egg changed its MR signal. The albumen of a fresh egg seems white on T2 images, but the signal is lost on cooking so the white turns to black. The change from white to black extends in from the outside as the egg cooks. When an egg is ready to eat and the albumen has solidified, the white of an egg is completely black on T2 images. This occurs, as may be guessed from breakfast experiences, after boiling for a little over three minutes.

Brian Witcombe
consultant in radiology, Gloucester Royal NHS Trust
brian.witcombe@glos.nhs.uk

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PREGNANCY PLUS

Eczema in pregnancy

Sophie Weatherhead,1 Steven C Robson,2 Nick J Reynolds3

Introduction

Atopic eczema has a reported lifetime prevalence of 8-17% in adults aged under 60.1 It is more common in women, affecting 16% in the United Kingdom, and in adults has its highest prevalence between the ages of 16 and 24.2 The incidence of eczema seems to be generally increasing, particularly in children.3,4 Moderate to severe eczema can be particularly difficult to manage, and second line treatments are often needed to control it.5

As the scenario suggests, treatment options become limited when a patient decides to try to conceive, and disease control is often suboptimal. This article discusses management of eczema in pregnancy.

SCENARIO

A 26 year old woman with lifelong moderate to severe atopic eczema had been unable to achieve good disease control with topical drugs. She received narrow band ultraviolet B phototherapy in 2001 but relapsed within a short time. As part of a randomised controlled trial she received 12 weeks of azathioprine,6 on which she greatly improved. She subsequently failed to respond to topical tacrolimus but received two further courses of azathioprine, both with an excellent response. Six months after stopping azathioprine she became pregnant, and her eczema quickly flared. This was managed with potent topical steroids, although her disease remained troublesome throughout the pregnancy. After the birth of her child, her eczema was managed with methotrexate with a good response.

Methods

We searched national health information sources, the Cochrane database and PubMed up to March 2007. Key search words used included “atopic dermatitis”, “eczema”, “pregnancy”, “maternal”, and “breastfeeding”. We used our personal archive of references and sought advice from the National Teratology Information Service, Drug Information Department, Royal Victoria Infirmary, Newcastle upon Tyne and from colleagues.

How common is eczema in pregnancy?

Eczema is the most common dermatosis of pregnancy, accounting for between a third and a half of all cases.7,8 Only 20-40% of patients are estimated to have a pre-existing history of eczema; the rest develop symptoms for the first time during pregnancy.9 Three quarters of these patients develop symptoms within the first two trimesters. The total prevalence of eczema in pregnancy is unknown.

Does pregnancy affect eczema?

Eczema has a fluctuating course in most patients and is influenced by environmental and internal triggers. However, pregnancy does seem to have an effect on eczema in most women with the condition—approximately 25% improve, and more than 50% experience a deterioration.9 Although available data are limited, pre-existing eczema may deteriorate at any stage of pregnancy, and a slightly higher rate is seen in the second trimester.9 About 10% of cases flare in the postpartum period.

In most cases, pregnancy biases T cell immunity towards a type 2 T helper response, and this is thought to be important for continuation of a normal pregnancy.10 However, a type 2 response is also associated with atopy, and this bias may explain why eczema can deteriorate during pregnancy. Whether skin barrier function or expression of filaggrin (a protein needed for terminal differentiation of cells within the epidermis, which is commonly mutated in eczema11,12) changes during pregnancy is unknown.

Does eczema affect the outcome of pregnancy?

Little or no evidence exists to suggest that eczema directly affects fertility or rates of miscarriage, birth defects, or premature birth. However, secondary skin infection with herpes simplex virus causes eczema herpeticum. Although eczema herpeticum has not been reported to cause intrauterine infection to date, herpes simplex virus is associated with premature delivery, intrauterine growth restriction, and miscarriage.13 Aciclovir seems to be safe in pregnancy,14 so prompt treatment is warranted if eczema herpeticum is suspected clinically. Infection can be confirmed by a viral swab taken before treatment.

Little evidence suggests that eczema is associated with illnesses such as depression. With the exception of infected eczema, the condition should not affect a woman’s birth plan or her obstetric outcome after delivery.

Good evidence suggests that both genetic and environmental factors are important in determining whether a child will develop eczema. Studies have shown a higher concordance of eczema in monozygotic twins (risk=0.86) than in dizygotic twins (risk=0.21).15 Moreover, recent genetic evidence indicates that an
Advice for eczema patients before conception

Eczema treatments in pregnancy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
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<tr>
<td><strong>Safe</strong></td>
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<tr>
<td>Emollients</td>
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<tr>
<td>Topical steroids (mild, moderate, or potent)</td>
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<tr>
<td>Ultraviolet B</td>
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<tr>
<td><strong>Relatively safe (caution)</strong></td>
<td></td>
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<tr>
<td>Very potent topical steroids (small quantities)</td>
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<tr>
<td>Oral steroids (in third trimester)</td>
<td></td>
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<tr>
<td>Ciclosporin* (Azathioprine)</td>
<td></td>
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<tr>
<td>Topical calcineurin inhibitors (small quantities)</td>
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<tr>
<td>Avoid</td>
<td></td>
</tr>
<tr>
<td>Methotrexate*</td>
<td></td>
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<tr>
<td>Psoralens plus ultraviolet A (PUVA)*</td>
<td></td>
</tr>
<tr>
<td><strong>Recommended minimum systemic drug-free interval before conception</strong></td>
<td></td>
</tr>
<tr>
<td>Methotrexate—three months (men and women)</td>
<td></td>
</tr>
<tr>
<td>PUVA—no minimum time but stop before conception</td>
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</tbody>
</table>

*Avoid in breastfeeding mothers

important proportion of atopic eczema is caused by non-functioning filaggrin that results in a primary skin barrier defect.11,12 This could potentially allow abnormal cutaneous penetration of environmental allergens and chemicals leading to increased immune activation. Some studies suggest a greater heritability of eczema maternally rather than paternally, although others do not.13 Maternal gene imprinting or transplacental fetal exposure to allergen could possibly contribute to this. A recent systematic review examined whether maternal dietary avoidance of cows’ milk or egg during pregnancy affects the subsequent development of eczema in the child, but the evidence did not support an effect.17

How is a patient with eczema managed in pregnancy?

Where possible, advice before conception should include strategies to minimise disease activity at baseline, as eczema may deteriorate during pregnancy. This should include advice about avoiding irritants and allergens, the use of emollients (see below), and how to apply topical treatments. A patient who is receiving systemic treatment for eczema should be made aware of the minimum time interval between stopping their treatment and safely getting pregnant, without increased risk to the child (box).

Emollients remain an integral part of eczema management in all patients. Taking tepid baths, using emollients, and avoiding soap can minimise barrier disruption, which may otherwise increase transepidermal water loss and exacerbate eczema. Moderate to potent topical steroids combined with moisturisers remain the mainstay of treatment for mild to moderate eczema and, with the exception of very potent topical steroids, can continue to be used relatively safely throughout pregnancy.19

Bacterial infections are an important cause of exacerbations and should be treated promptly to avoid further deterioration. *Staphylococcus aureus* colonises more than 90% of eczema lesions,16 but active infection may be suggested by the presence of increased pain or swelling, impetigo-like crustings, or inflammatory papules.

Moderate to severe eczema may need second line treatments when not controlled by the above measures. Systemic steroids are used only rarely by dermatologists for the treatment of eczema, and they may be associated with a rebound flare of disease when stopped. Oral steroids have been associated with cleft lip and palate defects in mice, but little evidence supports this occurring in humans.18,20,24 Oral steroids may also be linked to fetal growth restriction, although much of the evidence for this comes from their use in patients with asthma, and separating the effects of maternal disease from treatment is difficult. When eczema remains uncontrolled despite optimisation of topical steroids, narrowband ultraviolet B has been shown to reduce disease severity by more than 30% in a randomised controlled trial and is probably the safest second line treatment in pregnancy.21

Topical calcineurin inhibitors, such as tacrolimus and pimecrolimus, are increasingly used as second line agents in primary and secondary care. The manufacturers advise avoidance of topical calcineurin inhibitors during pregnancy. Although systemic tacrolimus is teratogenic, the bioavailability of the topical form is limited (<5%) and its use has not been associated with fetal anomalies.20 No epidemiological studies of pregnancy after use of systemic tacrolimus exist, and congenital malformations are not reported, although intrauterine growth restriction may occur. Therefore, if eczema remains poorly controlled despite optimal first line treatment and ultraviolet B is ineffective or contraindicated, topical calcineurin inhibitors may be considered after appropriate discussion; however, accepted practice is to restrict use to localised areas.

Patients who continue or start systemic treatment during pregnancy will need close monitoring in the hospital setting, by both dermatologists and obstetricians. If systemic agents are needed, the safest option is likely to be ciclosporin, although this should be used for the shortest duration possible (typically less than six months) to avoid the increasing risk of renal impairment in the mother. In a double blind randomised crossover trial, ciclosporin improved eczema by 39% over eight weeks,27 although no specific data exist for pregnant patients. Ciclosporin does cross the placenta, but information from organ transplantation suggests that it is relatively safe. Fetal growth restriction has been reported in this group but probably relates to underlying maternal disease.

Another important second line treatment is azathioprine. A recent randomised controlled trial in non-pregnant patients showed this reduced disease severity by approximately 37%.1 It readily crosses the placenta, and its use during pregnancy has been associated with miscarriage, preterm delivery, and fetal growth restriction.28 However, the fetus seems to be protected from teratogenic effects, as its liver lacks the enzyme needed to convert azathioprine into active metabolites,29 and no compelling evidence of an association with congenital malformations in humans exists. The case reports of azathioprine in pregnancy come from its use in pregnant transplant recipients, and current advice to these patients is to continue its use; no reports exist of patients taking azathioprine for eczema becoming pregnant. Rarely, it
has been associated with neonatal leucopenia, pancytopenia, or inhibition of neonatal haematopoiesis, although this should be predictable by maternal leucopenia in the third trimester. Use of azathioprine in severe eczema must be decided on a case by case basis.

Methotrexate, although likely to be effective in moderate to severe atopic eczema, is contraindicated in pregnancy and breastfeeding mothers. Patients established on ciclosporin or azathioprine before pregnancy will need careful counselling and liaison with obstetricians. Furthermore, those taking ciclosporin need regular monitoring of full blood count, renal function, and blood pressure, and those taking azathioprine need regular full blood count and liver function tests.

How is eczema managed in the postpartum period?

Mild to moderate eczema is managed routinely with emollients and topical steroids or topical calcineurin inhibitors. In breastfeeding women, topical calcineurin inhibitors are not recommended by the manufacturers, although early reports of women taking oral tacrolimus after transplantation suggest that minimal amounts of tacrolimus pass into milk. Further studies are needed to assess its safety. Up to 2% of breastfeeding mothers develop eczema of the areola or nipple. About 50% of these will have atopic eczema; other causes include food contact sensitivity or irritation as the baby is weaned on to solids. Moderate to low potency topical steroids and emollients are used to treat eczema in this area, although these should be applied after breast feeding and washed off thoroughly before the next feed.

Ultraviolet B is safe while breast feeding, but safety data are lacking for other second line treatments. However, in a recent cohort of 10 women receiving azathioprine while breast feeding, no adverse effects were seen in the babies, and it was not detected in most of the breast milk collected.

Ciclosporin and methotrexate should be avoided.

We thank Simon Meggitt for critically reviewing the manuscript and the National Teratology Information Service, Drug Information Department, Royal Victoria Infirmary, Newcastle upon Tyne for advice.

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PREGNANCY PLUS

Eczema in pregnancy

Sophie Weatherhead,1 Steven C Robson,2 Nick J Reynolds3

Introduction

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belief that he would escape poisoning by polonium-210, his will would probably be declared invalid.

The golden rule
In a judgment in the case of Kenward v Adams, Mr Justice (later Lord) Templeman stated:

“In the case of an aged testator or a testator who has suffered a serious illness, there is one golden rule which should always be observed, however straightforward matters may appear, and however difficult or tactless it may be to suggest that precautions be taken: [the rule is that] the making of a will by such a testator ought to be witnessed or approved by a medical practitioner who satisfies himself of the capacity and understanding of the testator, and records and preserves his examination and finding.”

Mr Justice Templeman’s golden rule is very important but is associated with potential pitfalls. Firstly, although the rule implies that the doctor should make an examination, we have found that some doctors are reluctant to get involved or do more than write a letter based on their knowledge of the patient (that is, without attention to the specific legal tests).

Secondly, solicitors sometimes ask general practitioners to witness a will without advising them of the legal tests. As a result, we have encountered practitioners who have done a mini-mental state examination and certified capacity on that basis. However, someone with a low score in that test, say 15/30, may have capacity to make a simple will leaving his entire estate to his spouse but be incapable of a more complex will dividing up his estate between several beneficiaries. Similarly, someone who scores 27/30 may lack capacity because of impaired judgment and reasoning due to frontal lobe impairment, which is not tested by the mini-mental state examination.

Thirdly, adherence to the golden rule does not guarantee the validity of a will; it merely provides strong evidence in the event of a future challenge. For example, in the Sharp v Adam case mentioned above, the golden rule was meticulously observed by a general practitioner, but the court none the less declared the will invalid. Thus, in a modern context, solicitors and doctors should consider the golden rule as best practice in providing high quality evidence in the event of a legal challenge—a point made by His Honour Judge Alastair Norris QC along with an interesting suggestion that medical assessments might in future be videotaped.

How to avoid embarrassment
Box 2 outlines some guidelines for doctors who are asked by a solicitor to assess testamentary capacity. Firstly, insist on a letter of instruction from the solicitor confirming that the patient has consented to examination and disclosure of the results. The solicitor should also provide the doctor at the outset with verifiable information about, for example, the patient’s estate and family and confirm in writing the legal test for capacity. (After all, the assessment is for legal not therapeutic reasons.) A reminder from the solicitor that the standard of proof in civil legal matters is the “balance of probabilities” (rather than “beyond reasonable doubt”) is helpful.

Secondly, allow enough time for assessment. The standard, seven minute consultation is wholly inadequate. Thirdly, have the legal tests to hand—such as a copy of box 1. If, as is usual, the problem is one of possible dementia, take a history and examine the patient’s cognitive state (this might well include administering the mini-mental state examination). A full record of the history and examination taken at the time adds force to the doctor’s conclusions. After this, go through the specific tests (box 1) systematically and record the answers verbatim. Contemporaneous notes are powerful evidence to put before a court.

You will probably have to explain to your patient why you are asking embarrassing questions, but embarrassment is best not deferred to the witness box, after the patient’s death. If not already provided, factual information—such as detail about the estate—should be cross checked with the solicitor. Third party information may be considered, but care should be taken with potential beneficiaries. The examination should be conducted in the absence of anyone who stands to benefit or might exert influence.

Witnessing (in accordance with the strict requirements of the Wills Act 1837) is an essential part of the process, but it authenticates only the testator’s signature, not his or her competence. The doctor does not, therefore, have to act as witness, but a doctor’s signature doubtless carries the implication that the testator had capacity. Conversely, it is extremely unwise for a doctor to witness a will without having properly assessed the testator’s capacity.

Because most trouble arises from disappointed potential beneficiaries, a doctor must ask whether the testator has ever made a will before and who is now going to be excluded and why. A person with dementia may not recall having made a previous will, so this must be checked with the solicitor. Some people make serial wills over their last years of life, so the doctor is wise to check the pattern of will making and review all previous wills. This process can expose impairments of memory, reasoning, judgment, and even delusions. Particular care is needed if close relatives such as children are to be excluded; the reasons should be explored in detail and meticulously recorded.

<table>
<thead>
<tr>
<th>Box 2</th>
<th>Process for assessing testamentary capacity</th>
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<tbody>
<tr>
<td>• Get a letter from the solicitor detailing legal tests</td>
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<tr>
<td>• Set aside enough time</td>
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<tr>
<td>• Assess (in the standard way) whether the patient has dementia</td>
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<tr>
<td>• Check that the patient understands each of the Banks v Goodfellow points (box 1)</td>
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<tr>
<td>• Record the patient’s answers verbatim</td>
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<tr>
<td>• Check facts, such as the extent of the estate, with the solicitor</td>
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<tr>
<td>• Ask about and review previous wills</td>
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<tr>
<td>• Ask why potential beneficiaries are included or excluded</td>
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<tr>
<td>• If in doubt about capacity, seek second opinion from an old age psychiatrist or other experienced professional</td>
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</table>
Dementia presents a challenge to doctors to assess correctly a person’s capacity to make a will

Deciding whether reasons for excluding offspring result from dementia or personality factors can sometimes be very difficult. In an example from our experience, an elderly dementing woman with a longstanding dependent and demanding personality, excluded her only daughter because she alleged that the latter was neglecting her. The general practitioner took the view that this attitude towards her daughter was a manifestation of the premorbid personality of his patient, whom he knew well. A psychiatrist who reviewed the papers only after she died considered that dementia had caused her to disinherit her daughter, which she would not otherwise have done. We cannot know who was correct, but some general practitioners may feel that assessment of testamentary capacity is beyond their expertise and may ask the solicitor to seek the opinion of a specialist. However, there is no reason why they should not assess testamentary capacity provided they are aware of the legal tests.

The parties in this case reached a compromise settlement before it came to court. Emotions and costs can run high in family battles. For example, the case earlier this year involving the widow of Richard Cox-Johnson, former banker of the Rolling Stones, was settled in mid-trial with estimated legal costs of £300000 (€443 000; $596 000). Ultimately, capacity is a question of fact, which the court must decide on the evidence as a whole. It is not a matter that a doctor can simply certify one way or another, but the evidence of a properly briefed doctor can greatly assist. We hope that fewer cases would get to the stage of litigation if the golden rule is observed in full measure and correct assessments of testamentary capacity are made and recorded at the time of making a will.

Contributors: RJ had the idea for the paper and wrote the first draft, on which PS made comments and suggestions that were all incorporated. Both authors helped to amend the paper in the light of the referees’ comments. RJ is the guarantor.

Competing interests: RJ writes expert reports for solicitors in contentious probate cases. PS is a solicitor specialising in acting for beneficiaries in contentious probate cases.

Provenance and peer review: Non-commissioned; peer reviewed.

1 Banks v Goodfellow [1870] 5 LR QB 549.
3 Kenward v Adams (1975) Times 29 Nov.
6 Norris A. An article overtaken by a decision by His Honour Judge Alastair Norris QC. Newsletter of the Association of Contentious Trust and Probate Specialists (ACTAPS) 2007;87:1-6.

Elephant neck

In India, the keeper and controller of an elephant is called a mahout. In Nepal, however, it takes three people to keep an elephant: the mahout finds and prepares the elephant’s food, the pachuwa cares for the elephant, while it is the phanit who does the driving of the elephant from his position on the elephant’s neck.

Any unexpected lurches as the elephant ascends or descends a steep slope tend to be applied to the phanit in the fore and aft (or pitch) direction. However, the elephant’s passengers sit at right angles to this, back to back and facing outwards from the flanks of the elephant. If a passenger is looking straight ahead, any jolt is felt in a combination of the yaw and roll directions. Passengers are frequently craning their necks, at the extreme of rotation, in order to photograph that elusive tiger or rhino. This is equivalent to the “check-6” position in a fighter aircraft. In the fighter environment, unexpected accelerational forces can cause acute soft tissue injury in the neck. Elephant passengers may therefore be expected to be vulnerable to similar injury in the case of unexpected acceleration.

A recent elephant safari in Nepal resulted in acute soft tissue injury to the neck of two passengers out of 30 exposures, but no history of equivalent injury among phanits. Holidaymakers, particularly elderly ones, should be warned about the risks of extremes of neck movement when riding on an elephant.

T M Gibson, medical director, Corporate Health, The Buckingham Centre, Slough, mike@bagpipe.wanadoo.co.uk

Can I be the only patient scratching my head about the BMA’s decision to advise general practitioners to boycott the creation of summary care records for their patients? The new record has two main purposes: to provide the NHS with crucial patient information when none is available from other sources, and to give people themselves access to a good summary of their health records whenever they need it.

For me as a patient this means that anyone I ask to help me at evenings and weekends will know basic information about me. This is particularly important now that GPs no longer provide their own out of hours cover for us. Unfortunately, I find that I usually develop a raging urinary tract infection on a Friday night and it would be really helpful for the stranger I ring to know what antibiotics worked for me before, which one caused me to come out in a rash and needs to be avoided lest I am allergic to it, which one made me vomit, and which gave me high fevers and the shakes. After a sleepless night, I can’t always remember their names, which aren’t very user friendly at the best of times.

I really want to be able to see my own records. Knowing that information passed around about me is correct would be reassuring. Also, when I am worried, I don’t always take in what I’ve been told if it’s complicated. I really would like to be able to review it when I am calmer. But more generally, it’s my life and my health and I don’t like making important decisions flying blind.

I can appreciate what GPs may be worried about. I would be the first to agree that my health information should remain confidential. But I also expect, as other patients do, that important information about me will be shared with others who need it to give me care. It is well documented that the balance isn’t right now, and that patients suffer harm as a result.

It would be very unfortunate if a patient complained about information being shared. All of medicine is a balance of risks, and risk needs to be weighed against the known risks to patients of poor information sharing. GPs worry, too, about information being shared that is not accurate. So do I. What better way to prevent inaccuracy than by giving me access to the information so that I can check it?

Are the risks of the summary care record great enough to justify a wholesale boycott by GPs, acting on my behalf? I find it reassuring that the record is being tried in a few areas first so that problems can be spotted early by an independent evaluation and fixed. If I don’t trust having my summary care record on the national database, when I receive my letter telling me it will happen in my surgery, I will have four months to tell my GP I don’t want one. Or I can say I want one to be created that only I can see. Or I can ask that certain information is not put on it. And I can change my mind at any time. The evaluation will assess how well people were informed of their options.

With all of these safeguards, why are some GPs trying to take this decision out of my hands? I wonder if they ever ask themselves why no major patient group or civil liberties group seems to agree that a boycott is the way to move things on? In the 1980s, I ran a support group for thousands of British women who had trusted their doctors to fit them with a contraceptive device that turned out to be faulty. At least 3000 got compensation from a $2.5bn (£1.2bn; €1.8bn) trust fund set up by the US courts. Judging from the many hundreds of letters and phone calls I had, GPs had been slow to act on these women’s symptoms—at great cost to their fertility. No one had the information they needed to avoid this tragedy, not least patients.

As Cyril Chantler has observed, treatments are becoming ever more complex and effective, and more dangerous with it. I don’t want my doctors taking all the responsibility for my health care and keeping all the information to themselves. I am not alone in this: Angela Coulter’s review of research last week (BMJ 2007;335:24-7) shows that evidence is mounting: true collaboration produces better outcomes for both patients and the NHS than paternalism. It is precisely why I went to work for NHS Connecting for Health.

Marlene Winfield is national patient lead, NHS Connecting for Health, London
marlene.winfield@nhs.net
Lethal practice

A new book chronicles insulin’s 50 year history as a murder weapon—including stories of doctors engaged in foul play. Wendy Moore reports

If one fact emerges with abundant clarity from Insulin Murders it is that coauthor Vincent Marks would make the ideal dinner party guest. As a world authority on criminal use of insulin, Marks could spin startling stories of bigamous murderers, serial killers, and bungled miscarriages of justice sufficient to last until well after the last wafer thin mint has been eaten.

Documenting 50 years of legal cases that have implicated insulin as a murder weapon, Marks and his coauthor, medical journalist Caroline Richmond, have produced a compelling account that is at least as thrilling as any best selling crime novel. Beginning in England in 1957 with the first murder proved to have involved insulin, though technically death was caused by drowning, the book details 14 of the most controversial trials in which insulin has played a determining role. In many—including the famous conviction and later acquittal of Claus von Bulow, wrongly accused of murdering his heiress wife by insulin injection, and the case of British nurse Beverly Allitt, convicted of killing four children in her care—Marks testified as an expert witness.

Just as the book provides a galloping account of ingenious attempts by fortune hunting husbands and money grabbing wives to pull off the perfect murder, it also charts the development of the laboratory tests that have often foiled their efforts—and also quite possibly led to wrongful convictions or erroneous acquittals. In this parallel journey, doctors and nurses are as often the villains as the heroes, just as likely to be clinically efficient killers as to be the medical sleuths who unmask them.

Kenneth Barlow, the first proved insulin murderer, convicted of killing his wife by injecting her with insulin then leaving her to drown in a bath, was an unemployed nurse. An astute forensic pathologist cast doubt on Barlow’s wife’s seemingly natural death, having discovered a tiny puddle of water in the crook of her arm, discrediting Barlow’s story that he had tried to resuscitate her. Tests with insulin antibodies on tissue taken from the suspected injection sites not only clinched Barlow’s conviction but for the first time destroyed the myth that insulin was the route to the perfect—undetected—murder.

Colin Bouwer, who was found guilty in 2001 of murdering his wife, probably by a succession of prescription drugs including insulin, was a professor of psychiatry at a New Zealand medical school. It was through emails he had sent to medical experts on hypoglycaemia, purporting to be a forensic psychiatrist investigating a possible insulin death, that his involvement was first suspected.

But if Insulin Murders is a roller coaster ride to equal any forensic detective television drama, it is also a cautionary tale of medical mishap, misdiagnosis, and misinterpretation. True life, unfortunately, is rarely as straightforward as fiction. Just as the laboratory tests to measure insulin and its criminal misuse have become ever more sophisticated, so evidence of their potential flaws has grown.

Himself a pioneer of the immunoassay test used to measure insulin in blood—first developed in 1960 and still the linchpin of criminal insulin investigations—Marks skilfully recounts the progress and the pitfalls. True life, unfortunately, is rarely as straightforward as any best selling crime novel. Beginning in England in 1957 with the first murder proved to have involved insulin, though technically death was caused by drowning, the book details 14 of the most controversial trials in which insulin has played a determining role. In many—including the famous conviction and later acquittal of Claus von Bulow, wrongly accused of murdering his heiress wife by insulin injection, and the case of British nurse Beverly Allitt, convicted of killing four children in her care—Marks testified as an expert witness.

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Himself a pioneer of the immunoassay test used to measure insulin in blood—first developed in 1960 and still the linchpin of criminal insulin investigations—Marks skilfully recounts the progress and the pitfalls. One difficulty is that tests that are both adequate and vital in diagnosing and treating patients on a hospital ward are not always foolproof in determining cause of death, proving murder, or fingerling the possible culprit. Postmortem tests for insulin in brain tissue, which helped convict serial wife killer William Archerd, for example, are now discredited. Postmortem urine tests for insulin and C peptide, instrumental in jailing nurse Maria Whiston, are similarly doubted—although both these cases also featured overwhelming circumstantial evidence. But, as conflicting opinions from medical experts in various trials make clear, many results are prone to misinterpretation, inaccuracy, and mix up.

Most fascinating is the case of Deborah Winzar, a nurse convicted in 2000 of murdering her husband by insulin injection, on the basis of a controversial immunoassay test and despite evidence of vomiting—a circumstance unheard of in insulin induced hypoglycaemia. Courageously casting doubt on the test he himself spearheaded, and indeed on the interpretation of his own colleagues who provided the critical result, Marks suggests that Winzar was wrongfully convicted. Tellingly, with the benefit of 50 years’ research on insulin measurement, Marks concludes that none of the available tests are sufficiently accurate on their own to provide a safe conviction of murder, unless backed by mass spectrometry.

Since Marks is probably unavailable for dinner party guest turns, his and Richmond’s powerful and enlightening book makes a gripping substitute.

Wendy Moore is a freelance writer and author, London
wendymoore@ntlworld.com
Cortina en France

I remember my family holidays. Lying on top of bags in the back of the Cortina as it careered through France. The wind deafened us because we kept the windows down, through fear of baking. We stopped at exotic service stations, full of the sound of crickets. We heard confused French rock music and smelt Gitanes smoke. These were solid 24 hour rallies from London to Spain. We had no in-car DVDs, no iPods, no games machines—just the hiss of cassettes. Seven of us were crammed in plus luggage. We played “knuckles,” “slap-pets,” and “paper, scissors, stone.” My father quizzed us on arithmetic, capital cities, and history. In the melting boredom we sang songs or enjoyed the sport of irritating a sibling until they became incandescent with rage. But mostly we just gazed through the window, sweating.

This summer, families will be spared these evocative and collective memories. Nowadays children slip through a largely homogenised and blander Europe. They are pinned down in their booster seats in silent, air conditioned capsules, plugged into a portable world of DVDs, computer games, and 30 gigabytes of music. Holidays have become yet more poor quality family time. Despite all the sugary emotion we express for our kids, there is a dissonance as we dump them at kids’ clubs and happily allow them to be glued to small screens the rest of the time. This is a variant of consumerism, anything for more “me time” to lounge and complain by the pool. Little wonder then that children struggle to speak to their parents: the truth is that we no longer seem to want share any real time together.

What is to be done? Ban the high tech social vacuums and boycott the kids’ clubs full of smiling kids’ leaders who wince when you tell them your children are theirs for two weeks. Instead, squabble over cards and board games. Kick a football, and throw a cricket ball. Sing a song or two. Ignore your children’s complaints about being bored. Life is not about being constantly entertained. Gazing through the window on holiday is time to reflect. And it is a catalyst for creativity and the gift that no expensive crammer school can give—imagination.

Share some misery this summer holiday. Perhaps our children might end up with their own collective family memories instead of multimedia shadows. Neil Diamond’s Cracklin’ Rose still makes me smell sweat, rub my knuckles, and smile.

Des Spence is a general practitioner, Glasgow destwo@yahoo.co.uk

Dunno, mate

Having produced a new treatment, drug companies take great care to avoid testing it too exhaustively in patients. Such an assertion would provoke howls of protest from the drug industry, which would no doubt point out just how much clinical research it does (lots) and contrast this with the amount of non-industry development of new drugs (very little).

While some of this counter-argument is half true, it doesn’t alter the fact that too much essential information about many new drugs is missing when they appear on the market. A simple demonstration of this fact involves subjecting examples of new drugs to two simple questions. Firstly, have they been directly compared with standard comparator treatments in appropriately designed trials? Secondly, does the available research allow confident prediction of the effects (both helpful and harmful) of the drugs in patients from the general population, particularly in the long term? The answer to both is often “No.”

In response, companies can say, correctly, they only do as they’re told by medicines regulators, the real villains of the piece. The framework that governs licensing of new drugs is ultimately responsible for the low standards that allow companies to conduct studies that duck away from answering key clinical questions. In particular, the overemphasis on inappropriately brief comparisons with placebo (despite the availability of well established alternative drugs or other treatments) is driven as much by the “don’t really care” attitude of regulators as by the commercial wellbeing of the industry.

This unsatisfactory situation is well entrenched and is unlikely to change soon. Ideally, therefore, it should prompt interested scepticism towards new products that have been inadequately tested before launch. Paradoxically, however, some prescribers take the opposite view, dazzled by promotional glamour and somehow reasoning that the absence of definitive evidence to indicate otherwise is in itself a good enough reason for trying out a new product in preference to tried and trusted older treatments. Such woolly thinking means that a new drug and its owners may enjoy a sort of “dunno dividend”—revenue where use of the treatment is catalysed by lack of knowledge about its real effects.

For truly innovative drugs this factor is relatively small, so robust, ever increasing and enduring is the evidence of net benefit to patients. But for others—noisily hyped but quietly under-researched—the dunno dividend is a crucial (if not dominant) component of the money making potential. And there is certainly no incentive for the companies to generate more complete data that could threaten such a position. Sometimes, for the drug industry, ignorance is bliss.

Ike Iheanacho is editor, Drug and Therapeutics Bulletin iiheanacho@bmjgroup.com
Ordinary people?

America is the land of opportunity, and everyone there can reach the maximum of their potential; perhaps that is why so much of its literature is tragic.

There must be failures—ever—or perhaps especially—in the most open of societies, and failure in such a society is more deeply felt than in a society that itself is a failure.

Raymond Carver is the poet of American failure. His short stories are what he calls “a long line of low rent tragedies.” He was born into a blue collar world; his father, an alcoholic, died young. Carver himself became an alcoholic, until he joined Alcoholics Anonymous, but died aged 50 from lung cancer.

In the world he describes, people have insufficient command of words to express themselves, and love turns to hate. People argue past the point, and never about what is really on their mind. In “One More Thing,” a drunk called L D, who is about to be thrown out of the house by his wife, Maxine, argues with his 15 year old daughter, Rae.

“Tell him, Mom,” Rae said. “Tell him it’s all in his head. Anyone who knows anything about it will tell you that’s where it is.”

“How about sugar diabetes?” L D said. “What about epilepsy? Can the brain control that?” He raised his glass under Maxine’s eyes and finished his drink.

“Diabetes, too,” Rae said. “Epilepsy. Anything! The brain is the most powerful organ in the body, for your information.” She picked up his cigarettes and lit one for herself.

“Cancer. What about cancer?” L D said. He thought he might have her there. He looked at Maxine. “I don’t know how we got started in this,” L D said to Maxine.

“Cancer,” Rae said, and shook her head at his simplicity. “Cancer, too. Cancer starts in the brain.”

We’ve all heard angry discussions about aetiology like this that are really about something quite different. In the story “What We Talk About When We Talk About Love,” one of the protagonists is a cardiologist, rather unusually for Carver, whose characters are usually at a much lower occupational level. Indeed, the story begins with the words: “My friend Mel McGinnis was talking, Mel McGinnis is a cardiologist, and sometimes that gives him the right.

“This rather implies that the right to silence in private life is not employed as often as it should be, and that the right to speak is conditional on possession of knowledge or skill of some kind.”

McGinnis and his second wife, Terri, are sitting round a table drinking gin with the narrator and his wife, Laura. A sense of dislocation—emotional, cultural, existential—is deftly conveyed: “We lived in Albuquerque then. But we were all from somewhere else.”

The four of them, progressively drunker, discuss the nature of love. The cardiologist and his second wife hover on the verge of an unpleasant, almost violent, dispute about whether her former lover, Ed—who beat her up, stalked McGinnis and eventually killed himself—really loved her. The subsequent discussion calls into question the reality, even the existence or possibility, of love.

What really disturbed me about this story, however, was not its scepticism about love but its suggestion that doctors were just the same as other people: illogical, inconstant, vulnerable.

Between the Lines

Theodore Dalrymple

What really disturbed me about this story was its suggestion that doctors were just the same as other people: illogical, inconstant, vulnerable.

It was five years after the end of the second world war. A young lecturer in orthopaedics from Manchester published a book titled The Closed Treatment of Common Fractures—a slim volume with a modest aim: “to re-emphasise the non-operative method.” His target readership was primarily junior trainees in accident and emergency and orthopaedics. His service as a military surgeon in the war almost certainly provided him with ammunition for his work. He had an important message for the hapless doctor left unsupervised to treat common fractures concerning why and how fractures displace and how best to reduce and hold them. His was a unique message, he thought, because after the description of detailed theory, larger textbooks had generally neglected to teach this small matter of practical treatment.

John Charnley (1911-82) was gifted with a superb technical mind. Within a decade he was set to forever transform the practice of hip replacement surgery. With this publication he tried to bring the ill defined art of fracture manipulation into the realms of practical science. He brilliantly explained fracture deformity and the soft tissue hinge by clever use of wooden blocks and leather strips. He was also not shy of borrowing from the industrial heritage of his Mancunian upbringing, using the analogy of gear wheels and crank and connecting rod.

Some of his line drawings might be accused of oversimplification yet are useful to help understand and treat fractures. His no-nonsense style of writing is a pleasure to read. He made his arguments confidently, deploying occasional bits of evidence based medicine from his own practice. With each common fracture he tried to present a “mental picture” of the deformity to the reader; once the mechanics of displacement were understood the reader could solve the puzzle of reduction. A well reduced fracture will often redisplace in a poorly applied cast. He then turned the reader’s attention to the proper application of casts. The chapters on treatment of particular fractures are full of practical tips. It is also instructive to see the respect he had for soft tissue preservation—he was, after all, advocating closed treatment mainly to avoid the unhappy consequences of poor handling of soft tissue. His interest in the non-operative treatment of fractured neck of femur and the like may be of historical interest, but more than 50 years, four editions, and three reprints later Charnley’s work is still essential reading for anyone managing fractures.

In many parts of the world today the prohibitive costs of orthopaedic implants mean that non-operative treatment is the only option left to the treating surgeon. However, even in the West, where internal fixation has supplanted non-operative treatment of many of the common fractures that Sir John describes so well, the message is still very pertinent. His interest was in highlighting the “principles,” and in so doing he set a standard that half a century later is still hard to beat.

Munier Hossian, staff grade in orthopaedics, Ysbyty Gwynedd, Bangor, Wales munierh@doctors.org.uk
Christopher John ("Jack") Dewhurst

Teacher and cofounder of paediatric and adolescent gynaecology

Jack Dewhurst was the first British obstetrician and gynaecologist to develop a particular interest in intersex disorders and congenital abnormalities in children and adolescents. He also wrote the current definitive text for trainee obstetricians and gynaecologists, was professor of obstetrics and gynaecology at Queen Charlotte's Hospital, London, and president of the Royal College of Obstetricians.

Jack was born in 1920 in Garstang, near Preston in Lancashire, the only son of John and Agnes Dewhurst, a market gardener and a district nurse. His father worked away from home during the week and his mother's commitment to nursing meant she was rarely at home. Jack recalled his childhood as being particularly lonely, and he was sent away to school at St Joseph's College in Dumfries. He was a very talented sportsman, and he spent all of his summer holidays at Fylde Cricket Club. At 16 he scored a century for the senior team and took a hat trick in the same season.

Cricket remained the sporting love of his life, and later, while pursuing his career in obstetrics and gynaecology, he played for six years at the highest club standard.

As a medical student Jack was university billiard champion until he graduated in 1943. After six months working in a local hospital he joined the Royal Naval Volunteer Reserve as a surgeon lieutenant. On D Day in 1944 he was in the fleet of ships which left Portsmouth for the Normandy beaches, landing troops and tanks on Sword Beach and carrying the wounded back to Britain. In 1945 and 1946 he was on the battleship King George V. After the war he returned to Manchester. He worked briefly in paediatrics but soon realised that his interest was more in the mother than the child, training as an obstetrician at St Mary's Hospital in Manchester between 1948 and 1951. In 1951 he became lecturer at the Jessop Hospital for Women in Sheffield, where he remained until 1967, ascending the academic tree to senior lecturer and then reader. He was professor at Queen Charlotte's Hospital in 1968 until his retirement in 1986.

Jack published his first book on gynaecological disorders in infants and children in 1963. In 1969 he published with R R Gordon, a paediatrician, Intersex Disorders, which was then the definitive text. As his reputation grew internationally, he stimulated two American gynaecologists, Vincent Capraro and John Huffman, to pursue similar interests, the three of them founding internationally a subspecialty and creating the world council and the first world congresses of paediatric and adolescent gynaecology.

Jack's first publication was in 1950, and he published 109 peer reviewed publications during his career. He became famous as a teacher and lecturer, being considered by many to be one of the best lecturers in the world. When asked whether lecturing came naturally to him, he admitted that in 1951 when he was appointed lecturer at Sheffield he had no idea how to lecture. He spent the next year attending lectures given by men he thought to be great lecturers and made notes on their style and technique. He found a number of common themes, which he translated into his own deliveries and thereafter became an outstanding speaker.

Jack was unselfish and generous, and not only in his personal life. He was a tremendous supporter and inspiration to young obstetricians and gynaecologists. His ability to obtain the best from people is probably epitomised by the fact that his seven senior lecturers all became full professors in their own right—a unique record for any professor of obstetrics and gynaecology in the United Kingdom.

The respect and admiration that Jack generated culminated in his being appointed president of the Royal College of Obstetricians and Gynaecologists in 1975, and in 1977 he was knighted for his services to medicine. Jack's legacy to obstetrics and gynaecology will undoubtedly be his passion for imparting knowledge. In 1972 he published Integrated Obstetrics and Gynaecology for Postgraduates, which remains the standard text for all trainees in obstetrics and gynaecology. The seventh edition has just been published, still bearing his name. In the latter part of his career, Jack became fascinated by history and published Royal Confinements, which became a classic.

Jack met his wife, Hazel, in 1951 on his first day in Sheffield: he was performing a caesarean section and she was giving the anaesthetic. As he had had such a lonely childhood himself he was completely dedicated to his family and despite travelling extensively never neglected his children. After retirement, he and Hazel decided to learn Italian but in true Dewhurst style: they gained a place at the University of Perugia and were the oldest students by 30 years. Jack became fluent in Italian, and he had a passion for Italian Renaissance painting. He was deeply religious and a devout Roman Catholic. He published Saints and Sickness, and he was able to recount the saints' days until his final illness. He leaves Hazel, two sons and a daughter; and six grandchildren.

D K Edmonds

Professor Sir Christopher John ("Jack") Dewhurst, former president of the Royal College of Obstetricians and Gynaecologists (b 1920; q Manchester 1943; FRCSed, FRCOG), died from bronchopneumonia and cerebral lymphoma on 1 December 2006.
Ywan Anthony
Former general practitioner east
Birmingham (b 1934; q Birmingham
1957; MRCGP, DPH), died from
Ywan Anthony was brought up bilingual in Welsh and English in
the west Midlands. After house jobs in Birmingham he studied at
the London School of Hygiene and Tropical Medicine for the DPH and
then took a short term commission in the army for three years, at
the same time developing his interest in sailing. He left the army in 1963
and after working as a locum in West Bromwich took up a post as
a junior partner in Hall Green, Birmingham. In 1967 he became a
partner in Small Heath, Birmingham, remaining there until his retirement
in 1994. He particularly enjoyed antenatal clinics and became a well
respected trainer, as well as working for the local bus company. He leaves
a wife, Clare; two children; and five grandchildren.
Richard Anthony

John Edward Barclay
Former consultant psychiatrist
Winwick Hospital, Warrington,
and Ormskirk General Hospital,
Lancashire (b 1929; q Liverpool
John Barclay did his national service in 1947 with the Household Cavalry
in Germany, from that time showing considerable sporting prowess in
fencing, rifle shooting, and skiing. In 1952 he won the fencing event
at the Winter Pentathlon in Bad Gastein, Austria. While in the army
he was awarded the bronze cross of
the Army Rifle Association and broke
the British 50 km cross-country
skiing record, which he held for
seven years, being selected for the
British Olympic ski team at the 1956 Winter Olympics. The following year
he was house surgeon at St Helen’s Hospital, going on to obstetrics and
gynaecology at Ormskirk Hospital, becoming consultant psychiatrist in
1964. He retired in 1988. He leaves a wife, Claire; seven children; and 14 grandchildren.
Emad Salib

Wilma Elizabeth Gemmell
Former general practitioner Barrhead,
Renfrewshire (b 1967; q Glasgow
1989; MRCGP, DRCOG, LFHom), died
Wilma Gemmell was appointed partner at Barrhead Health Centre
in 1993. Diagnosed with breast cancer in 1998, she returned to
work in the practice in 1999 after treatment but retired in 2003 after
further treatment for recurrence of the tumour. Wilma was committed
to raising awareness about breast cancer. She worked with Breast
Cancer Care as a support volunteer and enthusiastic ambassador. She
sang to large crowds to raise money for cancer charities. She ran the Race
for Life many times, once having just completed her chemotherapy. She
modelled in Breast Cancer Care’s Scottish fashion show twice. Her
attitude to her illness, her courage, and her dedication to helping others
was inspirational. She leaves a husband, Gordon, and two children.
Catriona MacRae, Catriona McHugh

Michael Gregory Price
Former general practitioner
Harpenden, Hertfordshire (b 1926; q
St Bartholomew’s Hospital 1952; MRCGP, DRCOG), d 6 January 2007.
Brought up in Jersey, Mike Price
escaped from the island in a small
boat with four friends during the
German occupation in 1944. They
were washed up near Cherbourg
before escaping to England with the
help of a French farmer. Mike
initially contemplated a career in
surgery before choosing general
practice. A founding member of the Royal College of General
Practitioners and active in the local
medical committee, he practised in
Harpenden for over 30 years until his
retirement in 1986. A keen golfer,
he also loved the sea and in 1982
took a six month sabbatical as ship’s
doctor in the Royal Fleet Auxiliary
to the Falkland Islands, a few
months after the conflict. He leaves
a wife, Enid, four children, and 11 grandchildren.
Jim Price

John William (“Jack”) Strain
Former general practitioner Egremont,
Cumbria, and medical officer
Sellafield (b 1921; q The London
Hospital 1953; DFM), died from
metastatic carcinoma of the prostate
on 29 April 2007.
Jack Strain started work in an
architect’s office, joining the Royal
Air Force in 1939 on the outbreak
of war and serving with distinction.
He was awarded the Distinguished
Flying Medal and the Polish Cross of
Valour. After the war Jack pursued
the career he had hankered after
and gained entry to The London as
an ex-serviceman. He returned to
his native Egremont as a general
practitioner until 1980, when he
joined British Nuclear Fuels as a
medical officer. He retired in 1986
but continued to work as a locum
at his original practice. A devout
Catholic, he loved rugby and was
passionate about fell walking. He
leaves a wife, Mary; five sons; and
10 grandchildren.
Greg Strain

John Robert Bentley Turner
Former consultant general physician
and cardiologist Pontefract General
Infirmary (b 1930; q Leeds 1954; FRCP), died from
After qualifying John Turner did
his national service in the Fleet Air
Arm and postgraduate training in
the Leeds hospitals. He became
consultant in 1968, retiring in
1990. He was held in high regard,
especially by general practitioners,
for whom he did many home visits.
John was a talented squash player,
winning the Yorkshire Plate twice.
He stopped playing squash at 56,
when he had a heart attack on
court. His main passion was cricket:
he was a life member of Yorkshire
County Cricket Club, serving on
the committee, and treasured
his membership of the MCC as
much as his FRCP. He travelled the
world following cricket and died at
Headingley as Vaughan was nearing
a century. He leaves a wife, Jean; four
children; and eight grandchildren.
Colin White

Advice
We will be pleased to receive
obituary notices of around 250
words. In most cases we will be able
to publish only about 100 words in
the printed journal, but we can run
a fuller version on our website. We will
take responsibility for shortening.
We do not send proofs. Please give
a contact telephone number and,
where possible, supply the obituary
by email to obituaries@bmj.com

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A 43 year old man who was returning after a week in Nigeria was seen behaving oddly at Heathrow airport. He was agitated, sweating profusely, and disoriented. Routine screening in customs found his urine tested positive for cocaine. A chest x ray showed multiple well defined objects in the stomach, and on admission to hospital he became tachycardic and hypertensive. He deteriorated, and cocaine poisoning was suspected. At emergency laparotomy 89 packets of cocaine were removed from his stomach and bowel (QJM 2007;100:461).

Obtaining travel insurance with a history of significant illness can be difficult and expensive. Macmillan Cancer Support is working with a banking group to find out more about customers’ experiences. People who have had cancer are invited to participate in the research by calling Direct Line Insurance for a quote—call 0845 246 1643 and quote marketing code 6000—before 25 July. Rest assured you don’t have to buy a policy to take part in the survey. Alternatively go to www.macmillan.org.uk/travelinsurance.

The concept of a “missed dose” is used in many studies of adherence to medication, but the term means different things to different people. Semi structured interviews with 45 HIV positive patients and 17 of their clinicians found a wide variation in what they thought “missed dose” meant: 55% of the patients thought that delaying taking a pill for more than six hours constituted a missed dose, but only one of the doctors agreed. Most patients thought the best thing would be not to take that dose at all after such a delay, but most doctors disagreed with this (AIDS Care 2007;19:775-80).

Are patients who don’t show up for their first appointment at specialist clinics putting themselves at risk? A retrospective analysis of 151 patients who failed to attend a “two week wait” or “urgent” appointment at a colorectal clinic between 1996 and 2004 found that 59 had also failed to attend other clinics. Of the 58 patients referred with suspicious colorectal symptoms (23 of whom were persistent non-attendees), five had colorectal cancers, 16 had benign disease, and 12 had entirely normal outcomes (Annals of the Royal College of Surgeons of England 2007;89:484-6).

The National Medical Journal of India (2007;20:56-8) offers advice to authors that is universally applicable. Don’t, an editorial says, let institutional politics make a liar of the scientific record. If you know authorship abuse is happening, take it seriously and create in-house policies on who can and should be listed as an author. The editorial goes on: if you’re already a senior author, show some humility—wouldn’t an acknowledgement suffice? And if you’re a junior author, be brave: clarify authorship rights at the start of a project to avoid disappointment at the end.

Minerva surmises that people with schizophrenia may have difficulties holding down jobs, but an interesting finding about employment patterns in the UK, France, and Germany is that local social contexts seem to be as important as factors related to the individual or the illness. Data from the European schizophrenia cohort study show that participants are working in all sections of the job market, and that those who are graduates, are living with their families, or have experienced just a single psychotic episode are more likely to be working. Germany enjoys the highest employment rate (British Journal of Psychiatry 2007;191:30-7).

Fire fighters have a higher than average prevalence of sarcoidosis. An investigation of exposure to “dust” from the World Trade Center after its collapse on 11 September 2001 reports that since then, new-onset sarcoidosis has been found in 26 members of New York’s fire department, significantly more than expected. Half presented during the first year after exposure, and 69% had findings consistent with asthma. Of those who agreed to challenge testing, eight had airway hyper-reactivity, findings not seen in fire fighters with sarcoidosis before the disaster (Chest 2007;131:1414-23).

Here’s a lesser known use for vitamin C. Following a report that vitamin C protects against complex regional pain syndrome, researchers designed a dose-response study of vitamin C in patients with wrist fractures. The double blind trial in 416 patients found that a daily dose of 500 mg of vitamin C for 50 days significantly reduced the prevalence of complex regional pain syndrome after wrist fractures. Complaints related to the use of plaster casts predicted the development of the syndrome (Journal of Bone and Joint Surgery 2007;89A:1424-31).

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A company that offers cremations in Israel has a lot to contend with. For example, there is no law allowing cremation in Israel, and yet there is no law forbidding it. There is no Hebrew word for “cremation”—the only term available is “burning bodies,” and that’s a hard concept to market in a country with strong memories of the holocaust. The company often refers to the Bible to prove cremation is a Jewish custom, and despite fierce objections raised by religious officialdom, the trend is growing (Pharos International summer 2007;(summer):4-9).