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(published 26 July 2007)

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Shortcuts from other journals: Lessons in pandemic flu from 1918

BMJ 2007;335:279, doi:10.1136/bmj.335.7614.279-a

Shortcuts from other journals: Screening by visual inspection protects Indian women against cervical cancer

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*10-minute consultation: Chronic knee pain*
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**Daniel Turnberg**
Caroline Richmond
BMJ 2007;335:308, doi:10.1136/bmj.39295.554792.BE

**Diana Margaret Riley (née Dean)**
Teresa Riley
BMJ 2007;335:308, doi:10.1136/bmj.39295.629850.BE
Tarsem Lal Garg  
Scot Garg  
BMJ 2007;335:309, doi:10.1136/bmj.39294.631481.BE

James Crawford Little of Morton Rig  
Alan Kerr  
BMJ 2007;335:309, doi:10.1136/bmj.39294.655567.BE

Edward Lawson McDonald  
Hazel M Baker  
BMJ 2007;335:309, doi:10.1136/bmj.39294.733727.BE

Sadie Bessie ("Bess") Michaels  
Andrew Coleman  
BMJ 2007;335:309, doi:10.1136/bmj.39294.531620.BE

Robert MacGregor ("Rab") Milne  
Alex Cargill  
BMJ 2007;335:309, doi:10.1136/bmj.39288.571227.BE

Patrick Joseph Evanson Smyth  
Elizabeth Smyth, Edward Smyth  
BMJ 2007;335:309, doi:10.1136/bmj.39288.533981.BE

Minerva  

Minerva  
BMJ 2007;335:310, doi:10.1136/bmj.39297.426273.BD1

Minerva  
Susan P Mollan, Deepun Gosrani, Andrew B Callear  
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Why don't doctors use HTML?  
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bmjupdates+: Soy phytoestrogen genistein increases bone mineral density in postmenopausal women

BMJ 2007;335:299, doi:10.1136/bmj.39287.690475.AD

Corrections  

Minerva  
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Read this week's articles on
Fast track referral for cancer
Has not improved patient outcomes in the UK

Most patients with cancer who are not diagnosed by screening will be diagnosed after symptoms develop, so timely referral of patients to specialists is essential. In this week’s BMJ Potter and colleagues assess the long term impact of the “two week wait” rule in the United Kingdom for breast cancer on referral patterns, diagnoses of cancer, and waiting times. Their study found that the diagnosis of cancer in people referred within two weeks significantly decreased in the period 1999-2005 (12.8% v 7.7%, P<0.001) and diagnoses in people referred through the routine route increased (2.5% v 5.3%, P<0.001). The study suggests that the current cancer referral policy in the UK—whereby patients with a given set of symptoms are seen within two weeks—results in more patients who have cancer being seen on routine waiting lists than on the fast track list. This means diagnosis is delayed even further. Why is this so, and how can it be rectified?

In formulating such rules, it is important to remember that waiting times for urgent appointments are only a surrogate end point. The main aim is to improve cancer survival, improve psychosocial outcomes for people with cancer and those who turn out not to have cancer, and to improve the general practitioner’s ability to diagnose cancer. This rule seems not to have led to any of these outcomes, although it has perhaps increased the proportion of patients with benign pathology referred for urgent specialist appointments.

Introduction of the two week standard clinics has not improved the outcomes for patients in some of the commonest cancers. The reason for this may be the complexity of the medical consultation. Many factors affect the decision to refer for an expert opinion, including a patient’s help seeking behaviour, doctor-patient communication, eliciting and interpreting signs and symptoms, applying evidence to decision making, negotiation with the patient about the need for and most appropriate route of referral, and conveying the information in sufficient detail to allow the patient to be fully informed about the need for urgency or otherwise. It has been calculated that if the practitioner successfully negotiates each of the above stages on 80% of occasions then only a small percentage of decisions will be evidence based.

A substantial proportion of patients with common cancers present as emergencies with advanced disease; in the case of colorectal cancer this has been estimated to be as high as 20%. This is especially true in deprived communities or in communities where people have cultural and linguistic differences.

A major step towards earlier diagnosis of cancer would be to raise awareness of the symptoms of cancer in the community. Furthermore, given that cancer is an uncommon diagnosis in general practice, practitioners are unlikely in most cases to opt to investigate symptomatic patients. Therefore patients with altered bowel habit may not be tested for iron deficiency anaemia or other signs of occult bleeding as symptoms are far more likely to be due to irritable bowel syndrome or diverticular disease than to colorectal cancer.

Bayes’s theorem demonstrates that the probability that a patient has cancer is affected by the prevalence. The prevalence of cancer in a primary care population depends on the symptoms in question. Such considerations should influence the selection of patients for referral. In practice, however, doctors will act on the basis of personal experience, respected local opinion, and anecdotal evidence rather than on high quality published research. Research about the positive predictive value of signs and symptoms of the common cancers in primary care does exist. Implementing these findings in practice, however, will require substantial effort.

General practitioners must also be able to persuade patients with suspicious symptoms that a specialist opinion is required. In practice, however, it is the patients with worrisome symptoms of benign pathology who are likely to demand an urgent specialist appointment. Given that cancers also present with symptoms associated with benign conditions and in view of the rising tide of litigation and complaint from patients sensitised to sensational stories of misdiagnosis, it is hardly surprising that patients are being inappropriately referred through the fast track route. This phenomenon can also be explained by Braess’s paradox, whereby “adding extra capacity to a network, when the moving entities selfishly choose their route, can in some cases reduce overall performance” (http://en.wikipedia.org/wiki/Braess’_paradox).

So what is the best strategy for deciding which patients to refer for specialist opinion? Maybe one day we will have a reliable and valid test to help identify cancer patients in primary care. Until then, general practitioners should make a provisional diagnosis on the basis of a history and a physical examination, paying particular attention to genetic predisposition, exposure to carcinogens, and the type and duration of symptoms. Effective lines of communication between general practitioners and cancer specialists or networks will help to relay these clinical details, leading...
Are health services in England failing our children?

Poor outcomes for major childhood diseases reflect the low status of children’s NHS services

In 2004, the UK government launched the national service framework for children in England.¹ It contained a comprehensive set of standards for children’s health services and a 10 year timescale for implementation. The framework was welcomed as the first real blueprint for children’s health since the Court Report² almost 30 years before. But with no extra money and no specific targets for health professionals or managers, progress has been slow. Children have been given a low priority, and managers are distracted by high profile government targets for emergency waiting times and surgical waiting lists. There is now real concern and increasing evidence that the National Health Service (NHS) is failing children.

The Healthcare Commission recently produced “Improving services for children in hospital,”³ a review of progress on national service framework standards in England. In 2006, only 4% of trusts were rated excellent and 21% were rated good. While the commission reported considerable progress in improving the hospital environment for children, their review noted a worrying potential for unsafe medical care. Surgeons trained to operate on adults were operating on children, many on only a handful each year. In a small number of NHS trusts too few trained staff were available to provide effective life support for children during the day. One in five trusts was unable to deal effectively with paediatric emergencies at night.

Children in England with diseases such as diabetes and cancer generally do badly, when compared with their peers in the rest of Europe. We have, for example, one of the highest incidences of type 1 diabetes and one of the worst records on diabetic control.⁴ This could be linked to differences in lifestyle and diet, but poor services are probably at least partly to blame.⁵ Good diabetic control is vitally important for children because we know that late complications of diabetes in adult life are determined by what happens in childhood. Our inadequate children’s services are inevitably storing up problems for the future and we can avoid them only by investing in better care now. Unfortunately, “short termism” has so far prevailed.

The picture is similar for children with cancer. According to recent estimates, children with cancer in Britain have a five year survival rate of 71%, compared with 77% for Scandinavian children and 75% for children elsewhere in western Europe (France, Germany, Netherlands, and Switzerland).⁶ British children possibly wait longer for diagnosis and referral to specialists. In Germany, for example, more than 27% of Wilms’s tumours are picked up by routine health surveillance by primary care paediatricians.⁷ This compares with less than 10% in the United Kingdom, where surveillance has been slimmed down, is largely done by nurses, and does not include abdominal palpation at regular intervals. Many office paediatricians in Germany have their own ultrasound machines and are trained to use them.

Our care of newborns also gives cause for concern. The Department of Health has recently reviewed the public services agreement target on health inequalities and infant mortality. The target aims by 2010 to reduce by at least 10% the gap in infant mortality between the socioeconomic class labelled the “routine and manual occupational group” and the English population as a whole.⁸ The NHS is falling behind in efforts to improve this important indicator of care during the antenatal and perinatal periods, and in the first year of life. England now lies 15th in the European league table for perinatal mortality. Much hope was built around the establishment in 2004 of neonatal networks of care—linked professional groups working across primary, secondary, and tertiary care to ensure equitable and clinically effective services—these have proved hard to establish and coordinate in the real world without adequate national direction and funding.⁹

All is not lost, however. For example, there have been substantial improvements in community child and adolescent mental health services during the past


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Neglected tropical diseases
These diseases could be controlled or eliminated in our lifetimes if efforts are better coordinated

In 2002 one of us wrote an editorial in the *BMJ* entitled “The world’s most neglected diseases,” referring to 13 ancient tropical infections of the poor (box). These diseases are disabling, disfiguring, and stigmatising; they impair children’s physical and cognitive growth; they promote poverty; and many of the drugs used to treat them are toxic, difficult to administer, and are more than 50 years old. Two years later, there was little news to report. But recently there has been a silent revolution in the attention being paid to these diseases.3

We see several reasons for optimism.

Firstly, the long held belief that it is not economically feasible to develop drugs, diagnostic methods, and vaccines specifically for the neglected tropical diseases has now been shattered.4 Although these conditions exclusively affect the world’s poorest people, product development partnerships have been established for at least six neglected tropical diseases in the past seven years without commercial markets or conventional business models, and several new drugs and vaccines are in the pipeline.5

This increase in drug development activity is not a passing trend. Moran and colleagues surveyed the landscape of drug development for neglected tropical diseases and found that 63 drug projects were under way at the end of 2004 (although some of these were for malaria and tuberculosis, diseases that are not considered to be among the most neglected).4 On the basis of these developments, we believe that the neglected tropical infections may be controlled or even eliminated in our lifetimes.

Competing interests: GY is consulting editor and PH is editor in chief of *PLoS Neglected Tropical Diseases*, which is funded through foundation support and publication charges. PH is president of the Sabin Vaccine Institute and inventor on two international patents on hookworm vaccines.

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

**Main neglected tropical diseases**

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<td>Buruli ulcer</td>
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**Neglected tropical diseases**

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This increase in drug development activity is not a passing trend. Moran and colleagues surveyed the landscape of drug development for neglected tropical diseases and found that 63 drug projects were under way at the end of 2004 (although some of these were for malaria and tuberculosis, diseases that are not considered to be among the most neglected).4 On the basis of these developments, we believe that the neglected tropical infections may be controlled or even eliminated in our lifetimes.
The penny has finally dropped among donors—they have realised that because chronic parasitic diseases leave people mired in poverty, controlling these diseases will help to achieve the Millennium Development Goal of halving the proportion of people living on less than a dollar a day by 2015 (www.undp.org/mdg/). Lymphatic filariasis, for example, is responsible for the loss of 0.63% of India’s gross national product, while the global annual loss of productivity related to impaired vision and blindness from trachoma is as high as $5.3bn.

The United States Agency for International Development has recently awarded a $100m grant to scale up integrated control of neglected diseases in Africa. This amount, however, is still less than 10% of the funds needed in sub-Saharan Africa alone for widescale implementation of interventions for neglected tropical diseases.

One problem facing the community working on controlling neglected tropical diseases is the lack of communication between the various players—researchers, policy makers, clinicians, public-private partnerships, donors, and patient advocacy groups. Finally, we have an online tool for such communication—the world’s first journal specifically devoted to these diseases. The Bill and Melinda Gates Foundation has awarded the Public Library of Science a grant of $1.1m to launch in October 2007 PLoS Neglected Tropical Diseases (www.plosntds.org), an open access, non-profit journal. One unusual feature of the journal is that, unlike other tropical medicine journals, 40% of the editors who handle peer review are from countries where the neglected tropical diseases are endemic.

of standard attrition rates, and assuming ongoing funding, we can expect to see eight or nine new drugs for neglected tropical diseases within the next five years. This increased pharmaceutical activity by public-private partnerships is now being complemented by the development capabilities of the so-called “innovative developing countries,” such as Brazil, India, and China. These countries have spent decades building infrastructures for developing their own drugs, vaccines, and diagnostics, with minimal financial or technical help from the rich world.

Furthermore, the moral duty to shape up use of the existing tools for controlling neglected diseases is becoming clearer. “A scientist who is also a human being,” said Albert B Sabin, who developed the oral polio vaccine, “cannot rest while knowledge might reduce suffering rests on the shelf.” For some of the neglected tropical diseases, the current drugs, if administered to everyone at risk, could certainly reduce suffering. Indeed, the World Health Assembly’s targets for controlling five of the neglected tropical diseases (lymphatic filariasis, onchocerciasis, trachoma, soil-transmitted helminth diseases, and schistosomiasis) emphasise mass drug administration. The African programme for onchocerciasis control is a good example—by the end of this year, treatment with ivermectin will have reached 65 million people (www.worldbank.org/afr/gper).

Given that the neglected tropical diseases often occur in the same geographical areas, and given evidence that a drug used by one disease specific vertical programme could simultaneously affect other diseases, there is now great interest in rolling out an integrated package of disease control. For example, a package of four drugs (albendazole, ivermectin, azithromycin, and praziquantel) could integrate the control of seven major neglected tropical diseases for 500 million people in Africa and could be delivered for about $50 (£25; €30) per person each year. Furthermore, tackling neglected parasitic diseases could enhance the effectiveness of antiretroviral therapy in endemic regions.
SELF MONITORING IN DIABETES

Useful in which patients?

The conclusion of the randomised trial reported by Farmer et al is in line with a recent systematic review of randomised trials (1000 patients, three trials) and observational studies (60 000 patients, 13 studies), which shows that only when the average starting HbA1c is above 8% do studies consistently show benefit of self monitoring.

The inference that self monitoring may be beneficial where control is poor is just common sense. That it is difficult to show benefit when control is already pretty good is also common sense—there is no sensitivity to show a difference even if there were one.

A different way of reporting results of trials like this would be interesting. Our interest is not in the average patient, since few patients are average: what we require is to know the number of patients who showed improvement (however defined, or perhaps at several levels of HbA1c) versus the number showing no change or an increase in HbA1c, as has been done before.

Generalised policy decisions should not be based on data like these. Extrapolating averages from trials into health economic models does disservice to patients and professionals in several ways. A more useful approach would be some operational and other research to identify the patients who would benefit most from self monitoring and the best way to engage them in actively helping themselves. This would build on professional skill and responsibility.

Where doctors make their own decisions, the results have been terrific, especially in clinical outcomes with major consequence. They did it by deciding which patients with type 2 diabetes would benefit from self monitoring, and prescribing self monitoring in those patients. Andrew Moore

Competing interests: The authors have written a recently published systematic review on this topic.


Education seems to work better

The article by Farmer et al reinforces our experiences in practice. We have not prescribed testing strips routinely to patients with stable type 2 diabetes for the past three years. Aggressive diabetic management based on principles of patient education, development of trust between trained diabetes nurses and the patient, and early use of oral agents to achieve target HbA1c levels have led to gratifyingly good outcome measures in our 3000 patient urban practice.

We discourage the use of self monitoring for several reasons: expense of testing strips and equipment, the anxiety generated by small variations in results and the subsequent medical time pressures in dealing with these, equipment failure, and the lack of evidence of any benefit. We have had pressure from hospital consultants, patients themselves, and pressure groups to provide testing strips, but we have firmly stuck to our guns. In the current state of knowledge, nothing would persuade us to go back to encouraging or supporting routine self monitoring in stable type 2 diabetes: our results are too good to justify the change.

Anthony) Listerv general practitioner, Old Palace Medical Practice, Norwich NR2 4JA

Competing interests: None declared.

Let me own my disease

As has been pointed out by several responders, the trial of Farmer et al was flawed in that those in the “intensive testing” group were not given the information to act on the results of their tests to bring their blood glucose down (take exercise), nor were they encouraged to use the results of the test to modify their diets to achieve greater control. On the contrary, they were encouraged to maintain their regimens.

Therefore I find the contention that self monitoring of blood glucose is not beneficial and the attitude of some of the medical profession towards their diabetic patients extremely arrogant and ill founded. It led me to think about how I would feel if I were refused strips and treated like a child with the diabetes specialist nurse prescribing my regimen—in effect, it would take away my “ownership” of the disease.

Surely it is possible for doctors to prescribe for motivated patients who will take advantage of the strips to modify their regimens accordingly and prove the worth of the prescription by saving the NHS money in the long run. There will, of course, be many patients who cannot cope with the necessary hard work (because it is hard work) and who would prefer to have their diabetes managed by the medical profession, but please do not deny the wherewithal to those who are both motivated and able to use the results.

Patti D Evans administrator, Lesodajck Centre, Penzance, Cornwall TR18 3PE

Competing interests: None declared.

Authors’ reply

We agree with Moore et al that the results of a clinical trial should be interpreted in the context of an individual patient. Our trial of self-monitoring of blood glucose does not exclude the possibility of a clinically important benefit for specific patient subgroups. While we welcome the improvements in care offered by Lister to his patients, personalising care on the basis of clinical judgment remains of critical importance. We agree with Evans that clinical judgment should be guided, rather than prescribed, by evidence from randomised trials. However, she has misunderstood the design of the more intensive self monitoring intervention where patients were provided with training and support to interpret readings and revise behavioural goals to reach treatment targets.

We take issue with Moore et al on several points. Firstly, it is not self evident that self monitoring will help where control is poor. We agree that the benefits of monitoring are self evident, but the relative benefits of self monitoring compared with repeated HbA1c measurements are unclear. We plan to explore this in exploratory subgroup analyses.

Secondly, we disagree with their comments about use of health economic models. The cost implications of routinely recommending self monitoring for all non-insulin treated patients with type 2 diabetes need to be carefully considered, and it would be unethical not to do so.

Finally, it is disappointing that they turn to a cohort study, which is likely to be confounded by unmeasured, and unmeasurable, individual characteristics, to claim “terrific” results for self monitoring. Randomised trials remain the gold standard for assessing an intervention.

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Competing interests: None declared.


INSOLVENT HOSPITALS

It’s not just whole hospitals

Ham points out the importance of the choices the government makes around failing hospitals. Almost every proposed reconfiguration will provoke local opposition from the people who live next door to the hospital. But what should matter for serious decision makers is not the views of the IMBYS (everyone wants a hospital “in my back yard”) but a rational standard of provision. For example, we might try to maintain general hospital levels of service in a certain travel time of the population (with perhaps a much less stringent limit for services that require substantial critical mass).

But this sort of analysis is rarely seen in the context of reconfiguration. For England we recently found that if we set an acceptable access standard of 30 minutes’ travel by road (actually quite a stringent target) we find that about 7% of the English population have no provision (this is mostly the rural fringes), but a remarkable 55% of the population have three or more hospitals available. Ten per cent have more than 10 choices at this standard of provision.

Thus there are parts of the country where even the complete closure of a major hospital would not leave a black hole for provision, and the government should stand up to the IMBYS. Many of the most controversial proposed reconfigurations are in well provisioned parts of the country, where the proposed changes could give people substantially better quality provision at an only marginally less convenient location.

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1 Ham C. What to do with insolvent hospitals. *BMJ* 2007;335:170. (29 July.)

LIFE SAVING GENERAL PRACTICE

Perhaps, if we work less hard

I agree with Heath, but the reality of being a general practitioner (GP) can quickly erode noble sentiments. In my 20 years as a full time GP I very much wanted to work by the tenets in this article. But being a full time GP with an average list is hard, hard work. It is not just easy to get it wrong: getting it wrong, very wrong, is part of the process.

The work rate of most GPs is damaging to both patients and doctors. That work rate or “busyness” is often used as an excuse for “getting it wrong.” However, it is that work rate which makes GPs so economical. To complete that argument, GPs are efficient and cheap because they half do things. Usually we get away with it and we will use our “luck” to rationalise our failures. But that is changing, and in my latter years I saw standards rising and GPs trying much harder to do a better job. The current system is not designed to deliver that service. Add in the internet and rising patient expectations, and the current system will probably fail.

Yes we can do more in practice, yes we can keep people out of hospital, yes we can really be that holistic ideal—but only with lots more time per patient. That of course means much smaller lists, lots more doctors, and in time perhaps less pay. At the moment it pays doctors to work too hard. That incentive may need to be removed.

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Competing interests: None declared.

1 Heath I. Only general practice can save the NHS. *BMJ* 2007;335:183. (28 July.)

Not with the state apparatus

Heath believes that it is governments which are sapping the morale of general practitioners (GPs), by introducing the twin evils of markets and private profit. She forgets that it was the GPs themselves who agreed a new contract that abolished their commitment to 24 hour “social solidarity,” while giving them better rewards.

The special role of primary care doctors in the United Kingdom is already nullified. The possibility of their recovery to a central “gatekeeping” role is offered by primary care commissioning. But the information technology and management add-ons make this peculiarly unattractive. Could it be the health service managers who are detrimentally undermining the GPs’ morale and esteem? The one continuous thread throughout the past 50 years of the NHS has been the desire of the state apparatus to “break the power” of doctors, and bring them to heel—while securing their own continued expansion of power and inefficiency.

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1 Heath I. Only general practice can save the NHS. *BMJ* 2007;335:183. (28 July.)
Government pushes ahead with plan for cheaper drugs deal

Nicholas Timmins FINANCIAL TIMES

Ministers want to switch the way the NHS pays for the £8bn (€12bn; $16bn) worth of branded drugs that it buys each year. They want to move to a system in which drug prices are based on the benefits they bring to patients—and it seems they want to do so quickly.

The radical move comes after a report from the Office of Fair Trading (OFT) in February that recommended such a shift from 2010, when the current 50 year old pharmaceutical price regulation scheme (PPRS) becomes due for its five yearly renewal (BMJ 2007;334:383).

The industry had been expecting a response but not last week's announcement that ministers want a renegotiation now.

A “value based” scheme would aim to allow higher prices for drugs that are more effective—a move that the OFT argues would stimulate innovation. Lower prices would be paid for more marginal or less effective products and certainly for so called “me too” drugs that are close to products already on the market.

Such a scheme differs sharply from the PPRS, which, despite being called a price regulation scheme, in practice places controls on drug companies’ profits rather than regulating the price of individual drugs. In its report the OFT argued that the change would provide better value for money while saving £500m a year—a figure the industry disputes.

The OFT set out various options for a value based scheme. Such a scheme could involve free price setting at a product’s introduction, with adjustment up or down as evidence of its cost effectiveness emerged. Alternatively—or in addition—prices could be set at the product’s launch, where there is enough evidence of its cost effectiveness, possibly shown at trial stage.

How quickly the new approach, in which the National Institute for Health and Clinical Excellence (NICE) would be likely to play a greater, price setting role—can be brought in remains to be seen. The view of the Association of the British Pharmaceutical Industry is that the OFT’s proposals are “unworkable in their current form.”

Court dismisses Novartis challenge to Indian patent law

Ganapati Mudur NEW DELHI

Patients’ groups and health organisations proclaimed victory this week after an Indian court dismissed a petition by the drug company Novartis challenging a section of the Indian law on patents.

Novartis had questioned section 3(d) of the law, which prohibits patents on new forms or new uses of known substances, arguing that it was in violation of the Indian constitution and that it did not meet international trade rules.

The Madras High Court dismissed the petition, ruling that the clause was not unconstitutional and that the issue of whether it complies with international law should be determined by the World Trade Organization.

Health agencies say the verdict is a victory for global public health. “This is a huge relief to millions of patients and doctors in developing countries,” said Tido von Schoen-Angerer, director of the campaign for access to essential medicines at Médecins Sans Frontières (MSF). Nearly 85% of the antiretrovirals that MSF procures for some 100,000 people infected with HIV across 30 countries come from Indian manufacturers of generic drugs.

“This ruling will allow the Indian generic industry to continue providing inexpensive drugs to the world’s poor,” said Anand Grover, director of Lawyers Collective HIV Unit, who had represented India’s Cancer Patients Aid Association against Novartis. The association had opposed a patent on Novartis’s drug imatinib (Glivec), used to treat chronic myeloid leukaemia.

Novartis challenged section 3(d) after India’s patent office had rejected the company’s application for a patent on imatinib on the grounds that the drug involved minor modifications of an old molecule.

Novartis has said that the verdict will have long term negative consequences for research into new drugs and that effective patent systems ensure that incentives are in place to stimulate long term research efforts needed for medical progress.

“If Indian patent law does not recognise these important advances, patients will be denied new and better medicines,” said Paul Herling, head of corporate research at Novartis.

The company disagrees with the ruling but is unlikely to appeal in the Indian Supreme Court. Its appeal against the decision on imatinib is still pending.
Overseas doctors work longer hours, says Australian study

Stephen Pincock SYDNEY
A study examining the practice patterns of overseas doctors working in Australia has shown that they work longer hours, prescribe more drugs, and order more tests than their counterparts who trained in Australia.

Australia relies heavily on medical graduates from overseas, said the study’s lead author, Clare Bayram, from Sydney University’s Family Medicine Research Centre. They make up 25% of the total workforce of doctors, but information on how they practise in the Australian setting is virtually non-existent, she said.

She and her colleagues compared 89 overseas trained doctors who were enrolled in a training programme with 1032 fellows of the Royal Australasian College of General Practitioners (Australian Health Review 2007;31:441-8). Each participant provided the details of 100 encounters with patients.

“We found that [overseas trained doctors] were significantly younger, had spent fewer years in general practice, worked more sessions per week, and were more likely to work in smaller practices than Australian trained doctors,” Ms Bayram said.

She said that these results weren’t surprising, given that many newly arrived doctors from overseas work in regional centres and remote parts of Australia.

A more surprising finding came when the researchers looked at the treatment patterns of the two groups. Doctors who had trained overseas were more likely to prescribe drugs, to offer clinical and procedural treatments, and to refer patients to allied health professionals and hospitals. They were also more likely to order pathology and imaging tests.

The differences in treatment patterns remained even when the researchers adjusted the results for mix of patients and the age, sex, and location of the doctor, she said. “There’s such a large difference in the prescribing rate that it can’t be accounted for by the characteristics of the patients they’re seeing.”

Overseas medical graduates are currently high on the political agenda in Australia. After the case of the Queensland based doctor Mohamed Haneef, who was accused of having links to the 30 June terrorist car bombing of Glasgow Airport, the country’s immigration minister this week ordered that all overseas trained doctors undergo security checks.

In a statement the trust’s chief executive, Mark Goldman, said, “Following the deaths of two patients at Heartlands Hospital we are carrying out a detailed investigation into the clinical care given to both of these patients.

“We have already met with both families, expressed our deepest sympathy, and advised them of this investigation.”

A hospital spokeswoman said she did not know when the inquiry would be complete, but she added: “The doctor and two nurses involved have not been suspended but are currently not working within the hospital and are deeply upset by the deaths.

“It has already been established that the two men received a higher dosage than normal.”

The National Patient Safety Agency, the government body that coordinates reporting of patient safety incidents, is tackling the issue of treatment errors nationally.

A review by the agency published in March showed that it received more than 14,000 reports between January 2005 and June 2006 relating to injectable drugs.

Of these, 92 incidents caused severe harm to patients or resulted in death. The agency also issued a patient safety alert on injectable medicines in March (BMJ 2007;334:714).

David Cousins, head of safe medication practice at the agency, said, “Injectable medicines are complex, and there is work under way. In a way, incidents such as [that at] Birmingham and others just underline the need to do something on injectable medicines.

“We are recommending that trusts purchase medicines that are safer to use in practice rather than those that are a concentrate and have to be mixed by doctors and nurses.”

Promoting Safer Use of Injectable Medicines is available at www.npsa.nhs.uk

Inquiry to be held after deaths of cancer patients

Adrian O’Dowd MARGATE
An inquiry has been launched after the deaths of two patients who may have been given an overdose of a drug intended to ease the side effects of cancer treatment.

The two men—Baljit Singh Sunner (aged 36) and Paul Richards (35)—both died within a day of being treated in an oncology ward at Birmingham’s Heartlands Hospital.

The Heart of England NHS Foundation Trust is not issuing details of the cases and would not say what drug or drugs had been involved, but the Birmingham Mail has claimed that the men were given five times the dosage they should have received (http://cbirmingham.icnetwork.co.uk/mail, 2 Aug, “Patients die after drug dose blunder”).

Incidents such as [this] … just underline the need to do something on injectable medicines

NHS fails to charge local authorities for delay

Roger Dobson ABERGAVENNY
Most hospitals in England do not charge local authorities for “bed blocking,” the term that describes extra stay in hospital because social services have failed to provide the care services that patients need after discharge, new research has found. However, it also found that the NHS, rather than local authorities, is responsible for two thirds of the number of bed days resulting from delayed discharge.

“There is no evidence to support government policy of charging social service departments for delay,” say the authors of the study, which provides data from across England on delays in discharge of patients from acute hospitals since the Community Care Act was introduced in 2003 (Journal of Public Health doi: 10.1093/pubmed/fdm026). This act gave NHS hospitals the power to charge social service departments a daily tariff (£120 (€180; $240) in the South East and £100 in the rest of England) where social services failed to provide the required care services, such as a place in a residential home.

The Community Care Act came in the wake of a
The rising number of morbidly obese people in the UK population has prompted anaesthetists to write new guidelines for managing these higher risk patients, emphasising the need for training and suitable equipment.

In England nearly 3% of women and 1% of men are morbidly obese (with a body mass index (BMI) of >40), and well over a fifth of the population are obese (BMI >30), government figures show.

The new guidelines, issued by the Association of Anaesthetists of Great Britain and Ireland, say that each hospital should have a named consultant anaesthetist responsible for making sure that staff and facilities are appropriately prepared for the perioperative management of morbidly obese patients. Each operating theatre should also have a member of staff with this responsibility.

“Many clinicians are aware of an increasing number of morbidly obese patients. It really is becoming significantly more common,” said Alastair Chambers, consultant anaesthetist at Aberdeen Royal Infirmary, who led the committee that wrote the guidelines.

The guidelines say that every major hospital is likely to encounter patients weighing more than 150 kg and that some of these patients will present in emergencies. In such patients intubation is often more difficult, low oxygen saturation during general anaesthesia is more common, and regional anaesthesia is harder where landmarks are obscured.

The guidelines say that anaesthetists should know how to manage such patients. “They need to be familiar with the equipment and the risks that these patients present. Formally recording a patient’s weight and height is a good start,” said Professor Chambers.

Clinicians need to make sure they know the weight tolerances of operating theatre beds, when flat and when tilted, he said. He pointed out that staff were also at risk, highlighting back pain as a potential consequence of unsafe lifting.

The guidelines are available at www.aagbi.org.
**German doctors fear performance-rating websites**

**Annette Tuffs**  
**HEIDELBERG**

As the number of German websites that try to judge doctors’ performances according to patients’ opinions rises, the National Association of Statutory Health Insurance Physicians (KBV) has warned doctors to contact the providers of websites they think may be libelling them.

However, doctors may not be aware of negative comments about them, because the websites are not obliged to inform the respective doctors when the comments appear.

Last week a Munich agency launched a new website [www.jameda.de](http://www.jameda.de) listing addresses of about 170,000 doctors and 120,000 other health professionals, such as midwives and alternative health practitioners. Patients can register free of charge, search for doctors by location and specialty, and post their comments on success of treatment, waiting times, and general service.

“We do not allow statements on medical competence,” says the website. “In contrast to other similar websites Jameda does not have the option of entering free statements by users.”

But other websites, such as [www.helpster.de](http://www.helpster.de) and [www.topmedic.de](http://www.topmedic.de), allow their users to add comments. Some of them also include hospitals and other healthcare institutions. Like its competitors the Jameda site will be financed mainly by advertising. Also, doctors can create their own home page on the site for just under €100 (£70; $140) a year.

Doctors’ representatives, such as Martin Eulitz of KBV, have said that the regional medical associations already provide complete addresses of all available doctors and psychotherapists. Also, numerous websites giving general health information and the home pages of health insurance companies have an internet link to a database of doctors’ addresses run by the Stiftung Gesundheit (Health Foundation) in Hamburg, a charity that aims to foster transparency in the healthcare system. However, none of these sites offers any information on quality.

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**Summer PSA tests may lead to more biopsies**

**Roger Dobson**  
**ABERGAVENNY**

Men who undertake the prostate specific antigen (PSA) screening test for prostate cancer in the summer are more likely to have a subsequent biopsy than men tested at any other time of the year.

A new study, published in *European Urology* ([doi: 10.1016/j.euro.2006.11.042](http://dx.doi.org/10.1016/j.euro.2006.11.042)) shows that concentrations of PSA are higher in the summer, resulting in a higher likelihood of referral for a biopsy of up to a quarter.

“We show that being screened during summer increased by 23% the likelihood of having a higher PSA than the cut-off value [for biopsy],” the authors write. “It may be prudent to confirm any isolated test result before biopsy, and even more so if this was obtained in summer.”

They add: “The present observation . . . is troubling as it suggests that rigid PSA cut-offs are ill-adapted to routine clinical practice.”

The authors say that measurement of PSA serum concentrations is central to all programmes for the early detection of prostate cancer but that the influence of season on PSA concentrations has been little investigated.

They looked at the relation between meteorological data and total PSA testing (which measures nanograms of PSA per millilitre of blood) as well as free PSA testing (which measures the percentage of PSA that is not bound to proteins in the blood) in 8644 men aged 55 to 70 in the French arm of the European randomised study of screening for prostate cancer (ERSPC).

Significantly higher PSA concentrations (P< 0.001) were found in summer (total PSA 1.87±0.06 ng/ml) than in autumn (1.71±0.07 ng/ml), winter (1.42±0.06 ng/ml), or spring (1.38±0.13 ng/ml).
Infant mortality and mental illness rise among Palestinians

Roger Dobson ABERG AVENNY

A new report calls for urgent international help in tackling health problems in the Palestinian territories. It shows an increase in infant mortality and a doubling of the number of cases of mental illness.

The authors also report increases in the numbers of cases of food poisoning, sexually transmitted diseases, and contaminated drinking water; a deterioration in nutrition; failure to achieve targets on mortality from heart disease and strokes; and poor provision of services for elderly and disabled people (Public Health doi: 10.1016/j.puhe.2007.04.017).

The report, which looks at the state of Palestinian primary health care and the achievements of the Palestine national strategic health plan 1999-2003, says, however, that a number of significant improvements have occurred, including a leap in the number of people being vaccinated, a drop in the incidence of HIV infection, and lower rates of smoking.

The authors, from the University of Crete School of Medicine, Al-Quds University in Jerusalem, and the Palestinian Ministry of Health, write, “Although there has been progress and promising changes in vital health, especially crude death rate and life expectancy, there are also alarming indicators that should attract the attention of Palestinian leaders.”

They add, “Certain health promotion and environmental health actions should be undertaken urgently by the Palestinian health care services to cope with environmental and sanitary conditions, and to further improve health status regarding communicable and non-communicable diseases in Palestinians. The main barrier to the success of the [plan] was the lack of follow-up due to political and socio-economic instability. There is an urgent need for international intervention and support.”

Their results show that from 1999 to 2003 the crude birth rate had fallen by 17.1%, the crude death rate by 0.6%, and the total fertility rate by 11.8%. Life expectancy had gone up by 0.8%.

The report lists a number of achievements over this period, including falls in mortality from breast cancer and lung cancer and in maternal mortality, a reduction of 64.3% in the incidence of HIV and AIDS, and a drop of 19% in the number of smokers aged over 10. There was also, it says, a “remarkable” improvement in immunisation coverage.

But infant mortality grew by 8.6%, and targets on heart disease had not been achieved. By 2003 heart disease mortality had fallen by 13.2%, against a target of 40%. Mortality from stroke fell by 6.5%, against a target of 40%.

Targets on sexually transmitted diseases had also not been achieved; the incidence of these diseases grew by 66%.

Proposals reopen debate over public and private practice

David Spurgeon QUEBEC

Reactions have been rapid to proposals from the outgoing president of the Canadian Medical Association that would allow doctors to work outside as well as inside the publicly funded national healthcare system, reviving a longstanding debate about “two tier medicine.”

Colin McMillan was reported in the Globe and Mail newspaper as saying that the issue has been simmering among doctors for the past two years and he wanted merely to “get it on the public discussion level” (www.heglobeandmail.com 1 Aug, “Debate among doctors builds over CMA health-care proposal”). Dr McMillan’s proposals were expanded on the association’s website, www.cmaj.ca (“CMA unveils plan to modernise Medicare” and “It’s still about Access”).

The Canada Health Act, which defines the national healthcare system, is generally interpreted as prohibiting doctors from working in the public and private systems at the same time.

Interest in the controversy had grown because Dr McMillan’s successor is Brian Day, who heads the private Cambie Surgery Centre in British Columbia.

He has said that if Canadians could not obtain essential medical services in a timely fashion they should not be forced into a lengthy queue where they could suffer or die. However, he also said he opposes privatising the national healthcare system (BMJ 2006;333:622).

The CMA has changed its official stance on the matter over the years, but on its website it says, “Governments should remove bans preventing physicians from opting out or preventing them from practising in both the public and private sectors, where it can be shown that this would improve access to services from the entire population, increase the capacity in the health-care system and reduce waiting times.”

“Ther is an urgent need for international intervention and support”
Unexploded munitions are a serious problem in Afghanistan

High profile campaigns have successfully highlighted the dangers of landmines, but data from Afghanistan show unexploded ordnance continues to harm a greater number of people, particularly children.

When researchers analysed 5471 incidents of individuals injured or killed by these devices between 2002 and 2006, they found that 2749 (50.3%) were caused by unexploded ordnance and 2314 (42.3%) by landmines. An unknown device caused the rest. The proportion of deaths and injuries caused by unexploded ordnance rose from 48.4% in 2002 to 58.8% in 2006 (P< 0.001). Almost half the deaths and injuries in this study were in children (2580, 47.2%), and of these 1687 (65%) were attributed to unexploded ordnance. Tampering accounted for an increasing proportion of injuries to children and adults, rising from 8.3% in 2002 to 25.6% by 2006 (P< 0.001). Most tampering incidents involved unexploded ordnance rather than landmines.

As the sensitivity of the data collection is not known the figures may be underestimated, say the authors. Both types of device continue to cause large numbers of injuries and deaths in Afghanistan. The increasing role of unexploded ordnance is particularly troubling, because these kinds of devices are cheaper and easier to clear up than landmines.

JAMA 2007;298:516-8

Interferon beta slightly delays disability in early MS

Interferon beta is a disease modifying treatment for multiple sclerosis. In patients who have had just one suggestive neurological event, treatment can delay progression to clinically definite disease. But can it delay or reduce disability, the outcome most feared by patients and their relatives? Extended follow-up of a randomised controlled trial for women at high risk of preterm delivery, says the editorial’s author. We will get a reliable answer sooner or later. At least 16 other trials are in the pipeline.


SHORT CUTS

WHAT’S NEW IN THE OTHER GENERAL JOURNALS

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

Unexplained progesterone and preterm birth. Trials have been inconsistent, however, and the latest two are no exception. In the first, vaginal progesterone (200 mg) used daily from 24 to 34 weeks’ gestation reduced the risk of preterm birth among high risk women with a short cervix (relative risk 0.56, 95% CI 0.36 to 0.86 among placebo controls). In the second, intramuscular 17 alpha-hydroxyprogesterone had no effect on the risk of birth or fetal death before 35 weeks among women with twins, another high risk group (1.1, 0.9 to 1.3). In both trials, the babies of treated mothers did no better than the babies of controls.

A linked editorial says the discrepancy between the trials is surprising, despite their methodological differences (p 499). If anything, progesterone should have worked better for women with twins. In singleton pregnancies, infection is likely to be a bigger contributor to preterm delivery than hormones. The data so far, along with ongoing worries about the effects of exogenous hormones on the growing fetus, mean that progesterone should probably remain an experimental treatment for women at high risk of preterm delivery, says the editorial’s author.

The war in northern Uganda between the rebel Lord’s Resistance Army and the government has devastated millions of lives since it began two decades ago. When researchers surveyed a sample of the region’s adult population, 40% (1018/2585) said they had been abducted by the rebels, almost one half (1259/2585) had been threatened with death, more than one half had seen a child abducted, and 31% (799/2585) had lost one or more of their own children. Physical and sexual violence, either witnessed or experienced first hand, was common. Perhaps unsurprisingly, 74% (1774/2389) of respondents had post-traumatic stress disorder and 44.5% (1151/2585) were clinically depressed. Both were associated with an inclination to favour violence as a way of achieving peace. Sixty one per cent of the 2585 respondents had been driven from their own children. Physical and sexual violence, either witnessed or experienced first hand, was common. Perhaps unsurprisingly, 74% (1774/2389) of respondents had post-traumatic stress disorder and 44.5% (1151/2585) were clinically depressed. Both were associated with an inclination to favour violence as a way of achieving peace. Sixty one per cent of the 2585 respondents had been driven from


Adapted from N Engl J Med 2007;357:462-9
their villages and were living in camps. This survey found a higher prevalence of severe mental illness than other surveys in Cambodia, Ethiopia, Gaza, Afghanistan, and Rwanda, although the various methods weren’t strictly comparable. The length of the Ugandan conflict, its brutality towards civilians, and mass displacement are all to blame, say the authors. The Lord’s Resistance Army used civilian abduction to conscript soldiers and other personnel, including sex workers. JAMA 2007;298:543-54

Vulnerable families suffer when soldiers go to war
Children in some military families are more likely to be mistreated when a parent goes to war, say US researchers. In a retrospective analysis of routinely collected child protection data, deployment to a combat zone was associated with a 40% increase in the rate of child mistreatment among families with at least one recorded incident (rate ratio, 1.42, 95% CI, 1.31 to 1.54). The rate of moderate or serious mistreatment went up by 60% (1.61, 1.45 to 1.77).

Most of the increase was due to mothers neglecting children aged between 2 and 12 while their husbands were on active duty in combat zones (3.88, 3.43 to 4.34). Physical abuse by mothers was also more likely during these periods (1.91, 1.33 to 2.49). Increased stress is one possible explanation, although deployment of female soldiers was not associated with a significant increase in mistreatment by civilian fathers. Deployment of either parent had no effect on the rate of sexual abuse.

These findings are consistent with other observational work suggesting that vulnerable children are at risk when soldiers go to war, say the authors. The current support networks may not be enough for families already registered for mistreating their children. JAMA 2007;298:528-35

Lessons in pandemic flu from 1918
Preparations for pandemic influenza tend to focus on vaccines and antiviral drugs. Neither were available in 1918 during the last pandemic, when city authorities had to rely on classical public health measures to limit the spread of disease. A careful trawl through over 1000 historical documents and an epidemiological analysis of the pandemic’s trajectory in 43 US cities suggests these measures can work. Closing schools, preventing public gatherings, and setting up mandatory quarantine for sick people and their contacts were all associated with slower rise in deaths and a lower overall death rate. Cities, such as St Louis, that introduced multiple public health measures early in the pandemic and sustained them through the riskiest period, seemed to lose the fewest citizens overall, although it’s impossible to say for certain whether these authorities’ timely actions were responsible. The authors note that successful strategies in one city didn’t necessarily translate to other cities in the study.

In 1918, timing was critical. In New York, the authorities introduced rigorous isolation and quarantine before any excess deaths had occurred. It had the lowest death rate on the eastern seaboard. JAMA 2007;298:644-54

Simple screening protects Indian women against cervical cancer
A quick, easy, and affordable screening test reduced the risk of cervical cancer by 25% among women in rural India, in a recent cluster randomised trial (hazard ratio 0.75, 95% CI 0.59 to 0.95). A single visual inspection of the cervix with acetic acid followed by treatment for positive patients reduced deaths from cervical cancer by 35% (0.65, 0.47 to 0.89), and all cause mortality by 13% (0.87, 0.78 to 0.96) during a follow-up of seven years. The authors say the test looks like a good option for resource poor countries without the facilities, personnel, or infrastructure required to screen with cytology. The women in this study were screened just once, and those aged between 30 and 39 benefited most. Older women may not do so well once the transformation zone, where cervical intraepithelial neoplasia occurs, moves into the endocervical canal and out of sight.

As with all screening tests, the success of this one depends on well trained health workers, good quality control, and a high uptake. Poor performance at all three may limit the benefits of screening in other developing countries, says a linked editorial (pp 365-6).

But if it’s done properly, once in a lifetime visual inspection could be a workable stop gap until vaccines against human papillomaviruses become affordable and widely available. Lancet 2007;370:398-406

Children in developing countries have silent rheumatic heart disease
Rheumatic heart disease is already a leading cause of death and disability in developing countries, and clinical disease is just the tip of a large iceberg, according to a study of schoolchildren in Mozambique and Cambodia. Researchers looked proactively for rheumatic valve lesions using portable echocardiography, and found 10 times more than expected. Around nine out of 10 affected children were asymptomatic without an audible heart murmur, and would have been missed by traditional screening for clinical disease.

Among 3677 children in Cambodia, 79 had ultrasound evidence of rheumatic heart disease (2.1 per 1000, 95% CI 1.68 to 2.62). Only eight had clinical symptoms or signs (2.2 per 1000, 0.7 to 3.7). The findings were similar among children in Mozambique, where echocardiography picked up 13 times more cases than would have been found by clinical screening (30.4 per 1000, 23.2 to 37.6 v 2.3 per 1000, 0.3 to 4.3).

Screening with echocardiography may be relatively expensive, but it’s important that the authorities in endemic areas learn the true extent of the problem, say the authors. Only then can they plan services and offer treatment, surveillance, and prophylactic antibiotics to affected children. The challenge now is to find a way to make echocardiography affordable to the countries that need it most. N Engl J Med 2007;357:470-6
It is not often that publishers of scientific material get a good press. Their main customers—the funders of research, scientists, and librarians—have long resented the unfairness of a system that sees their library coffers squeezed dry to purchase reports about their own science, resulting in a fractious, if co-dependent, relationship. But away from the animosity of rich countries’ labs and libraries, the world’s biggest publishers have been challenging their heartless image.

Since 2000, when the World Health Organization (WHO) first broached the idea of increasing access to scientific information in the developing world by supplying electronic content free of charge (phase 1) or at low cost (phase 2), publishers have been falling over themselves to take part. Last month, more than 100 of the world’s largest publishing companies further extended their commitment to this philanthropic project by pledging to support WHO’s “health internet-work access to research initiative” (HINARI) to at least 2015.¹

Some observers question whether the industry’s motives are purely altruistic. It is conceivable that pitifully poor countries in 2007 may later follow China along the path to rampant consumerism, making HINARI a useful mechanism for pre-emptive brand recognition. Nevertheless, the commitment of publishers—and the rapid success they have helped HINARI achieve—has provided a valuable opportunity for scientists in developing countries to engage in the global scientific conversation.

“Developing country researchers who don’t have access to the internet will put together a proposal and then get it immediately turned down by a funder, who says the proposal is out of date,” explains Barbara Aronson, HINARI’s project manager and one of only two full time staff working on the project based at WHO, “but when you allow these researchers access to current journals they can contribute and be involved in the biomedical research community.”

Access restrictions
This opportunity, HINARI’s first proponents confidently predicted, would not only improve research in developing countries but would lead to knock-on effects that boosted health outcomes and much more besides. But, five years on, HINARI has become bogged down by some of the technical challenges of delivering electronic content. Many users have internet connection speeds so slow that downloading a single article can absorb an entire afternoon.
In institutions that register for the content, librarians often control or restrict access so researchers cannot use the system as freely as they need. So are developing countries’ scientists and healthcare workers really getting a good deal?

HINARI was conceived as a way of helping WHO better meet the information needs of researchers. “We got several people together for a workshop, after a questionnaire had been sent out and researchers were unanimous that the one thing they needed was access to journals. So we set about doing something about that,” explains Aronson. HINARI offers a simple user interface over the web serving as a gateway to full-text journal articles at publishers’ websites that can be accessed directly from PubMed.

As the only surviving element of Kofi Annan’s internet commitment in the UN millennium declaration—which pledged to “ensure that the benefits of new technologies, especially information and communication technologies are available to all”—the scale of HINARI’s success took even its organisers by surprise. The scheme now gives its registered users, spread among 113 countries and 2500 institutions, access to almost 80% of the published literature indexed in Medline since 2000, and the number of available articles is now climbing towards 6200000. Aronson believes that this growth is explained by the fortuitous timing of the launch, which capitalised on both the growing importance of the internet as an information resource and the changing nature of the publishing industry—from one which delivered printed products to readers to a much broader information distribution business.

Maurice Long, former head of development at the BMJ Publishing Group and now publisher coordinator for HINARI and its sister projects AGORA (for agricultural literature) and OARE (environmental material), says there was an opportunity in 2000 where one had not previously existed: “In the mid-1990s, we calculated that it would cost £80 to send a free copy of the BMJ to an institution in a developing country.” But with the internet that cost was suddenly gone.

An editorial published simultaneously by the editors of the Lancet (Richard Horton), BMJ (Richard Smith), and BioMedCentral (Fiona Godlee) in September 2000, calling for publishers to provide free health information to resource-poor countries, spelt out the part industry should play in taking the advantages of this new technology to the developing world. For WHO, this was all the encouragement that was needed. Aronson recalls: “I rang up Richard Smith [after the editorial was published] and said ‘We want to do this. Can we talk?’ She asked Smith to chair a meeting of the chief executive officers of top publishing companies. “He said he was the worst person to do it because he was a loose cannon, but instead suggested Maurice Long—and that’s how he became involved.”

Getting the publishers to agree
The HINARI team predicted that their biggest challenge would be getting publishers to agree to the idea of providing free content. However, even during initial negotiations in 2000, when Aronson and her team first set about approaching big publishers, the enthusiasm that would later drive HINARI’s success was clear. The fact that HINARI came along at a time when the publishing industry was just starting to view the open-access movement as a commercial concern may have played a part. By mid-March, Long had managed to charm the six biggest publishers to New York for a remarkable meeting. “In the first 10 minutes of the meeting we had consensus,” he recalls. What they decided on was a non-binding agreement—“There are no contracts in HINARI,” says Aronson—between publishers and WHO to provide their content free to developing countries.

Yale University stepped in to design an appropriate web based system for authentication and registration of HINARI’s users, and in January 2002 the programme’s launch was announced. After little more than a year in gestation, HINARI’s birth was so quick that it led Sheldon Kotzin, executive editor of Medline, to joke about the team’s tactics. Aronson reports: “He said ‘How the hell did you get this done so quickly? You must have told the publishers that WHO was going to organise it, and they thought it would never get done and said yes,’” she laughs.

One issue of administrative concern was how to identify countries that should receive free access. The decision made by the HINARI team in 2000 was to delineate eligible countries according to their ranking on the World Bank development list. Those
with a yearly per capita gross national product (GNP) of less than US$1000 (£500; €730) were to get free access to HINARI’s content, while countries with a yearly per capita GNP of $1000–$3000 were asked to pay a $1000 fee—a sum that, according to Long, would buy “about two and a bit journals”—with that money being reinvested in training.

The aim was, and is, to get HINARI’s content to as many people involved in medicine and biomedical science as possible. “We want HINARI to reach people where teaching is done, where research is done, and where policy is being made,” explains Aronson. This definition includes all sorts of government offices, teaching hospitals, professional schools outside universities, national medical libraries, and occasionally non-governmental organisations. “In special cases—for example, a country like Afghanistan, where the country has contractted out the provision of health care to NGOs in whole provinces—we accept that they are the people who are providing the health care,” Aronson says. “The people we don’t want to have access are the local offices of Glaxo,” adds Long.

More than research
HINARI provides researchers with access to scientific literature, but that is not all it does by any means. According to Aronson, the initiative has proved a spur for widening internet access in general in developing countries, thanks to the fact that anyone can register to get access for their institution or organisation. “The internet has arrived. It is just a question of giving the institutions and the ministries or organisations that fund them the incentive to get it,” she explains. “[Institutions] can now say to their funders, ‘We have access to HINARI. How about giving us a few computers?’ That seems to work.”

The “HINARI effect” has seen improvements in poor network connections, inadequate electricity supply, equipment shortages, and even poor English skills among staff. “From anecdotal evidence what we have seen is that, once they have HINARI, they have a reason to fix some of those problems,” says Aronson. She adds that some research done by the WHO-sponsored Special Programme for Research and Training in Tropical Diseases suggested HINARI was advancing capacity building programmes, such as training in ethics and techniques for research, by 10 years.

The training that HINARI’s decentralised network provides—which is essential for many first-time users who may have used the internet only for email—is also helping to improve internet literacy in developing countries. Training courses lasting four or five days familiarise institutional representatives with different publishers’ web interfaces, searching, categorisation, and downloading, along with general internet concepts such as browsing, evaluating health information, and useful sources such as WHO and PubMed. “Everywhere we do training there is a burst in use,” says Aronson.

However, recent surveys of users of HINARI in five African countries, done by Helen Smith and colleagues from the Liverpool School of Tropical Medicine, suggest that there are bottlenecks within institutions that prevent researchers taking full advantage of the free content.4 Part of the problem, according to Smith, is that obtaining HINARI access requires institutions to register with WHO and obtain a password, which must subsequently be disseminated to researchers. The password often does not work when users attempt to download articles that should be free, and some librarians discourage users from requesting full-text access. “Our research suggests that librarians control access by keeping the HINARI password and insisting users go through them for access,” explains Smith. The HINARI team at WHO counters that they encourage dissemination of the passwords as widely as possible, but when Smith and colleagues questioned several potential users about their awareness of online services and internet use, they found that librarians are often not publicising the fact that the content is available—a particular problem for researchers who use internet cafes as their main source of internet access—and uncovered numerous examples of passwords not providing the access they should.

Does HINARI advance health?
A broader issue of concern is whether HINARI’s efforts to disseminate medical science to researchers in developing countries is actually improving health and health care. According to Neil Pakenham-Walsh, coordinator of the Global Healthcare Information Network and a long-time observer of HINARI, although it is incredibly important for the health system at all levels to be managed by people that are fully informed (as HINARI allows), if health workers don’t have access to the information they need at the point of care then the direct health benefits are limited.

Smith and colleagues’ study of electronic access to health knowledge confirms that, when it comes to treating the sick, journal articles are not the sort of information that health workers refer to during their day to day work: generic formularies or textbooks are more likely to guide clinical decision making.4 They explain this finding indicates that clinical competence in developing countries does not necessarily involve applying the most recent research findings to practice. Pakenham-Walsh believes it also exposes an information gap: “The whole issue of availability of health information is much broader than what HINARI is doing. They are setting an important foundation for a future when every person worldwide will have health information necessary to improve health. But researchers and academics are a very small proportion of those who need information.”

Clinical competence in the developing world does not necessarily involve applying the most recent research findings to practice

Translating the research: nurses using computers in a Kenyan hospital
There are other problems with the system. Most of the journal literature available via HINARI is in English, which means that many health workers and researchers in developing countries cannot benefit from the literature simply because they can’t speak the right language. Content remains available only in registered institutions, so, explains Pakenham-Walsh, “even if you are in an HINARI eligible country that doesn’t mean you have access. It means that somewhere in your country there are a couple of institutions where you can go and log on.” Several critics point out that middle income countries such as India, China, South Africa, and Pakistan are not included within the list of eligible countries, thus depriving thousands of needy researchers from the service. And one consistent complaint from users is the slowness of responses to user queries, if they are acknowledged at all, by WHO headquarters.

Improving resources

Pakenham-Walsh suggests that the system would be improved if more resources were directed at the WHO Geneva office to help the currently tiny team give a better service to users. He believes that HINARI’s users would also benefit from better access to electronic textbooks and other non-journal resources. There should be some way to rank the content according to relevance to users, he adds. “One of the issues with HINARI is that it has so many different journals that there is a lot of noise,” he explains. “Because most journals are published in developed countries, the content is high tech. It might be good to separate out the developing country-relevant stuff.”

Helen Smith adds that more needs to be done to ensure that people who currently should have access to literature via HINARI, those in registered institutions, are reaping the full benefits.

The technology problem

There remains a limiting factor to HINARI’s influence—poor internet connectivity in much of the developing world. WHO gives informal advice to institutions about ways to lobby for improving their connections or funding, but this remains a serious problem. Furthermore, WHO itself has been struggling with the technology challenge of HINARI. One of the deals that WHO made with publishers initially was that WHO would guarantee to identify who qualified for HINARI access. Aronson explains: “We said we would do the authentication. We first used a system done by Yale, who had off-site users, but it didn’t work for any of our institutions. It required something that you can do in the US but you can’t in developing countries. We went for a system that worked quite well for two years, but, starting in the summer of 2005, the system was overloaded. By March 2006, it was a catastrophe.”

Two external reviews of HINARI’s operations funded by the UK Department for International Development pinpointed the problem. “The biggest issue was this problem of authentication, that meant very often a significant number of times users in Africa couldn’t get through to the original article,” explains Aronson. Luckily, just as HINARI’s technical infrastructure was collapsing under the strain, a volunteer from Microsoft walked into WHO in May 2006 looking for ways to collaborate with UN agencies. “They said they would be interested in collaborating. We said we have a technological problem and they said they would solve it. And they did,” recalls Aronson.

As of July this year, Microsoft became an official HINARI partner, and the project’s technological infrastructure is now functioning well. This outcome, according to Aronson, demonstrates one of the less well known aspects of HINARI’s success—it inspires people. “People get very involved and committed. They become champions within their companies and put in huge amounts of personal time,” she says.

But is a scheme so dependent on the goodwill of individuals a sustainable one? Long and Aronson believe so. “What we are really pleased about is that we have developed this diffuse network of people in different institutions that form a collaborative framework,” Aronson enthuses. “If we have people at WHO doing all the work, that might be unsustainable. But in a network like that you have great commitment to the programme, and that gives a very stable model.” However, she believes the most important stabilising influence of HINARI is the change in attitude it has brought about. “The big thing is we have brought in developing countries like any other users. Now, even if HINARI were to disappear after 2015—which we don’t anticipate it will—the notion that developing countries have researchers who need information will not.”

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How not to win friends and influence people

The debacle concerning the UK medical training application service (MTAS) has flushed out what people really think of the Postgraduate Medical Education and Training Board.

As the MTAS shenanigans have emerged it has been interesting to discover how many organisations and individuals are not responsible for them. Failure is an orphan, they say, but seldom such a threadbare and friendless waif as this.

Foremost among those who deny any responsibility is the government organisation charged with the higher training of doctors, the Postgraduate Medical Education and Training Board. Let's count the number of words in its name that relate to the issues affected by MTAS: education, postgraduate, training, medical. That leaves only “board” unaccounted for.

The board was supposed to bring organisation and method to the often haphazard arrangements for postgraduate education and training of doctors. In evidence to the High Court in the case brought by the campaigning group Remedy UK, the board admitted it was responsible for laying down the basic principles of recruitment to specialist training posts. But its chairman, Peter Rubin, has said—rightly—that its powers do not encompass choosing between eligible candidates.

In disavowing responsibility for the mess he is at least in the best of company. When the chief medical officer, Liam Donaldson, was asked if he felt any responsibility for MTAS, he said: “The implementation went wrong. But responsibility is very widely distributed. It is very difficult to point to any single individual who could be said to be accountable." I’ll take that as a no, then.

Those who devise new policies or who are given the task of managing them are apparently unaccountable when implementation goes awry. Responsibility is so subdivided that, ultimately, nobody is to blame. But regardless of whether the board deserves criticism over MTAS the affair has at least flushed out what people really think of it.

It might be a slight exaggeration to say that the board is friendless, but there is little risk of being trampled in the rush to come to its defence. All the old animosities, swelled at the time of its creation, have resurfaced. Even the Academy of the Medical Royal Colleges, normally not a body to foster discord, has expressed its anxieties in a nine page memorandum, leaked to the magazine Hospital Doctor, accusing the board of inefficiency, poor communication, bad judgment, and a reluctance to consult the colleges or even care what they think.

The academy should not have been surprised. The board was set up by Alan Milburn when he was health secretary, with the intention of clipping the colleges’ wings. Although nominally independent, it is largely a creature of the Department of Health. The colleges were allowed, on sufferance, to nominate members (through the academy), but it is the health secretary who makes appointments from the names put in front of him. Those appointed serve in their own right, not as college representatives.

The charges against the board include a lack of cooperation with the colleges, inefficient management, high handedness, steep fees, and lengthy and complex application forms. As one senior college president put it, “We’re not trying to turn the clock back, but we wanted a light touch regulator. What we got was a body with a large staff and an apparent desire to go into every possible detail.”

There is particular rancour over the board’s readiness to overturn the colleges’ advice over applications to join the specialist register. The colleges are paid for processing these applications—though not enough to cover their costs, they say—but their advice is often ignored, usually through the granting of registration to candidates that the colleges believe are unfit or insufficiently experienced.

Roger Greenhalgh, president of the European Federation of Surgical Specialties, called a meeting at the Royal College of Surgeons earlier this year of European surgeons, who agreed that only surgeons in a particular specialty were qualified to assess proficiency and competency. The board, by contrast, makes a point of excluding from its panels members of the same specialty as the applicant. Opinions among surgeons are running so high that in June the college passed a resolution suggesting that the college dissociate itself from the board and take no part in its affairs until all the college’s concerns are met in full.

The board’s most cogent defence of its role came in its evidence to John Tooke’s inquiry into Modernising Medical Careers. It argues there that in less than two years it has published standards for postgraduate training and approved curriculums across 57 medical specialties; issued more than 7500 CCTs; organised the first ever national survey of postgraduate trainees; and put in place a system for awarding CCTs to doctors who have not followed a formal training programme but have achieved the same levels of skills and knowledge as those who have. This long list of the board’s achievements makes you wonder how we ever produced doctors at all in the past.

The board’s only concession to criticism is to admit that “any organisation would expect to take time to establish itself, and PMETB is no exception.” Since the publication of the academy’s memorandum, there have been meetings between the board and the colleges, with some evidence of a desire for compromise. One college president saw this as a chance for a new start but warned that the issue of whether the profession has lost faith in the board has not yet been resolved.

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Preventive health care aims to delay the onset of illness and disease and to prevent untimely and premature deaths. But the theory and rhetoric of prevention do not deal with the problem of how such health care applies to people who have already exceeded an average lifespan. In recent years, concerns about equity of access to treatments have focused on ageism. As a result, preventive interventions are encouraged regardless of age, and this can be harmful to the patient and expensive for the health service. In rapidly ageing populations, we urgently need to reappraise the complex and uncomfortable relations between age discrimination, distributive justice, quality, and length of life.

**The epidemic of cardiovascular disease**

In the richer countries of the world, improved social conditions combined with immunisations and antibiotics have rapidly reduced the rates of death from infectious diseases. People saved from these epidemics now live long enough to face the new “epidemic” of cardiovascular disease, which is the focus of huge investment and endeavour in health promotion. The national service framework for cardiovascular disease aims to reduce the number of people dying from coronary heart disease by 40% by the year 2010 with advice that standards set out in this framework apply to all people, irrespective of age.1 But what will be the next most common cause of death—the next epidemic? Our bodies have a finite functional life and age is a fundamental cause of disease.2 By using preventive treatments to reduce the risk of a particular cause of death in elderly people are we simply changing the cause of death rather than prolonging life?

Three factors fuel this possibility. **Firstly, single disease perspectives lure researchers and guideline groups into assuming that improved outcomes for the index condition mean that everybody with that condition should be treated, irrespective of the overall effect on population mortality and morbidity. Secondly, sensitivity about age discrimination prevents us from looking at things differently when dealing with an elderly population. Finally, drug companies make huge financial gains if effective interventions in relatively small populations become standard care for all people at risk of that condition.**

Research estimates of differences in the absolute risk of an adverse outcome enable us to assess the potential benefits of treatments. The number needed to treat is calculated from the reduction in absolute risk and can help clinicians assess the balance between the burden of treatment and possible benefit. This measure is most useful for younger people in whom a single disease is more likely to have a significant effect on mortality and morbidity. The number needed to treat works best with acute conditions and less well with chronic conditions.3 In older people, the likelihood of many compounding diseases increases, and the absolute risk of dying is higher because they are nearer the end of their life. This may magnify the apparent effect of a single intervention for a specific condition while overall survival is only minimally affected. **The use of statins to prevent cardiovascular disease provides a case study for examining these issues further.**

**Lipid lowering treatments in elderly people**

Currently, we use evidence from younger populations and extrapolate this to elderly ones. Anxiety about age discrimination means that no upper age limit exists for assessing cardiovascular risk. However, evidence for the effects of prevention of heart disease with drugs is scant in elderly people. The largest study in this group is the pravastatin in elderly individuals at risk of vascular disease (PROSPER) trial. In this trial more than 5000 participants, aged 70-82 years, were followed up for an average of 3.2 years.4 Pravastatin had a clear but small effect on mortality and morbidity from cardiovascular disease using the primary composite end point (absolute risk reduction

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**Preventive health care in elderly people needs rethinking**

Dee Mangin, Kieran Sweeney, and Iona Heath argue that, rather than prolonging life, preventive treatments in elderly people simply change the cause of death—the manner of our dying.

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**Cardiovascular outcomes, all cause mortality, and cancer outcomes in the PROSPER study**

Dee Mangin, Kieran Sweeney, and Iona Heath argue that, rather than prolonging life, preventive treatments in elderly people simply change the cause of death—the manner of our dying.

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**ANALYSIS**

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2.1%, number needed to treat 48; figure). These data are used to underpin the study conclusions and those of subsequent guidelines that vascular prevention strategies in middle aged people should also be applied to elderly people. However, examination of all mortality and morbidity data is revealing. Pravastatin showed no benefit over placebo for any outcome in elderly women and despite a change in composite cardiovascular outcomes, all cause mortality stayed the same (hazard ratio 0.97, 95% confidence interval 0.83 to 1.14; figure), inferring that mortality and morbidity from other causes must have increased. Rates of cancer diagnosis and death were higher in the treatment group than in the placebo group. The difference was significant for a new diagnosis of cancer (1.25, 1.04 to 1.51; absolute risk increase 1.7%, number needed to treat 59; figure) and almost significant for mortality from cancer (1.28, 0.97 to 1.68). Treatment can sometimes be justified because of reduced morbidity even if mortality does not change, but the increase in cancer diagnoses in the PROSPER trial counters this argument. To assess whether pravastatin caused cancer, the authors of the study conducted a brief meta-analysis of the incidence of cancer in major statin trials; they found no difference between the statin and placebo arms. A more extensive meta-analysis also found no convincing evidence for this hypothesis. As none of the studies apart from PROSPER looked at elderly patients, the more likely reason for the results seen in elderly patients is substitution of cause of death, and the meta-analysis does not test this hypothesis. Perhaps we are seeing diminishing returns of prevention on overall life extension in older age.

Are we further blighting old age?
We are describing a contemporary phenomenon that is historically unprecedented. When we vaccinate children in infancy, we are selecting out a cause of death for them, in this case justifiably, because deaths from infectious disease tend to occur prematurely. It is only when we select out causes of death for people who have already exceeded the average lifespan that the endeavour becomes morally questionable. Many patients fear the manner of their dying more than death itself and, despite the distressing nature of some cardiac deaths, many people regard coronary heart disease as a “good way to go” in old age. By providing treatments designed to prevent particular diseases, we may be selecting for another cause of death unknowingly, and certainly without the patient’s informed consent. This is fundamentally unethical and undermines the principle of respect for autonomy.

Clinical decision making in relation to disease prevention carries extra responsibilities. Preventive treatments do not relieve suffering directly but reduce the risk of future suffering. As a degree of persuasion is involved in starting preventive treatments, clinicians must be reasonably certain they will fulfil their promise. Prevention has side effects other than the hazards of the treatment—in particular, the shadow cast over a currently healthy life by the threat of disease, which might be magnified in elderly people for whom mortality looms closer. When we convey risk to any patient we should be cautious—it is like putting a drop of ink into the clear water of the patient’s identity, which can never be quite clear again. Financial incentives for doctors that are linked to guidelines and targets, such as the quality and outcomes framework in the United Kingdom, may coerce doctors into persuading patients to accept such preventive treatments. The evidence that paying for performance changes health care is clear. Whether it improves health care is not always so clear.
Attesting to reduce the costs of these epidemics may be a motivator for the government, but the cost of health care is greatest in the year before death whenever it occurs. The best interests of elderly people, who have paid a lifetime of taxes, might lie in investing that money in health care that will genuinely relieve suffering. Cataract operations, joint replacement surgery, and personal care of people with dementia are obvious examples. This may explain why general practitioners are not comfortable about applying the national service framework for heart disease in elderly people and their reluctance to follow guidelines for cholesterol measurement and lipid lowering agents in people over 75.

This predicament shows how using fragments of information can make the answer to a complex clinical situation less clear. The problem is not the data—it is the way they are interpreted and communicated to practitioners and to patients. We need a way to assess prevention and treatment of risk factors in the elderly that takes a wider perspective when balancing potential harms against putative benefits. Instead of looking at absolute risks and death prevention, we should consider overall life extension and reduction in overall morbidity, taking the duration of treatment into account. The balance of risks will need to be assessed in broader terms than the adverse effects of drugs. What risk of cancer is acceptable to prevent death from a myocardial infarction? We should not carry on extrapolating data from younger populations and using linear models that use absolute risks of disease specific mortality and morbidity rather than all cause mortality and morbidity. If we do, the only ones to benefit will be drug companies, with increasing profits from an ageing population consumed by epidemics rather than enjoying their long life.

**Summary Points**

- Single disease models should not be applied to preventive treatments in elderly people.
- Preventive treatments in elderly people may select cause of death without the patient’s informed consent.
- Preventive use of statins shows no overall benefit in elderly people as cardiovascular mortality and morbidity are replaced by cancer.
- A more sophisticated model is needed to assess the benefits and harms of preventive treatment in elderly people.

**Contributors and sources:** DM, KS, and IH are general practitioners and the ideas in this article arose from thinking, researching, and reading around the experience of clinical care for patients in general practice. DM conceived the paper and wrote the first draft. KS contributed to the initial conversations about the essay, and all authors contributed to the serial drafts and conversations and agreed the final submission. DM is guarantor.

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**Why don’t doctors use HTML?**

As a regular browser of the BMJ’s online Rapid Responses, I’ve noticed that most contributors don’t format their entries in HTML (hypertext markup language). Perhaps they don’t know basic HTML code, or they just don’t bother to use it. Either way, it’s a great shame because HTML is extremely easy to learn and use, and formatted letters are a lot more aesthetically pleasing and therefore easier to read.

I’ve performed a quick audit of recent Rapid Responses. In the past 21 days, 334 responses have been accepted. Of these, 318 (95.2%) were completely unformatted, and 15 (4.5%) were formatted. Special mention goes to the author who used “XX” to separate paragraphs, making his contribution (0.3%) readable without the use of HTML code. Of the 15 formatted responses, five were authored by clinicians; the others were submitted by software developers, an author, a lawyer, a professor of computer science, a medical student, and a naturopathic medic.

Appearances are important, and when I read unformatted but otherwise excellent Rapid Responses, I often think the contributors’ gems of wisdom and knowledge have been done no justice by being squashed into a single paragraph devoid of indentation or font formatting.

If you learn only one piece of HTML code it should be the paragraph code, which allows you to leave line spaces between paragraphs simply by inserting `<p>` at the beginning of each paragraph and `</p>` at the end.

If you’re adding references to your letter, you might also want to remember the code for italic and bold letters: `<i>` italic `<b>` bold `<br>` becomes italic `<b>` bold `<br>` becomes bold.

If you’re using quotations or excerpts, the `</blockquote>` code can be useful. The wrapped text will be presented in its own indented paragraph.

Alternatively (and if this brief educational intervention is inconsequential), it might be worth badgering the BMJ for a WYSIWYG (what you see is what you get) web editor, so that contributors can submit beautifully formatted letters without having to bother with HTML code at all.

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We welcome articles up to 600 words on topics such as a memorable patient, a paper that changed my practice, My most unfortunate mistake, or any other piece conveying instruction, pathos or humour. Please submit the article on http://submit.bmj.com

Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for “Endpieces,” consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.
Referral patterns, cancer diagnoses, and waiting times after introduction of two week wait rule for breast cancer: prospective cohort study

Shelley Potter, clinical fellow,1 Sasi Govindarajulu, staff grade breast surgeon,1 Mike Shere, associate specialist breast physician,1 Fiona Braddon, clinical information systems manager,2 Geoffrey Curran, cancer analyst,3 Rosemary Greenwood, medical statistician,4 Ajay K Sahu, consultant surgeon,1 Simon J Cawthorn, consultant surgeon1

ABSTRACT

Objective To investigate the long term impact of the two week wait rule for breast cancer on referral patterns, cancer diagnoses, and waiting times.

Design Prospective cohort study.

Setting A specialist breast clinic in a teaching hospital in Bristol.

Participants All patients referred to breast clinic from primary care between 1999 and 2005.

Main outcome measures Number, route, and outcome of referrals from primary care and waiting times for urgent and routine appointments.

Results The annual number of referrals increased by 9% over the seven years from 3499 in 1999 to 3821 in 2005. Routine referrals decreased by 24% (from 1748 to 1331), but two week wait referrals increased by 42% (from 1751 to 2490) during this time. The percentage of patients diagnosed with cancer in the two week wait group decreased from 12.8% (224/1751) in 1999 to 7.7% (191/2490) in 2005 (P<0.001), while the number of cancers detected in the “routine” group increased from 2.5% (43/1748) to 5.3% (70/1331) (P<0.001) over the same period. About 27% (70/261) of people with cancer are currently referred in the non-urgent group. Waiting times for routine referrals have increased with time.

Conclusion The two week wait rule for breast cancer is failing patients. The number of cancers detected in this group of patients has been low, and the poor predictive value of fast track referral guidelines together with poor adherence in primary care has flooded one stop clinics with large numbers of inappropriate referrals. As a result, waiting times for those patients deemed non-urgent by the general practitioner have significantly increased, prompting considerable criticism because up to a third of cancers are ultimately diagnosed from this group. No survival benefit has been shown, and several authors have called for a re-evaluation of the system.

INTRODUCTION

At the end of the 20th century, cancer services in the United Kingdom were in a state of disarray. Mortality for a range of malignancies, including breast cancer, was among the highest in Europe and “disgracefully” long waiting lists resulting in delayed diagnosis and treatment were thought to be at least partly responsible. In 1998, in an attempt to address these inequalities and to improve outcomes for patients with breast cancer, the Department of Health issued a circular titled Breast cancer waiting times—achieving the two week target. The aim of this circular and the later NHS Cancer Plan was to improve access to specialist services, thus facilitating early diagnosis and treatment. The resultant fast track or two week wait rule stipulated that, by April 1999, all patients with suspected breast cancer should be seen by a specialist within two weeks of referral by a general practitioner, and, despite having little scientific foundation, this “guarantee” conveyed a genuine sense of commitment to improving cancer services in the UK.

This initial optimism, however, was short lived. From the beginning, the value and effectiveness of the two week wait rule have been questioned. The number of cancers detected in this group of patients has been low, and the poor predictive value of fast track referral guidelines together with poor adherence in primary care has flooded one stop clinics with large numbers of inappropriate referrals. As a result, waiting times for those patients deemed non-urgent by the general practitioner have significantly increased, prompting considerable criticism because up to a third of cancers are ultimately diagnosed from this group. No survival benefit has been shown, and several authors have called for a re-evaluation of the system.

METHODS

The Frenchay Breast Care Centre serves a population of 500 000 in Bristol and northeast Somerset and is one of two centres providing services for the Avon breast screening programme. Each year, we see over 4000 new patients and close to 400 new cases of cancer are diagnosed. The centre is staffed by two consultant surgeons, one associate specialist breast physician, one
Fixed, hard, or enlarging lump
Discrete lump persisting after period/menopause
Spontaneous unilateral bloody discharge from nipple
Skin distortion, tethering, discoulouration, nodule, or ulceration
New lump or suspicious features in patient with previous diagnosis of breast cancer
Female aged >30 years with:
Discrete lump persisting after period/menopause
Fixed, hard, or enlarging lump
Male aged >50 with:
A unilateral firm subareolar mass with or without nipple distortion or associated skin changes

Fig 1 Trends in referral patterns from primary care to breast clinic, 1999-2005

Fig 2 Cancers diagnosed in patients referred from primary care, 1999-2005. Overall number of cancers referred has remained constant. The number of cancers diagnosed from the two week wait group has decreased, increasing by an apparent 42% (n=739) from 1751 in 1999 to 2493 in 2005, an estimated increase of 5.8% a year (5.0% to 6.7%, P=0.001). By contrast, the number of routine referrals has declined over the same period by an estimated 4.3% a year (3.3% to 5.2%, P<0.001), giving an apparent reduction of 24% (n=417) from 1999 to 2005.

Despite the changes in referral patterns, the total number of cancers diagnosed in those referred from primary care has remained fairly constant over the seven years, with a mean of 263 (SD 18) new cancers diagnosed annually from this group (fig 2). Initially, in 1999, most of these cancers presented in the two week wait group (n=224, 84% of all cancers referred by general practitioner, 12.8% of all urgent/two week wait referrals) with only a small number (n=43, 16% of all cancers referred by general practitioners, 2.5% of all routine referrals) referred as routine. With time, however, despite the increasing numbers of urgent two week wait referrals, the actual number of cancers diagnosed in this group has fallen. In 2005, only 191 out of 261 cancers (73% of all cancers referred by general practitioners, 7.7% of all urgent referrals) were referred as two week waits while the number of cancers diagnosed in the routine group increased over the same period. The chances of being diagnosed with cancer in the two week wait group have decreased each year with an odds ratio of 0.91 (0.89 to 0.94), meaning patients in this group are 0.91 times as likely to be diagnosed with cancer in each subsequent year, which is highly significant (P<0.001). In 2005, 70 out of 261 cancers (27% of all cancers referred via the general practitioner, 5.3% of all routine referrals) were referred as non-urgent. This constitutes an increase in the chances of being diagnosed with cancer in the routine group with an odds ratio of 1.21 (1.14 to 1.28); thus...
patients are 1.21 times more likely to be diagnosed with cancer in the routine group in each subsequent year, which is, again, a highly significant change (P<0.001). These trends are summarised in figure 3 and the table.

Despite increasing numbers of referrals, waiting times in the two week wait group have always been maintained well within the target range, but, as predicted, this increasing demand on services has affected non-urgent patients and the waiting times for routine referrals have increased. The decrease in waiting times from 2000 to 2002 seen in figure 4 reflects an increase in clinic capacity created by the introduction of a new follow-up policy. After 2003, however, waiting times have steadily increased, reflecting the increasing numbers of patients referred under the two week wait. The current waiting time for a routine referral is 30 days.

We also analysed the demographics of the population served by the centre and the general practitioners referring to breast clinics from 1999 to 2005. Over this time, the population of general practitioners referring to the clinic did not change significantly, nor did the demographics of the population served by the hospital.

**DISCUSSION**

The two week wait rule was supposed to improve access to specialist services for all patients with suspected breast cancer and to facilitate early diagnosis and treatment. This policy has failed to achieve its goal. Since the introduction of the rule, while the number of patients referred under the urgent or two week wait rule has steadily increased by about 5.8% a year from 1751 in 1999 to 2490 in 2005, the percentage of these patients ultimately diagnosed with cancer has significantly decreased from 12.8% in 1999 to 7.7% in 2005. More worryingly, however, despite a significant decrease in number of routine referrals (1748 in 1999 to 1331 in 2005), the proportion of cancers diagnosed in this group has significantly increased (2.5% in 1999 to 5.3% in 2005) over the same period. These patients are also potentially being disadvantaged by longer clinic waits and delays in diagnosis as waiting times for routine referrals have increased in the face of increasing service demands from the dramatically increased number of patients referred under the two week wait rule, over 90% of whom have benign disease.

**Strengths and weaknesses**

We evaluated a large cohort of patients over a prolonged period and assessed the resultant trends. We used robust diagnostic and outcome data recorded from forms subsequently used to generate letters to primary care on almost 25 000 referrals over the seven years. Our results are therefore an accurate reflection of the impact of the policy on referrals and diagnoses of cancer in our centre. Though we evaluated referrals to a single centre only, because of the size of the study population and the workload of the clinic we consider that these findings could be extrapolated to other centres and probably reflect the referral patterns and rates of cancer diagnosis seen by other specialist breast units nationwide.

**Comparison with other studies**

Many studies have questioned the validity of the two week wait rule, particularly with respect to the low number of cancers detected in this group, and have discussed the unacceptability of what is effectively a two tier system, whereby so called “non-urgent referrals” have to wait longer to see a specialist. Concerns are justified given the fact that a large proportion of cancers detected are in patients referred by this route. In our study, more than one in four (27%) patients ultimately diagnosed with cancer in 2005 was referred non-urgently, which is consistent with earlier findings of between 20% and 36%. Many of these studies, however, were conducted soon after the introduction of the policy and offer no information regarding the long term impact of the two week wait rule or how this has changed with time. With the exception of a study of 15 breast units conducted by Sauven, which evaluated over 12 000 referrals, many of these early studies were also small. Our study is based on robust
The two week wait rule for patients with suspected breast cancer was introduced in 1999 to improve access by improving access to specialist services and facilitating prompt diagnosis and treatment. Its effectiveness has been questioned because of the low number of cancers detected in the two week referral group and poor prognostic value of the referral guidelines. Over a seven year period, the number of two week referrals has dramatically increased, but more cancers are now detected in this group. The two week wait for patients with suspected breast cancer was introduced in 1999 to improve outcomes by improving access to specialist services and facilitating prompt diagnosis and treatment. Its effectiveness has been questioned because of the low number of cancers detected in the two week referral group and poor prognostic value of the referral guidelines. Prospective data collected from 25,000 referrals over seven years and assesses the long term impact of the two week wait rule policy on numbers of referrals and cancer diagnoses in a specialist setting. It extends previous findings and shows several worrying trends, which add further weight to the debate over the two week wait rule.

Why is the two week wait rule failing?

In 2005, only 7.7% of all two week wait referrals were ultimately diagnosed with cancer compared with 12.8% of urgent referrals when the two week wait was first introduced. This is compared with the alarming increase in cancers diagnosed from the “routine” population, from 2.5% (n=43) in 1999 to 5.3% (n=70) in 2005. These data support other studies in suggesting that the diagnostic accuracy of general practitioners has decreased since the introduction of the two week wait. It has been suggested that general practitioners might not suspect cancer in many patients presenting to them with malignancy. It is more likely, however, that this apparent decrease in “diagnostic accuracy” is the result of the poor predictive value of the two week referral criteria rather than a decline in general practitioners’ diagnostic skills. The guidelines are less discerning than traditional clinical judgment and general practitioners’ skills are being undermined by the need to adhere to the two week wait guidelines. General practitioners themselves have expressed concerns about the system and clinical uncertainty, often over-referring as a result of media pressure and patients’ expectations. Indeed, a recent study showed identical presenting symptoms in patients diagnosed with breast cancer regardless of their route of referral. Waiting times for routine referrals have also increased as clinic capacity has been diverted to meet increasing demands from the two week wait population. The current waiting time for a routine appointment is 30 days, but in some centres may be significantly longer. This has considerable psychological impact for any patient, regardless of their diagnosis, but for the one in four patients with cancer in this group, the additional wait constitutes yet another unacceptable delay for definitive diagnosis and treatment. The system is failing patients and a change is urgently needed.

Contributors: SP performed the literature search, collected and analysed the data, and wrote the paper. SG, MS, and AKS were involved in data collection and writing. FB and GC were involved in data collation and analysis. Helen Cooke analysed the demographics of the hospital catchment area to ensure this has remained stable. RG performed the statistical analysis. SG was responsible for the design and conception of the study, assisted in writing, and is guarantor.

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Competing interests: None declared.

Ethical approval: Not required.

8 Sauven P. Impact of the “2 week wait” on referrals to breast units in the UK. Breast 2002;11:262-4.
13 Sauven P. Specialists, not GPs may be best qualified to assess urgency. BMJ 2001;323:864-5.

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Cost effectiveness of home based population screening for *Chlamydia trachomatis* in the UK: economic evaluation of chlamydia screening studies (ClaSS) project

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**ABSTRACT**

**Objective** To investigate the cost effectiveness of screening for *Chlamydia trachomatis* compared with a policy of no organised screening in the United Kingdom.  
**Design** Economic evaluation using a transmission dynamic mathematical model.  
**Setting** Central and southwest England.  
**Participants** Hypothetical population of 50 000 men and women, in which all those aged 16-24 years were invited to be screened each year.  
**Main outcome measures** Cost effectiveness based on major outcomes averted, defined as pelvic inflammatory disease, ectopic pregnancy, infertility, or neonatal complications.  
**Results** The incremental cost per major outcome averted for a programme of screening women only (assuming eight years of screening) was £22 300 (£33 000; $45 000) compared with no organised screening. For a programme screening both men and women, the incremental cost effectiveness ratio was approximately £28 900. Pelvic inflammatory disease leading to hospital admission was the most frequently averted major outcome. The model was highly sensitive to the incidence of major outcomes and to uptake of screening. When both were increased the cost effectiveness ratio fell to £6200 per major outcome averted for screening women only.  
**Conclusions** Proactive register based screening for chlamydia is not cost effective if the uptake of screening and incidence of complications are based on contemporary empirical studies, which show lower rates than commonly assumed. These data are relevant to discussions about the cost effectiveness of the opportunistic model of chlamydia screening being introduced in England.

**INTRODUCTION**  
*Chlamydia trachomatis* is the most commonly reported sexually transmissible infection in developed countries. The asymptomatic nature of the disease means that treatment is often delayed, leading to an increased risk of complications and transmission to partners. Complications in women include pelvic inflammatory disease, ectopic pregnancy, and infertility, along with neonatal complications in their children.1

In April 2003 the national chlamydia screening programme began its roll-out across England.2 No organised screening existed before this. The programme is managed nationally by the Health Protection Agency, but the way in which screening is delivered is decided locally and run from a chlamydia screening office. The main approach is opportunistic, but in some areas general practice registers are being used to send proactive invitations to potentially eligible people or to remind them to be re-screened.

Most published economic evaluations have suggested that screening for chlamydia is cost effective.3 The validity of this conclusion has been questioned by a systematic review showing that all but two of the evaluations used static decision analytic models.4,5 These models do not incorporate the dynamic effects of transmission of infectious diseases and can produce misleading results. Whether opportunistic screening approaches can control transmission of *C trachomatis* in the long term is also debated.6 An alternative approach is to use population registers to proactively invite young adults to be screened.1,7 This is the only screening approach that has been shown in randomised trials to reduce the incidence of pelvic inflammatory disease.8

Here we report the results of an economic evaluation comparing proactive register based screening with a policy of no organised screening. The evaluation was a cost effectiveness analysis, carried out from the perspective of the National Health Service, based on “major outcome averted,” which we defined as the occurrence of at least one episode of pelvic inflammatory disease leading to hospital admission, ectopic pregnancy, infertility, or neonatal complications due to chlamydia. We used a modelling approach, as opposed to direct estimation, because of the time lag between implementation and the realisation of any future benefits of chlamydia screening. We chose a transmission dynamic model, which is appropriate...
for evaluating the impact of screening for an infectious disease.19

The chlamydia screening studies (ClasS) project, in the United Kingdom, collected empirical data on the coverage and uptake of screening, the population prevalence of chlamydia infection,2 the effectiveness of partner notification,10 the performance characteristics of different laboratory tests, and the costs of screening.11 Screening was offered proactively to women and men identified from patient registers of 27 general practices in the Bristol and Birmingham areas. Participants were invited to collect vulvo-vaginal specimens, urine specimens, or both at home and to send these in prepaid envelopes to a local laboratory for testing. People with positive results received these at their general practice and those with negative results were informed by mail. Notification of partners took place at the general practice or at a local genitourinary medicine clinic (www.chlamydia.ac.uk).11

METHODS

We developed a new transmission dynamic simulation model based on a framework created by Kretzschmar.12 The model, programmed in Borland Delphi (version 4, Borland International, Scotts Valley, CA, USA), used discrete event simulation. The modelling methods are described elsewhere,1 including details of the calibration process in which the model data were adjusted to fit the observed prevalence by age and sexual behaviour. The population was simulated over time, with individual characteristics changing on a daily basis. The initial population was 50,000 virtual people aged between 12 and 62 years with ages drawn from a uniform distribution. As the model runs, people die in line with standard UK life tables and new people at the minimum age are added. During the running of the model, partnerships were formed and dissolved. The model needed a warm-up period to reach a steady state. We introduced screening into the model after the warm-up period. We ran the model 40 times against the scenario of no organised screening for a total of 15,000 (simulated) days each time. Each run was based on a different set of randomly generated numbers and took approximately three hours of processor time. At any time a person’s chlamydia status could be one of the following: none, latent, asymptomatic, having symptoms, or experiencing inflammation. In the absence of a population screening programme, we assumed that people could be treated either by presenting with symptoms or through background opportunistic testing.

We parameterised the model wherever possible by using empirical data collected in one of the four components of the chlamydia screening studies project outlined above.17 10 11 We used nationally representative data from studies such as the second national survey of sexual attitudes and lifestyles where necessary.13 We based incidence rates of long term complications associated with chlamydia that necessitated admission to hospital on data from the Uppsala women’s cohort study,14 as no equivalent UK data were available. We

Table 1 | Inputs relating to transmission and progression of chlamydia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average probability of transmission, men to women per day</td>
<td>0.077</td>
</tr>
<tr>
<td>Average probability of transmission, women to men per day</td>
<td>0.061</td>
</tr>
<tr>
<td>Incubation period—men (days)</td>
<td>10</td>
</tr>
<tr>
<td>Incubation period—women (days)</td>
<td>12</td>
</tr>
<tr>
<td>Probability asymptomatic—women</td>
<td>0.7</td>
</tr>
<tr>
<td>Probability asymptomatic—men</td>
<td>0.25</td>
</tr>
<tr>
<td>Recovery rate per day—asymptomatic women</td>
<td>0.005</td>
</tr>
<tr>
<td>Recovery rate per day—women with symptoms</td>
<td>0.025</td>
</tr>
<tr>
<td>Recovery rate per day—asymptomatic men</td>
<td>0.005</td>
</tr>
<tr>
<td>Recovery rate per day—men with symptoms</td>
<td>0.03</td>
</tr>
<tr>
<td>Progression per day, chlamydia to epididymitis</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(Estimate per episode)</th>
<th>(Progression per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression of chlamydia to severe PID‡</td>
<td>0.036</td>
</tr>
<tr>
<td>Infertility§</td>
<td>NA 0.0005</td>
</tr>
<tr>
<td>Ectopic pregnancy§</td>
<td>NA 0.008</td>
</tr>
<tr>
<td>Neonatal complications</td>
<td>0.45 0.013</td>
</tr>
</tbody>
</table>

NA Not applicable; PID pelvic inflammatory disease.
*Drawn from Kretzschmar et al 2001.† Based on partnership specific rate of sexual contact multiplied by transmission per contact based on Kretzschmar et al 2001.‡ Probability of transmission not related to duration of partnership.
‡Model input calibrated to incidence of PID estimated from Uppsala women’s cohort study.14 Estimated progression per day of chlamydia to PID achieved through process of calibration in dynamic model. Comparable figure to probability estimates typically presented in literature,15 which are in terms of probability of PID per episode of infection with chlamydia, estimated by multiplying daily rate found in calibration process by duration of infection, estimated in dynamic model to be 200 days.12 Thus 0.00018×200 days×0.036, which is probability of developing PID per episode of infection with Chlamydia.
§Ectopic pregnancy and infertility are not considered sequelae of PID but are based on tubal damage; risk of these outcomes increases with repeated reinfection. Different assumptions about PID in the model would therefore not affect other sequelae. Dynamic model allows risk of ectopic pregnancy and infertility to depend on past chlamydia, so comparable figures to those typically presented in published studies cannot be given.
identified additional data on the probabilities of long term sequelae in our review of economic evaluations, and we used these in the sensitivity analyses.

We based the main inputs relating to transmission and progression of chlamydia on those in the original models (table 1). We incorporated the probability estimates for pelvic inflammatory disease, ectopic pregnancy, and infertility into the model dynamically and independently. By considering each complication separately, we could examine uncertainty about rates of progression to severe and mild pelvic inflammatory disease, independently from progression rates to ectopic pregnancy and infertility. We used empirical data from the chlamydia screening studies project and from other sources to provide likely values for the number of partners, the frequency of changes of partner, and changes in these parameters by age (table 2). The exact values used in the model were determined as part of the calibration process. This means that we did not directly enter critical parameters such as population prevalence of chlamydia by age but made adjustments until the model reproduced the observed prevalence pattern by age and also had as close a fit as possible to the sexual behaviour parameters. Table 2 shows the comparison between the observed and calibrated data.

We prospectively collected primary data on costs and resource use, including the private costs to patients of participating in the screening programme. We used the costs of running the chlamydia screening studies project, including laboratory staff and tests, treatment, and partner notification, as a proxy for NHS costs of running a population screening programme. We converted all costs to 2005 prices (£ 1) by using the combined hospital and community index. We applied the recommended discount rate of 3.5% to costs and outcomes in the base case.

**Analysis**

In the base case analysis we compared proactive population screening with no organised screening but assumed that some background chlamydia testing would occur. We assumed that screening was offered annually for people aged 16-24 years. The screening test used was Cobas Amplicor CT (Roche Diagnostics, Basel) for both population screening and background screening. We assumed that notification of partners took place at the general practice surgery.

We based the evaluation on three comparisons: screening women only versus no organised screening; screening men and women versus no organised screening; and screening men and women versus screening women only. No robust information exists for quality adjusted life years (QALYs) relevant to the sequelae associated with chlamydia. The only published source of estimates for these QALY weights was based on expert opinion rather than empirical research. We therefore present our results as incremental cost effectiveness ratios in terms of the cost per additional major outcome averted by proactive population screening compared with a policy of no organised screening. The lower the incremental cost effectiveness ratio, the more cost effective the intervention. We carried out a one way sensitivity analysis, in which the perspective was widened to represent a societal perspective by including the private cost to individuals, response rate and screening interval were each varied, the discount rate was varied, the incidence of pelvic inflammatory disease was replaced by estimates from the literature, a scenario combining high uptake and high incidence of pelvic inflammatory disease was considered, and the costs of pelvic inflammatory disease and infertility were varied according to alternative assumptions about resource use.

Table 2 | Comparisons between model outputs and prevalence data from chlamydia screening studies (ClaSS) project

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Model results</th>
<th>ClaSS survey</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td><strong>Prevalence (%)</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19†</td>
<td>4.09</td>
<td>6.25</td>
</tr>
<tr>
<td>20-24</td>
<td>7.51</td>
<td>6.53</td>
</tr>
<tr>
<td>25-29</td>
<td>3.30</td>
<td>2.13</td>
</tr>
<tr>
<td>30-39</td>
<td>0.63</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Mean age difference with partner (years)</strong>‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-19</td>
<td>0.83</td>
<td>-2.41</td>
</tr>
<tr>
<td>20-24</td>
<td>1.65</td>
<td>-1.74</td>
</tr>
<tr>
<td><strong>Percentage reporting ever had sex</strong>§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-19</td>
<td>57.78</td>
<td>85.81</td>
</tr>
<tr>
<td>20-24</td>
<td>94.16</td>
<td>99.63</td>
</tr>
<tr>
<td><strong>Mean length of reported partnership (months)</strong>†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-19</td>
<td>7.80</td>
<td>10.98</td>
</tr>
<tr>
<td>20-24</td>
<td>16.82</td>
<td>17.81</td>
</tr>
</tbody>
</table>

**Sexual activity groups (%)¶ | | | | |
| 16-24: | | | | |
| Periphery | 71.71 | 72.64 | 72.6 | 79.2 |
| Adjacent | 16.03 | 21.36 | 17.4 | 15.1 |
| Core | 12.26 | 6.00 | 10.0 | 5.7 |
| 25-39: | | | | |
| Periphery | 84.21 | 89.20 | 80.5 | 91.0 |
| Adjacent | 13.23 | 8.05 | 12.7 | 6.6 |
| Core | 2.56 | 2.75 | 6.8 | 2.4 |

Values in parentheses are 95% confidence intervals.

*Data taken from table 64 of report by Low et al.
†Data taken from table 63 of report by Low et al.
‡Data based on case-control study in report by Low et al.
¶Laumann and Youm use activity groups defined by number of partners in previous 12 months, calling those with no or one partner the “periphery,” those with two or three partners the “adjacent,” and those with four or more partners the “core.”

**RESULTS**

Table 3 presents the base case parameters relating to the screening programme, based on the chlamydia screening studies project. Table 4 presents the unit costs, which show that the cost per screening invitation was estimated to be £14.65 (€21.69; $29.54). The baseline results suggest that, after the introduction of home based postal screening, the prevalence of chlamydia would drop to a new equilibrium value, particularly in the younger age groups in whom prevalence
was higher (see supplementary figure at www.chlamydia.ac.uk). Figure 1 presents the impact of screening on the individual outcomes over time. Pelvic inflammatory disease and neonatal complications were by far the most frequent outcomes.

Table 5 presents the results of screening under different scenarios up to eight years after the introduction of an annual invitation to be screened. We assumed that once introduced, the screening programme would continue indefinitely. In the base case, the incremental cost effectiveness ratio per major outcome averted for screening men and women, compared with no organised screening, after eight years, was approximately £28 900. It was less costly to screen women only but also less effective, and the incremental cost effectiveness ratio per major outcome averted was approximately £22 300.

Figure 2 shows the results for a range of time horizons from four to 20 years. The gradual fall in the incremental cost effectiveness ratios over time reflects the delay inherent in a screening programme in which a lag is seen before the full effect of the major outcomes averted as a result of screening becomes apparent.

In the sensitivity analysis when the response rate for men and women was equated to that found for women only, the incremental cost effectiveness ratio for screening men and women improved. The ratio improved further when the response rates were increased to 60% for women and 40% for men. Decreasing the screening interval to six months led to less favourable ratios. Two yearly screening gave a slightly lower incremental cost effectiveness ratio. Applying the discount rate for outcomes as recommended by the UK Treasury (1.5%) had a slightly more favourable effect on the incremental cost effectiveness ratio, as did not discounting outcomes at all. Including the person’s private costs of screening, to adopt a societal perspective, increased the incremental cost effectiveness ratio for screening men and women to £41 300 per major outcome averted compared with no screening.

The assumptions surrounding the probability of developing pelvic inflammatory disease had the biggest single impact on the incremental cost effectiveness ratio. The cost applied to pelvic inflammatory disease in the base case was that for an episode needing inpatient treatment. When we used an estimated probability for developing pelvic inflammatory disease of 25%,15 and assumed that all cases were admitted to hospital, the incremental cost effectiveness ratio fell by almost half to £10 200 per major outcome averted. When we assumed that the probability of developing pelvic inflammatory disease was 25%, and that 10% of cases were treated in hospital and 90% treated in primary care,20 the ratio increased to £12 000 per major outcome averted.

Table 3 | Parameters for population screening

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population prevalence of chlamydia (age 16-24)</td>
<td>0.062</td>
<td>ClaSS1 7</td>
</tr>
<tr>
<td>Compliance with screening (women)</td>
<td>0.39</td>
<td>ClaSS1 7</td>
</tr>
<tr>
<td>Compliance with screening (men)</td>
<td>0.29</td>
<td>ClaSS1 7</td>
</tr>
<tr>
<td>Waiting time for result of screening (days)</td>
<td>30</td>
<td>Assumption</td>
</tr>
<tr>
<td>Sensitivity of screening test (men)</td>
<td>0.999</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Specificity of screening test (men)</td>
<td>0.998</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Sensitivity of screening test (women)</td>
<td>0.973</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Specificity of screening test (women)</td>
<td>0.997</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Maximum time (days) since last sexual contact for partner to be considered recent</td>
<td>120</td>
<td>Assumption</td>
</tr>
<tr>
<td>Probability that partner will attend for treatment</td>
<td>0.45</td>
<td>ClaSS1 10</td>
</tr>
<tr>
<td>Delay (days) for partner to receive treatment</td>
<td>3</td>
<td>Assumption</td>
</tr>
</tbody>
</table>

ClaSS = chlamydia screening studies.
Screening tests are Cobas Amplicor CT test (Roche Diagnostics, Basel) on urine specimen for men and vulvo-vaginal swab for women.
Probability of partner attending for treatment applied independently to each partner.
outcome averted (table 5). The unit costs associated with other sequelae had to increase substantially to have a noticeable effect on the incremental cost effectiveness ratios. In the best case scenario for screening, which combined high uptake and high incidence of pelvic inflammatory disease, the incremental cost effectiveness ratio fell dramatically.

**DISCUSSION**

The results of this economic evaluation suggest that proactively offered register based screening for *C. trachomatis* with home collected specimens is an expensive intervention, on the basis of levels of uptake achieved in our cross sectional survey and assuming that the incidence of chlamydia associated complications is lower than previously believed. No pre-defined accepted threshold for incremental cost effectiveness ratios in terms of major outcomes averted exists for decision makers, but this result is unlikely to be considered cost effective. We draw this conclusion from the incremental cost effectiveness ratios based on major outcomes averted, in which pelvic inflammatory disease is the most commonly avoided outcome.

**Strengths and limitations**

The main strength of our study is that we collected cost data prospectively alongside a series of empirical epidemiological and laboratory studies and used these in an individual level dynamic mathematical model that gave the closest approximation to the real sexual behaviour of the population. The limitations of the study include the complexity of the model and the fact that the results are based on a single set of assumptions about mixing of partners and background rates of opportunistic screening and thus represent only one plausible scenario. This scenario is consistent with empirical data, however, as the model was able to recapture the prevalence by age group observed in the chlamydia screening studies project. The large number of replications and the size of the hypothetical population also support the robustness of the model and the results. As the clinical parameters are the results of calibration to the empirical data observed in the chlamydia screening studies project, we could not produce 95% confidence intervals. The large number of runs of the model needed to produce estimates of uncertainty would reflect only randomness in the model and not parameter uncertainty.

**Comparison with other studies**

The structure and dynamics of our model are comparable to those on which the evaluation of the English national chlamydia screening programme is based. The assumptions about duration of infection, transmission, and symptoms have also been used to evaluate both proactive and opportunistic screening approaches in other studies using the model developed by Kretzschmar. The sensitivities and specificities of the tests obtained from laboratory based studies in the chlamydia screening studies project were higher than those reported by a recent meta-analysis. This would improve the cost effectiveness of our screening intervention.

Our results contrast with the very low reported incremental cost effectiveness ratios per major outcome averted that have often been found in studies using static decision models. A fundamental difference is that our evaluation was based, appropriately, on a transmission dynamic model. The different results between static and dynamic models of chlamydia screening have been reported. Three evaluations based on a similar dynamic model to ours found opportunistic and proactive screening to be cost effective. Two principal factors contribute to the differences in these results.

Firstly, the incidences of long term outcomes used in our model were based on population based cohort data from Sweden, which observed a lower incidence of complications than the clinic based estimates used by other studies. The most recent economic

---

**Table 4 | Unit costs in model (2005)**

<table>
<thead>
<tr>
<th>Resource use data needed</th>
<th>Unit cost (£)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per screening invitation (including administration)</td>
<td>14.65</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Average private cost to people being screened</td>
<td>6.82</td>
<td>ClaSS1,11</td>
</tr>
<tr>
<td>Screening tests, men</td>
<td>7.72</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Screening tests, women</td>
<td>7.35</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Background screening tests, men</td>
<td>7.05</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Background screening tests, women</td>
<td>6.68</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Treatment of index case, including partner notification</td>
<td>25.12</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Treatment of partners</td>
<td>17.12</td>
<td>ClaSS1</td>
</tr>
<tr>
<td>Infertility*</td>
<td>453</td>
<td>NICE guidelines12</td>
</tr>
<tr>
<td>Ectopic pregnancy†</td>
<td>2456</td>
<td>HRG costs</td>
</tr>
<tr>
<td>Pelvic inflammatory disease§</td>
<td>3014</td>
<td>HRG costs</td>
</tr>
<tr>
<td>Epididymitis</td>
<td>836</td>
<td>Welte§15</td>
</tr>
<tr>
<td>Neonatal complications</td>
<td>749</td>
<td>HRG costs</td>
</tr>
</tbody>
</table>

ClaSS = chlamydia screening studies; HRG = health resource groups; NICE = National Institute for Health and Clinical Excellence.

* NICE baseline costs for one cycle converted to 2005 costs.
† NICE baseline costs converted to 2005 costs.
§ Weighted average of Welte et al 2000,15 converted to 2005 UK costs.
evaluation, which used an individual based dynamic model to examine the opportunistic screening used in the national chlamydia screening programme in England, showed that screening was not cost effective when the incidence of pelvic inflammatory disease was less than 10%. In the base case, we included only severe pelvic inflammatory disease leading to hospital admission, because this was the most costly. If the incidence of mild pelvic inflammatory disease treated in primary care was very high, screening would become more cost effective. When we increased the incidence of pelvic inflammatory disease in the model to that typically used in other studies, and apportioned the associated costs between severe and mild disease, the incremental cost effectiveness ratio was lower. However, even at the higher incidence of pelvic inflammatory disease and assuming all cases to be severe, the ratio of £10,200 per major outcome averted is unlikely to be low enough for population screening for chlamydia to be considered cost effective. These sensitivity analyses did not affect the estimated incidence of ectopic pregnancy and infertility, which were incorporated independently in the model.

Secondly, the screening uptake rate used by other studies is typically higher than we found in the chlamydia screening studies project. One recent study used a combined uptake rate in men and women of 48%. In the sensitivity analysis, we showed that a scenario that assumes 10% of cases are severe and cost £3014 each, other 90% of cases cost £30 each, assumed a similar uptake and a high incidence of pelvic inflammatory disease had a much more favourable incremental cost effectiveness ratio of £6,200 per major outcome averted. The combined effect of higher uptake and higher probability of sequelae has been shown to reduce the incremental cost effectiveness ratio considerably.

### Meanings of the study

The base case incremental cost effectiveness ratio suggests that screening women only, compared with no active screening, costs an additional £22,300 per major outcome averted. We were unable to present the incremental cost effectiveness ratios in terms of a cost per QALY, as the data available on quality of life associated with pelvic inflammatory disease and other sequelae were inadequate. UK decision makers suggest that programmes with an incremental cost effectiveness ratio of greater than £30,000 per QALY gained, for proactive screening to be considered cost effective the value for each case of pelvic inflammatory disease avoided would have to be more than 0.74 of a QALY. In other words, having pelvic inflammatory disease would have to be considered equivalent to being in a state equal to death for almost nine months. Adams et al presented their results in terms of both cost per major outcome averted and cost per QALY based on the only available estimated quality adjusted life year weights. If we had used these same weights, our base case incremental cost effectiveness ratio expressed in terms of the incremental cost per QALY is likely to have been considerably more than £0.5 million per QALY.

### Implications for research and policy

Our results are relevant to the national chlamydia screening programme. Our model could also be further refined to explore the importance of differential uptake of chlamydia screening and re-screening according to factors including socioeconomic deprivation and sexual behaviour. A future objective will be to provide a model that captures the most important human interactions influencing transmission and control of Chlamydia, while excluding unnecessary detail.

The programme costs of a proactive register based approach described in this study were similar to those estimated for opportunistic screening. Opportunistic screening programmes are also known to have problems with sustaining regular uptake over time, so the disappointing uptake of proactive screening might also apply to the future uptake of opportunistic screening. Evidence from the chlamydia screening studies project shows that a mixed model combining elements of opportunistic and systematic screening might achieve optimal coverage and uptake. Future research should focus on rigorous evaluation in randomised controlled trials of the relative effectiveness and cost effectiveness of alternative strategies to improve

### Table 5: Summary of incremental cost effectiveness ratios after eight years

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Incremental cost effectiveness ratios (£/MOA)</th>
<th>Women only v no screening</th>
<th>Men and women v no screening</th>
<th>Men and women v women only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case*, outcomes discounted at 3.5% (NICE)</td>
<td>22 300</td>
<td>28 900</td>
<td>41 300</td>
<td></td>
</tr>
<tr>
<td>Equal response rate 39%</td>
<td>22 300</td>
<td>25 200</td>
<td>28 900</td>
<td></td>
</tr>
<tr>
<td>Response 60% women, 40% men</td>
<td>18 200</td>
<td>22 400</td>
<td>29 300</td>
<td></td>
</tr>
<tr>
<td>Six monthly screening</td>
<td>29 800</td>
<td>34 200</td>
<td>40 400</td>
<td></td>
</tr>
<tr>
<td>Two yearly screening</td>
<td>19 600</td>
<td>27 100</td>
<td>44 000</td>
<td></td>
</tr>
<tr>
<td>Base case, outcomes discounted at 1.5% (UK Treasury)</td>
<td>20 600</td>
<td>26 600</td>
<td>37 900</td>
<td></td>
</tr>
<tr>
<td>Base case, outcomes not discounted</td>
<td>19 300</td>
<td>24 900</td>
<td>35 400</td>
<td></td>
</tr>
<tr>
<td>Incidence of PID=0.25, equivalent to Welte et al</td>
<td>10 200</td>
<td>12 200</td>
<td>15 200</td>
<td></td>
</tr>
<tr>
<td>PID 25%; response rate 60% women, 40% men</td>
<td>6 200</td>
<td>9 400</td>
<td>17 000</td>
<td></td>
</tr>
<tr>
<td>Including private patient costs of attending for screening†</td>
<td>31 800</td>
<td>41 300</td>
<td>59 300</td>
<td></td>
</tr>
<tr>
<td>Adjustment in unit costs applied to sequelae</td>
<td>23 700</td>
<td>33 600</td>
<td>43 600</td>
<td></td>
</tr>
<tr>
<td>PID £30 (based on outpatient visit and course of antibiotics)†</td>
<td>23 600</td>
<td>30 500</td>
<td>43 400</td>
<td></td>
</tr>
<tr>
<td>PID £30, infertility £3014 (based on intensive inpatient IVF treatment)†</td>
<td>22 200</td>
<td>28 800</td>
<td>41 100</td>
<td></td>
</tr>
<tr>
<td>Omit complication costs†</td>
<td>24 300</td>
<td>31 200</td>
<td>46 100</td>
<td></td>
</tr>
<tr>
<td>All complications £3014†</td>
<td>21 100</td>
<td>27 300</td>
<td>39 000</td>
<td></td>
</tr>
<tr>
<td>All complications £6028†</td>
<td>17 900</td>
<td>23 400</td>
<td>33 800</td>
<td></td>
</tr>
<tr>
<td>Incidence equivalent to Welte, PID cost average £328†</td>
<td>12 000</td>
<td>14 100</td>
<td>17 200</td>
<td></td>
</tr>
</tbody>
</table>

IVF=in vitro fertilisation; MOA= major outcome averted; NICE= National Institute for Health and Clinical Excellence; PID=pelvic Inflammatory disease.

All results presented from perspective of NHS, with exception of "Including private patient costs of attending for screening."

*Base case response rate=39% women, 29% men.
†All other parameters as base case.
‡Assumes 10% of cases are severe and cost £3014 each, other 90% of cases cost £30 each.
the uptake and regularity of chlamydia screening. More reliable data about the long term sequelae associated with chlamydia are also needed to reduce the uncertainty associated with this parameter in future modelling studies. Value for money of screening programmes crucially depends on the values attributed to the adverse outcomes averted by screening, and these should be the subject of explicit public debate. Our evaluation of proactive population chlamydia screening, using a dynamic model incorporating realistic estimates of partner notification, the uptake of screening, and the incidence of severe complications, has shown it to be an expensive intervention that probably does not represent good value for money.

Contributors: TER, JM, ME, and NL contributed to the design of the chlamydia screening studies (ClaSS) project and obtained funding. TER designed the economic evaluation for the study, was chair of the ClaSS Economics Working Group and prepared the manuscript as the lead writer. SR was principal economic researcher for the project and, with TER, was responsible for collating the primary data. PNB constructed and developed the transmission dynamic model and carried out the analysis using the model. SB advised on the economic evaluation. AJMc was the project manager. MJKe/Birmingham based aspects of ClaSS fieldwork. NJ was acting principal investigator and helped to revise the manuscript. ME was principal investigator of the ClaSS project. All authors were members ClaSS Economics Working Group. All authors commented on and approved the final manuscript. TR is the guarantor.

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Gallstones
Grant Sanders, Andrew N Kingsnorth

About 10-15% of the adult Western population will develop gallstones, with between 1% and 4% a year developing symptoms. From April 2005 to March 2006, 49,077 cholecystectomy procedures took place in England, a 10th of the number of procedures in the United States.

The management of gallstone disease is changing rapidly, with an increase in day case surgery and in cholecystectomy during the index admission for cholecystitis and with the advent of natural orifice transluminal endoscopic surgery.

This review focuses on the problems that gallstones cause and their optimal treatment based on current evidence.

Who gets gallstones?
Gallstones occur when there is an imbalance in the chemical constituents of bile that results in precipitation of one or more of the components. Why this occurs is unclear, although certain risk factors are known.

Gallstones are seen in all age groups but the incidence increases with age. The old adage “fat and fertile, female and forty” tells only part of the story. Oestrogen does cause more cholesterol to be excreted into bile, and obesity (body mass index >30) is a risk factor. However, genetics also plays a part, accounting for 25% of the phenotypic variance among twins, thereby adding a fifth “f” (family history) to the adage. Other risk factors include pregnancy, rapid weight loss (such as after obesity surgery), parenteral nutrition, loss of bile salts (terminal ileitis or after ileal resection), and diabetes via the metabolic syndrome.

What problems do gallstones cause?
Gallstones can cause various problems (fig 1), the most common being biliary colic (56%) (fig 2) and acute cholecystitis (36%) (fig 3), as shown in a study from the United States, which mirrors our experience in the United Kingdom.

Biliary colic/cholecystitis
Biliary colic and cholecystitis share a spectrum of symptoms, and no exact time course or definition exists to separate them. The table outlines the symptoms and signs.

Jaundice
If the bile duct becomes partially or completely obstructed, bilirubin, conjugated in the liver with glucoronate acid, cannot be excreted into the bowel and the levels increase in the bloodstream. The patient becomes jaundiced, and as a result of excretion of the water soluble conjugated bilirubin, the urine becomes dark. The stools are pale owing to an absence in the faeces of stercobilin, a breakdown product of bilirubin in the intestine. Obstruction leading to jaundice is caused most commonly by a stone migrating into the bile duct but can be due to compression of the common hepatic duct by a stone in the neck of the gall bladder or cystic duct (Mirizzi’s syndrome).

Ascending cholangitis
Ascending cholangitis results from infection in a partially or completely obstructed bile duct. Stasis leads to an increase in the resident bacterial flora. The risk is increased if there is potential for added infection to be introduced into the obstructed biliary system—for example, during endoscopic retrograde cholangiopancreatography. Charcot’s triad is diagnostic (fever—usually with rigors—jaundice, and right upper quadrant pain).

Pancreatitis
During the passage of stones from the gallbladder into the bowel, transitory obstruction of the biliopancreatic duct (the common channel) occurs in the region of the ampulla, which initiates premature activation of enzymes in the pancreas, leading to pancreatitis (gallstone migration theory). The resulting pain is classically epigastric, constant, radiating through to the
back, and relieved by bending forwards. Vomiting is often profuse.

Bouveret’s syndrome and gallstone ileus
Gallstones may fistulate directly into the duodenum from the gallbladder during a period of often silent inflammation. The stone can impact in the duodenum leading to duodenal obstruction (Bouveret’s syndrome). Alternatively, it can impact at the narrowest section of healthy small bowel, situated where the embryological vitello-intestinal duct once existed in the terminal ileum (a Meckel’s diverticulum is the embryological remnant). This leads to small bowel obstruction known as gallstone ileus—a misnomer, as the small bowel obstruction is mechanical and not an ileus. Gallstone ileus is often diagnosed intraoperatively, though supine abdominal radiography may show air in the biliary tree (as a result of the fistula) or indeed the stone.

Gallbladder cancer
Gallstones are a known risk factor for gallbladder cancer. However, this cancer is rare, accounting for 0.3% of patients with gallstone disease in a study from the United States. Furthermore, it is usually either advanced at presentation or discovered as an incidental finding during cholecystectomy.6

How are biliary colic and cholecystitis diagnosed?
The patient’s history is crucial in diagnosing biliary colic or cholecystitis. Examination will help to identify the presence of biliary inflammation and exclude the presence of masses or hepatomegaly, which can cause pain in the right upper quadrant. Liver function tests are a useful indicator of a possible stone in the bile duct. Ultrasonography is the key diagnostic test used to identify the presence of stones, biliary tract dilatation, and thickening of the wall of the gall bladder indicating chronic disease. However, although the accuracy of ultrasonography in detecting gallstones is quoted as 98% in textbooks7 we could find no studies showing this. Certainly the absence of stones on ultrasound scans does not exclude their existence, as very small stones or sludge can be missed. If clinically the diagnosis is highly likely, an interval ultrasound scan should be performed.

What if gallstones are found incidentally?
People with asymptomatic gallstones develop problems related to gallstones at a rate of 1%-4% a year.1 This means that for most of the population, prophylactic cholecystectomy is unnecessary as the balance of risks and benefits is in favour of “watch and wait.” However, a young patient will have a higher risk of developing problems, as there is more time in which to do so, and the balance may therefore favour treatment. In addition, small stones can be more dangerous than large ones. A well conducted case series study from the Netherlands involving 528 patients identified small stones as an independent risk factor for pancreatitis.8

In general, the decision to treat should be made on a case by case basis, taking into account the age of the patient, the ultrasound findings, and the presence of any symptoms, regardless of how vague these are.

Treatment
Non-surgical
Analgesia for acute attack of biliary colic or cholecystitis
In the acute, out of hospital setting, diclofenac and an opioid (morphine or pethidine) are very effective, used in combination or separately. Since the symptoms are
often associated with vomiting, a suppository or injection is recommended.

**Drug dissolution therapy**

Ursodeoxycholic acid has been shown to be useful in preventing gallstones. A prospective study examining the rate of formation of gallstones in 152 patients after obesity surgery (a known risk factor for developing gallstones) randomised patients to 500 mg of daily ursodeoxycholic acid or to placebo, for six months or until stones developed. The researchers found that gallstone formation was significantly less likely to occur with ursodeoxycholic acid than with placebo at 12 months (3% vs 22%) and at 24 months (8% vs 30%).9

However, ursodeoxycholic acid does not seem to be useful once stones have developed. A prospective, randomised, double blind, placebo controlled trial from the Netherlands in 177 highly symptomatic patients with gallstones scheduled for cholecystectomy found that ursodeoxycholic acid did not reduce biliary symptoms.10

**Percutaneous drainage**

Percutaneous cholecystostomy allows resolution of sepsis in patients at high surgical risk. A retrospective review of 55 patients treated by percutaneous trans-hepatic cholecystostomy found a successful biliary drainage rate of 98%; 95% of patients recovered well and left hospital.11

**Surgical**

**Laparoscopic versus open surgery**

A Cochrane review comparing laparoscopic with open cholecystectomy found no differences in mortality, complications, or operative time.3 However, laparoscopic cholecystectomy, when compared with classic open cholecystectomy, was associated with a significantly shorter hospital stay (difference, −3 days [95% confidence interval −3.9 days to −2.3 days]) and quicker convalescence (−22.5 days (−36.9 days to −8.1 days)). These results support the recommendation by surgeons for laparoscopic cholecystectomy rather than open cholecystectomy.

However, a Cochrane review comparing laparoscopic with small incision (<8 cm) cholecystectomy found no differences in mortality, complications, and postoperative recovery.12 In addition, small incision cholecystectomy had a significantly shorter operative time. The complication rate in the studies reviewed was high: 17% in the laparoscopic group versus 17.5% in the small incision group, if gallbladder perforation is excluded as a complication. These rates are higher than those in the Cochrane review comparing laparoscopic with open cholecystectomy (5.4% and 10.1% respectively).3

The conclusions of the Cochrane reviews are reinforced by more recent publications from Finland and Sweden.13 14

**Day case surgery**

A randomised clinical trial of day case versus “overnight stay” laparoscopic cholecystectomy from Sweden found no difference in complication rate or patients’ acceptance, though the day case procedures cost less.15 A feasibility study from the Royal Berkshire Hospital identified an acceptable complication rate for overnight stay surgery of 14.3% and readmission rate of 1.9% among 154 patients having day case surgery.

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**A Patient’s Story**

About two years ago, I started to experience bouts of abdominal pain, initially low grade but increasing to crescendos of severe pain lasting several hours. It was often associated with nausea but no vomiting. My symptoms initially occurred once every month or two, but more recently, every few weeks. My general practitioner organised an ultrasound scan, which showed that I had gallstones. I was referred to a specialist. However, while waiting to be seen in the clinic, I had two visits to the accident and emergency department and received morphine for pain control. After my second visit to the emergency department, I saw my general practitioner again, who did a blood test, only to find my liver tests were abnormal, and urgent admission to hospital was arranged. An ultrasound scan showed I now had a stone in my bile duct. I was operated on during that hospital stay, which included laparoscopic removal of my gall bladder and the bile duct stone. I had a drain left in when I went home, but I came back to the outpatient department two days later for the drain to be removed. I now feel well and am pain free; long may it last.

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**Fig 2** Laparoscopic photograph of gall bladder in patient with symptoms of biliary colic

**Fig 3** Laparoscopic photograph of gall bladder in patient with symptoms of cholecystitis
Cholecystectomy should be performed on the index admission for biliary symptoms. Day case laparoscopic cholecystectomy should be the default for elective procedures. Preventing their formation in high risk groups.

People with asymptomatic gallstones develop gallstone related problems at a rate of 1%-4% a year, with small stones being more dangerous than large as they can cause pancreatitis. Ursoodeoxycholic acid does not reduce symptoms from gallstones but may be useful in preventing their formation in high risk groups. Percutaneous cholecystostomy is a good treatment for patients at high surgical risk. Day case laparoscopic cholecystectomy should be the default for elective procedures. Cholecystectomy should be performed on the index admission for biliary symptoms.

SUMMARY POINTS

Of the adult Western population, 10-15% will develop gallstones, with between 1% and 4% a year developing symptoms. The incidence of gallstones increases with age, with family history being an important risk factor. People with asymptomatic gallstones develop gallstone related problems at a rate of 1%-4% a year, with small stones being more dangerous than large as they can cause pancreatitis. Ursoodeoxycholic acid does not reduce symptoms from gallstones but may be useful in preventing their formation in high risk groups. Percutaneous cholecystostomy is a good treatment for patients at high surgical risk. Day case laparoscopic cholecystectomy should be the default for elective procedures. Cholecystectomy should be performed on the index admission for biliary symptoms. Intervals were wide. Further evidence for early cholecystectomy comes from a prospective case series from Taunton.18 This study showed a 28.5% readmission rate with gallstone related complications for people on the waiting list for surgery after emergency admission with acute cholecystitis. The authors concluded that all patients presenting as an emergency with symptomatic gallstones and are admitted should be offered cholecystectomy, a point echoed by the NHS Institute for Innovation and Improvement.2

Although the conversion rate (from laparoscopic to open surgery) was high in the randomised studies included in the Cochrane review, an audit before and after implementation of a specialist led service for urgent cholecystectomy in Portsmouth illustrated a fall in the conversion rate from 32% to 12%.19 The same study showed a reduction in the rate of unplanned readmissions, from 19% to 3.6%.

Postoperative complications

Cholecystectomy is not without risk. Complications include haematoma in the gall bladder bed, infection (usually of the haematoma), bile leak, inadvertent injury (to the bowel or bile duct), and retained stone in the bile duct. The most serious is bile duct injury, occurring at a rate of 0.2% in both laparoscopic and open surgery.2 Further surgery may be needed to repair the bile duct or to join the bile duct to the bowel by anastomosis. In addition, bile duct injury is often further complicated by concomitant hepatic vascular injury.

Possibilities for the future

A new era is developing in the treatment of gastrointestinal conditions. It seems feasible that major intra-peritoneal surgery may be performed without skin incisions, with access to the peritoneal cavity via natural orifices, the mouth (via the stomach), the rectum, and the vagina, using flexible endoscopes. This experimental technique is known as natural orifice transluminal endoscopic surgery. Although no research has yet been published on resections in humans, the first report of cholecystectomy in a porcine model was published in 2005.20 The principle is gathering momentum, and developments are likely to be rapid, with working groups set up to move the concept forward.21

Contributors: Both authors performed the literature search. GS wrote the article and ANK edited it. Both authors are guarantors.

Competing interests: None declared.

Provenance and peer review: Commissioned and externally peer reviewed.

Soy phytoestrogen genistein increases bone mineral density in postmenopausal women

**Research question**
Can genistein reduce bone loss in osteopenic postmenopausal women?

**Answer**
Yes, but it's still unclear whether genistein helps prevent fractures.

**Why did the authors do the study?**
Small, brief trials suggest that the phytoestrogen genistein, found in many soy products, can help prevent bone loss after the menopause. These authors wanted to extend and confirm these preliminary findings.

**What did they do?**
389 Italian women took part in a double blind, randomised, controlled trial. All were postmenopausal and had osteopenia (with a bone mineral density at the femoral neck of <0.795 g/cm²) but were otherwise well.

After randomisation, 198 women took a pill containing 54 mg genistein and 198 women took a placebo pill. They were asked to take the pill for 2 years. They were followed-up annually.

**What did they find?**
Bone mineral density increased among the women taking genistein and decreased among those taking placebo, leading to a difference at two years of 0.10 g/cm² (95% CI 0.08 to 0.12, P < 0.001) at the lumbar spine and 0.062 g/cm² (0.049 to 0.073, P < 0.001) at the femoral neck.

Women taking genistein reported significantly fewer hot flushes than those on placebo. But about one in five women in this trial stopped taking the treatment early, primarily because of pyridinoline and deoxypyridinoline (markers of bone resorption). It had no measurable effect on endometrial thickness.

**What does it mean?**
Genistein, an isoflavone phytoestrogen, seems to have positive effects on bone mineral density and bone turnover in osteopenic women who are at least one year past the menopause. But about one in five women in this trial stopped their treatment early, so gastrointestinal side effects may be a problem.

Although these data look encouraging, the authors looked only at surrogate measures of effectiveness and safety. Bigger trials are now required with the power to find out if genistein can reduce the risk of osteoporotic fractures without increasing women’s risk of uterine cancer.

**BMJ UPDATES**
Soy phytoestrogen genistein increases bone mineral density in postmenopausal women


Diagnosing and managing hypothyroidism during pregnancy can be problematic. The scenario box on this page illustrates some typical problems encountered and raises pertinent questions concerning good medical practice. In this article, we define autoimmune thyroiditis as the presence of measurable circulating antithyroid autoantibodies (to thyroglobulin or thyroperoxidase), irrespective of abnormalities of thyroid function. Subclinical hypothyroidism is defined as an increase in serum thyroid stimulating hormone (TSH; usually >10 mU/l) associated with normal concentrations of serum thyroxine and triiodothyronine. Overt hypothyroidism is defined as an increase in serum TSH (usually >10 mU/l) associated with a decreased concentration of thyroxine, as a result of negative feedback; at that stage, most patients have symptoms and benefit from treatment.

**How common is hypothyroidism in pregnant women?**

The prevalence of autoimmune thyroiditis in women of childbearing age in the developed world is 15%; that of overt hypothyroidism is estimated at 0.3-0.5% and subclinical hypothyroidism at 2-3%. In a prospective population study of 9471 pregnant women, autoimmune thyroiditis was present in 5.5% of the women with subclinical hypothyroidism (serum TSH 6-10 mU/l) and in more than 80% of women with overt hypothyroidism (serum TSH 11-200 m U/l). Thus, the main cause of hypothyroidism during pregnancy is chronic autoimmune thyroiditis, at least when iodine intake is adequate. On a worldwide basis, however, the most common cause of thyroid insufficiency is iodine deficiency, which affects more than 1.2 billion people.

**How does pregnancy affect hypothyroidism?**

Pregnant women with hypothyroidism have a reduced functional reserve in the thyroid, so hypothyroidism often develops or worsens as gestation progresses.

**How does hypothyroidism affect pregnancy and pregnancy outcome?**

Women with hypothyroidism can still conceive, although infertility rates are higher and failure of in vitro fertilisation is more likely. Pregnant women with hypothyroidism have a greater risk of early and late obstetric complications such as miscarriage, anaemia, gestational hypertension, placental abruption, premature delivery, postpartum haemorrhage, and admission of their baby to neonatal intensive care (particularly for respiratory distress syndromes). Obstetric complications are associated with both

Table 1 | Dose of serum thyroid stimulating hormone (TSH) and thyroxine in the patient during pregnancy (see Scenario box)

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Weeks of gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mU/l)</td>
<td>14</td>
</tr>
<tr>
<td>Thyroxine (µg/day)</td>
<td>150</td>
</tr>
</tbody>
</table>

**SCENARIO**

Mrs SC, aged 29 years, has a family history of goitre. Nine months after a first delivery in 1999, she had positive antithyroid peroxidase antibodies and a serum thyroid stimulating hormone (TSH) concentration of 3.1 mU/l. No treatment was given, but she was told that she should have her thyroid function monitored, advice that she did not follow. Two years later, when she was six weeks pregnant, she was diagnosed with hypothyroidism of autoimmune origin: serum TSH 150 mU/l, free thyroxine 2.6 pmol/l (normal 10-26), antithyroid peroxidase antibodies 990 U/ml (normal <60). She presented with severe hypothyroidism during the first weeks of pregnancy, although we cannot tell whether it was present before conception (though this is likely) or developed after the onset of pregnancy. Treatment with thyroxine was started immediately, and thyroid function returned to normal and remained so throughout the remainder of her pregnancy (table 1). Delivery was full term and obstetrically uneventful. After parturition, the mother’s thyroid function was equilibrated with 75 µg thyroxine/day. Six months postpartum, TSH rose transiently to 10.4 mU/l, as a result of postpartum thyroiditis, and thyroxine was increased to 100 µg/day.
overt and subclinical hypothyroidism. Adequate treatment with thyroxine, with subsequent restoration of normal thyroid function, greatly reduces the frequency of such complications. In a recent prospective randomised intervention trial, miscarriage and preterm delivery rates were much lower in women with autoimmune thyroiditis given thyroxine (started at five to 10 weeks) throughout gestation to keep them euthyroid than in controls. The miscarriage rate was reduced by 75% and preterm delivery by 69% in women given thyroxine.

The detrimental effects of maternal thyroid deficiency on fetal development are thought to depend on the severity and early onset of a reduced availability of maternal thyroid hormone. Severe impairment of fetal neurodevelopment is also thought to require prolonged hypothyroxinaemia. Recent studies indicate that undiagnosed (and hence untreated) hypothyroidism during the first half of pregnancy is associated with a risk of a poorer neurodevelopmental outcome in the progeny. In iodine deficiency, maternal and fetal thyroid glands are affected early on, and maternal hypothyroidism is present during early gestation. Severe iodine deficiency leads to endemic cretinism, as a result of irreversible damage to the fetal brain. Even in less severe iodine deficiency, a meta-analysis showed an overall reduction in cognitive functions of 13.5 IQ points. A recent study showed that when maternal hypothyroidism is due to chronic autoimmune thyroiditis, the offspring of untreated (or suboptimally treated) women are at risk for clinically relevant cognitive deficits. Even isolated hypothyroxinaemia during early gestation (defined as serum free thyroxine near the lower limit of normality, normal TSH, and no detectable thyroid antibodies) may be associated with a lower psychodevelopmental index in the offspring. None the less, free thyroxine values spontaneously returned to normal during later gestation in most of these women and their fetuses developed normally. It is unclear whether women with isolated hypothyroxinaemia need treatment, as no evidence based information is available to prove that such patients benefit from thyroxine administration. The results of a large scale randomised trial presently under way will be important for developing screening and management guidelines.

What are the unresolved questions?

We do not know how low maternal serum free thyroxine values need to be before normal fetal development is affected. The relative roles of early versus late gestational hypothyroidism are also unclear. Moreover, maternal hypothyroidism may not be diagnosed (and therefore not treated) during pregnancy and may even remain undiagnosed for several months after delivery. It is unclear how detrimental this may be for the development of the neonate. The consequences of maternal hypothyroidism on the fetus or neonate are probably the result of several factors acting in combination, such as decreased availability of maternal thyroid hormones at crucial times in fetal brain development, obstetric events associated with maternal hypothyroidism, and possibly prolonged undisclosed maternal hypothyroidism during pregnancy.

Answers to these questions are needed to help us improve guidance for clinical management, such as how and when screening programmes should be established during pregnancy. In the meantime, we have to rely on individual clinical judgment to decide how and when to diagnose and treat women at risk of hypothyroidism during pregnancy.

Another ethically important—but debatable—question is whether clinicians should recommend terminating pregnancy when severe hypothyroidism is diagnosed late in gestation. Present consensus among obstetric care providers and endocrinologists is against recommending abortion, but despite the administration of thyroxine future parents cannot be fully reassured about potential brain damage as a result of longstanding and severe intrauterine undiagnosed hypothyroidism.

How should we manage hypothyroidism during pregnancy?

An international ad hoc committee under the auspices of the American Endocrine Society has recently produced consensus guidelines for managing thyroid disease during pregnancy. The guidelines have not officially been published, but they recommend adjusting the dosage of thyroxine to reach a serum TSH value not higher than 2.5 mU/L in women with hypothyroidism who intend to conceive and are taking thyroxine. This recommendation could be extended to euthyroid women with autoimmune thyroiditis, although the proof of a clear benefit in such women is lacking. It is regrettable that thyroid function was not closely monitored in the case presented here (because of the patient’s non-compliance; see scenario box). Whether the patient should have received thyroxine at the time of initial investigation is debatable. Some authors have recommended that the reference range for serum TSH should be narrowed from 0.40-4.0 mU/L to 0.40-2.5 mU/L to make it more representative of the normal physiological range.

Because of the potentially serious adverse effects of maternal hypothyroidism on the fetus, targeted case finding is recommended at the first prenatal visit. For women taking thyroxine before conception, the dosage should normally be incremented as early as four to eight weeks’ gestation, usually by 30-50%. It has been suggested that women who are already taking thyroxine should increase the dosage by about 30% as soon as they know they are

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Guide to managing hypothyroidism during pregnancy</th>
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</thead>
<tbody>
<tr>
<td>Serum TSH (mU/L)</td>
<td>Increase in thyroxine (µg/day)</td>
</tr>
<tr>
<td>5-10</td>
<td>25-50</td>
</tr>
<tr>
<td>10-20</td>
<td>50-75</td>
</tr>
<tr>
<td>20</td>
<td>100</td>
</tr>
</tbody>
</table>

TSH, thyroid stimulating hormone.
pregnant (before seeking evaluation) to avoid early maternal hypothyroidism. The size of this increase depends on the cause of hypothyroidism—women with no residual thyroid tissue need a greater and more rapid increment than those with Hashimoto’s thyroiditis. A simple rule of thumb has been established to guide the clinician (table 2).\(^6\)

When overt hypothyroidism is diagnosed during pregnancy, thyroid function tests should be normalised as rapidly as possible. To achieve this aim, and to rapidly normalise the extrathyroidal thyroxine pool, some authors recommend using two to three times the estimated final daily dose. However, presently we have no proof of a real advantage in doing this. Thyroid function tests should be performed again four to five weeks after the onset of treatment and every six weeks thereafter, until after mid gestation at least. The dose of thyroxine should be titrated to reach and maintain serum TSH concentrations no more than 2.5 mU/l in the first trimester (<3 mU/l in the second and third trimester).

In principle, the administration of thyroxine should be straightforward. However, this is not the case in clinical practice (table 3).\(^6\) A retrospective study of 167 pregnant women with hypothyroidism showed that despite increasing the mean dosage of thyroxine (from 100 to 150 µg/day between the first and third trimester) and adequate median serum TSH values, thyroxine dosage varied greatly (25-325 µg/day). Also, some women had raised serum TSH (almost 100 mU/l), indicating that increases in thyroxine dose were insufficient or came too late.

### Postpartum period

After parturition, the dosage of thyroxine should be decreased in most women, over a period of two to four weeks.\(^6\) Women with features of thyroid autoimmunity are at risk of developing postpartum thyroiditis, which may justify differences in thyroxine requirements before and after pregnancy.\(^6\)

### METHODS

This review was based on personal reference archives, including references used to write the chapter on pregnancy in Thyroid Disease Manager (www.thyroidmanager.org). We also used references that were reviewed by the ad hoc international guidelines committee of the American Endocrine Society, of which we are active participants.

### Conclusions

Because hypothyroidism has potentially serious adverse effects on the mother and the fetus, targeted case finding is recommended at the first prenatal visit. If hypothyroidism is diagnosed before pregnancy, the dose of thyroxine should be adjusted to reach a serum TSH not higher than 2.5 mU/l and the dosage should be increased further by four to eight weeks’ gestation. When overt hypothyroidism is diagnosed during pregnancy, thyroid function tests should be normalised as soon as possible. Because euthyroid women with features of thyroid autoimmunity are at risk of developing hypothyroidism during pregnancy, they should be monitored for an increase in serum TSH. Subclinical hypothyroidism is associated with an adverse outcome in pregnancy. Although the efficacy of treating women with subclinical disease has not been proved, thyroxine administration is recommended, as the potential benefits greatly outweigh the potential risks. In addition, undiagnosed (or untreated) hypothyroidism and hypothyroxinaemia in the first half of pregnancy (when availability of maternal thyroxine is particularly important for the fetus) are associated with a risk of cognitive impairment in the progeny.

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#### Competing interests

None declared.

#### Provenance and peer review

Commissioned; externally peer reviewed.


### Table 3

<table>
<thead>
<tr>
<th>Trimester</th>
<th>First</th>
<th>Second</th>
<th>Third</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average dose of thyroxine (µg/day)</td>
<td>100</td>
<td>125</td>
<td>150</td>
</tr>
<tr>
<td>Range of thyroxine doses (µg/day)</td>
<td>25-275</td>
<td>25-300</td>
<td>25-325</td>
</tr>
<tr>
<td>Median serum TSH value (mU/l)</td>
<td>2.6</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Upper TSH value (mU/l)</td>
<td>34.6</td>
<td>68.7</td>
<td>95.7</td>
</tr>
</tbody>
</table>

TSH, thyroid stimulating hormone.

Thyroid function tests should therefore be monitored in the mother for at least six months after delivery.
10-MINUTE CONSULTATION

Chronic knee pain

Christian David Mallen, George Peat, Mark Porcheret

A 57 year old self employed painter and decorator presents with a six month history of pain and stiffness in his left knee. The onset was insidious, and the pain has worsened over the past few weeks.

What issues you should cover

• Chronic knee pain affects one in four people aged above 55 years. Usually symptoms are mild to moderate. Osteoarthritis—presenting as activity related pain and limitation of movement, crepitus, and intermittent swelling in the absence of constitutional symptoms—is the commonest working diagnosis. Routine blood tests are not needed in these patients. Up to 70% of people with chronic knee pain will have radiographic evidence of osteoarthritis, but radiography results are only weakly related to symptoms. Plain radiography is not recommended for routine confirmation of the clinical diagnosis of osteoarthritis.

• Exclude “red flags” signs and symptoms that indicate immediate referral (significant trauma, evidence of severe local inflammation, sepsis). Do an initial investigation before specialist referral if you suspect an inflammatory cause. Consider extra-articular (referred pain from hip or back) and peri-articular (bursitis) causes.

• Useful indicators of prognosis are level of disability, severity of pain, body mass index, and psychological status. His occupation and employment status may be important in deciding management options.

• Be alert to comorbid conditions that may affect the pain and its management (such as further mobility restriction, polypharmacy).

What you should do

• Aim to reach a shared understanding of the problem and formulate a management plan that will enable him to control his pain, minimise disability, and prevent progression.

• Have a look at both knees and assess the joint. This will help form your differential diagnosis. Basic examination should include range of movement (including hip rotation), muscle strength, ligament stability, and varus or valgus malalignment. The absence of findings such as crepitus and bony enlargement does not rule out osteoarthritis.

• Discuss his worries and the probable cause of his pain and disability and disabuse him of common myths about arthritis (see box). Reassure him and be positive—referring, for example, to “wear and repair” of the joint, not “wear and tear.”

• Written material and contact details (such as those of the Arthritis Research Campaign) may help him understand the diagnosis and in self help. Find out what treatments he has already tried and what his preferences are.

• Non-pharmacological interventions are an important part of management for all patients. Encourage him to stay active, lose weight (if he is overweight or obese), consider a regular exercise routine, and, if necessary, modify his occupational activities.

• Review his treatment, including over the counter painkillers and supplements. He may want advice on glucosamine or chondroitin sulphate; results of trials have been mixed, and the latest show little benefit to symptoms. Paracetamol is the recommended first-line oral analgesic, with the option of moving up (and down) the analgesic ladder when appropriate. Discuss the risks and benefits of oral non-steroidal anti-inflammatory drugs (NSAIDs) if these are being considered. He may prefer to live with slightly more pain for less chance of serious side effects or to use topical NSAIDs. Injections of corticosteroid into the joint are also a future option for pain relief.

• Referral to physiotherapy can give him access to a range of effective non-pharmacological treatments, including exercise instruction and supervision, acupuncture, walking aids, and advice on activity.

• Consider referral to rheumatology or orthopaedics only if he has red flag symptoms or an unclear diagnosis; if he needs surgery; or if he does not respond to primary care treatment.

Common myths about arthritis

• Nothing can be done about it
• You mustn’t exercise if you have it
• Only elderly people get it
• Surgery always makes you better
• The only options are paracetamol and surgery
• You can’t work if you have arthritis

Source: Department of Health, Musculoskeletal Services Framework

USEFUL RESOURCES

Arthritis and Musculoskeletal Alliance Standards of Care. www.ama.uk.net


Department of Health. Musculoskeletal Services Framework. Available at www.18weeks.nhs.uk


UK Arthritis Research Campaign. www.arc.org.uk
Why do collaborative research?

PERSONAL VIEW Anisur Rahman

Much of the most valuable medical research is done by large teams of people, often collaborating across several centres. Examples include randomised controlled trials that prove the efficacy of new forms of treatment and genetic studies that use clinical data from many hospitals to establish the linkage of genes to specific diseases.

Such collaborative efforts are undervalued by academic institutions, to the extent that it could be argued that clinical academics who wish to thrive should avoid taking part in such collaborations—unless they are a lead author. Without colleagues who are prepared to collaborate without gaining the kudos of leading, however, none of these studies could be done.

Are the disincentives to collaboration worse than before? One disincentive is the increasing complexity of documentation that researchers need to carry out any form of study involving patients. A researcher who signs up to recruit patients into any multicentre project—even if only blood samples are needed, or a review of case notes—will have to submit several forms to the local ethics committee and may have to deal with the research and development departments of several trusts. All of this may require hours of work spread over several months before the research can even begin.

Once the project starts much time may be invested in recruiting participants, collecting samples, and collating information from case notes. In studies that are not funded by drug companies, often no funding is available for staff outside the lead centre. Collaborators at peripheral centres can either do this work themselves, which is laborious, or try to delegate it to junior staff. This could be considered exploitation if the juniors in question are unlikely to be listed as authors in the final paper.

What reward will ensue from this investment of time and effort? When the research is finally published, there will be a long list of authors. Most of the collaborators will be somewhere in the middle of this list. To get some idea of how this outcome will be viewed by academic departments we can consider the “publication score” recently proposed by Imperial College London as a part of the mechanism for assessing academic performance. The contribution of a particular paper to a person’s score is calculated by multiplying the impact factor of the journal that published it by an author position weight and then dividing by the number of authors. The author position weight is 5 for the first and last authors and 1 for any other position from fourth onwards. It is immediately obvious that the amount of credit to be obtained from being part of a large collaboration is very small. Although this publication score has been criticised and has not been adopted by other institutions, many may feel that it simply formalises a mode of thinking that already exists. This model implies that clinical academics should concentrate on papers with few authors in which they can lay claim to first or last authorship. Anything else is a mark of failure.

Is this too cynical? Why not just accept that collaboration is a virtue in itself without expecting any other reward? If you have helped to bring a new form of treatment to patients, is that not reward enough? Isn’t that why we chose to be clinical academics in the first place? Maybe all this is true, but why should involvement in multicentre collaborative research be a cross to bear? Why shouldn’t we actually assess whether individuals or departments are successful collaborators and include that assessment when judging their contribution to research? It shouldn’t be difficult. Does a person do any collaborative research? What do the lead authors of the collaboration think of that person’s contribution? What was the impact of the resulting research?

Whether as researchers or patients we all benefit from the fact that people in different institutions work together. Let us make it more attractive for individuals to choose that option. Otherwise, one possibility is that the only large scale collaborations will be those funded by the drug industry. The industry can pay people to deal with the bureaucracy and data entry needed and can reward institutions financially for taking part in the research. Do we want this to be the only incentive that persuades people to collaborate?

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Competing interests: AR is a clinical academic who has been involved in six multicentre collaborative projects since 2000.
Rage against the dying of the light

A film about the last days of an Alzheimer’s patient has undeservedly been mired in bad publicity about a “faked” TV death, finds Richard Huxtable

Malcolm and Barbara: Love’s Farewell
ITV 1, 8 August at 9 pm
Rating: ★★★★★

Although they are more familiar with subjecting other institutions—not least the NHS—to critical scrutiny, some broadcasters in the UK are currently at the unwelcome centre of national attention, amid allegations of unethical and deceptive practices. Such scrutiny is only proper. However, it is regrettable that the questions raised by this powerful and poignant documentary risk being obscured by reports that the film was falsely publicised as depicting the “passing away” of Malcolm Pointon, whose life with Alzheimer’s is unflinchingly traced.

We are first introduced to Malcolm in 1995, three years after he, alongside his wife Barbara, first learnt that the “silent physical buzzing” in his head marked the early onset of Alzheimer’s, at the age of 51. In this film, a sequel to his 1999 documentary Malcolm and Barbara: A Love Story, the filmmaker Paul Watson was granted permission by the couple to document Malcolm’s illness, through to his death earlier this year.

As the film begins, Malcolm—formerly a composer, lecturer, and BBC broadcaster—appears physically well but, as his son Martin observes, he is increasingly drawn into his “own little world.” From losing his way on (previously familiar) journeys, to expressing frustration at himself and those around him, Malcolm gradually transforms from the “most gentle” man that Barbara married into one that is—sometimes literally—“knocking all the love I have for him out of me.”

It is Barbara’s journey, as much as Malcolm’s, that is at the heart of this film, and her compassion, patience, and candour, while occasionally shaken, remain as firm at the close of the film, 11 years on, as they were at the outset. Save for respite care—which is, Barbara says, neither as frequent nor as capably provided as she would wish—Barbara remains Malcolm’s main carer throughout his illness.

She finds her relationship with her spouse transformed into one that resembles that of a parent to a child, and her home transforms too, with her dining room becoming “a hospital ward for one.”

Throughout these changes, Barbara remains humane, articulate, and direct and it is obvious how committed she is to ensuring that her family’s situation is documented: she declines Watson’s offer that he turn off the camera when she weeps, and it is she who asks him, “Do you want to film the bitter end, Paul?” To his credit, Watson quickly seeks to know whether this is what Malcolm would have wanted; it is, says Barbara, since the filmmaker has become “almost like a friend of the family.”

Barbara intimates why a documentary like this is so important; it seems, to her, that it should help raise awareness of the difficulties faced by patients with dementia, a condition she dubs “the scourge of the century,” and their carers. Awarded an OBE for her work advising policymakers on how to care for people with Alzheimer’s, Barbara does not shy away from asking difficult questions: “Where”, she asks, “is the money for our most vulnerable members of society?”

As for Malcolm’s final conscious moments, there appears nothing prurient or voyeuristic in these closing scenes. It is, it seems, not quite the “bitter end” that has dominated the headlines: certainly, the family members are shown gathered at Malcolm’s bedside, and in the last footage we see of him, Malcolm’s consciousness may be dwindling but he is breathing yet. Whether the broadcasting media ought to be entitled to show a person’s demise is an ethical debate for elsewhere; a debate, indeed, that might just as equally have been initiated by a previous documentary by Watson, Rain in my Heart, in which Nigel, a patient with cirrhosis, died in his partner’s arms (BMJ2006;332:1127). There are, of course, ethical and social questions to be asked here, but the real story concerns not simply the final failings of Malcolm’s body but also what Barbara refers to as the “little bit of Malcolm [that] has been dying for the last 15 years.” The questions raised about the care provided both to those with dementia and, in turn, to their carers should remain the primary focus, long after the credits, over which one of Malcolm’s compositions is played, have rolled.

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The return of the Saturday surgery?

I sighed. Glasgow’s tower blocks, heavy skies, and the sprawling postwar housing schemes that aimed to offer a better life than did the inner city slums disappeared in my rear view mirror. We headed for a better life in rural Suffolk, where I had taken up a GP partnership. The move from the electoral wards with the shortest life spans in Britain to those with the longest was just an eight hour drive. All my training, however, had not prepared me for the reality of general practice. Fifty consultations every day, five house calls at lunchtime, call-outs in the midst of surgery, 7 pm finishes, Saturday morning surgeries that ran till 3 pm. But I considered myself lucky, for the fledgling out of hours cooperatives had freed us from the 24 hour commitment that had crushed previous generations. I struggled, suffering near constant chest pain induced by stress. This was the 1990s: the Great Depression of general practice. Recruitment was at an all time low, and partnerships were worthless, receiving no applicants. It was a bankrupt specialty standing on the edge of the abyss, and the term “burn-out” was on everyone’s lips. Desperation forced change in Suffolk, and we reorganised. But that was the past, and general practice is now booming.

The government wants to extend general practice opening hours into the evening and weekends. For many this is a step back into the darkness of the past and to be resisted at all costs. But our working lives have been transformed by the new GP contract, so we owe our patients and the government an opportunity to explore these suggestions.

If these plans were not about offering more appointments but merely offering different times of availability this would suit many practices, with no need for coercion. With out of hours services covering emergencies during weekends, early mornings, and evenings, standard routine appointments could be offered at these times. The traditional two session day could be extended to a more flexible three session day, offering GPs the possibility of an early start and early finish or a later start and later finish—or even swapping a weekend morning for a midweek session. Such flexibility is much more compatible with family life. Extended opening may present problems with support staff; but with the development of paperless records systems and online booking the need for clerical staff is in steep decline. Offering extended opening is simply an issue of organisation—it is in our interests and possible. What goes around comes around.

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Gifts

This June, the 21 year old son of our closest family friends was stabbed to death as he slept. The next days were a blur. Friends, neighbours, and relatives gathered around and stayed close to the family. Everyone brought gifts; the fridge was kept full, the house swept, cold water kept ready for the hot, hot days. My husband rigged sails up to shade the veranda for the hot, hot days. All my training, however, had not prepared me for the reality of general practice. Fifty consultations every day, five house calls at lunchtime, call-outs in the midst of surgery, 7 pm finishes, Saturday morning surgeries that ran till 3 pm. But I considered myself lucky, for the fledgling out of hours cooperatives had freed us from the 24 hour commitment that had crushed previous generations. I struggled, suffering near constant chest pain induced by stress. This was the 1990s: the Great Depression of general practice. Recruitment was at an all time low, and partnerships were worthless, receiving no applicants. It was a bankrupt specialty standing on the edge of the abyss, and the term “burn-out” was on everyone’s lips. Desperation forced change in Suffolk, and we reorganised. But that was the past, and general practice is now booming.

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Mary E Black is a public health physician, Belgrade, Serbia dmaryblack@gmail.com
A Donne deal

John Donne, dean of St Paul’s, is among the greatest poets in the English language. He was also a great meditator on disease: not surprisingly, perhaps, for in his day there was a lot of it about. In the 22nd of his Devotions on Emergent Occasions, which he wrote in response to a severe fever that nearly killed him, he says: “How ruinous a farme hath man taken, in taking himselfe! How ready is the house every day to fall downe, and how is all the ground overspread with weeds, all the body with diseases! where not onely every turfe, but every stone, bearres weedes; not onely every mus cle of the flesh, but every bone of the body, hath some infirmitie; every little flint upon the face of this soile, hath some infectious weede, every tooth on our head, such a paine as a constant man is afraid of, and yet ashamed of that feare, of that sense of the paine.”

This can hardly have been an exaggeration, though it reads like such today. But for Donne, it was all Man’s own fault: until Adam ate of the fruit of the Tree of Knowledge, God did not intend for Man to die.

“O miserable condition of Man, which was not imprinted by God, who as he is immortall himselfe, had put a coale, a beame of Immortalitie into us, upon which we might have blown into a flame, but blew it out, by our first sinne; wee beggard our selves by hearkening unto false riches, and infatuated our selves by hearkening after false knowl edge. So that now, we doe not onely die, but die upon the Rack, die by the torment of sickness . . . ”

Man for Donne is a great self destroyer:’ ’Fevers upon wilful distempers of drink, and surfeits, Consumptions upon intem perences, and licentiousness, Madnes upon misplacings, or overbending our natural faculties, proceed from our selves, and so, as that our selves are in the plot, and wee are not onely passive, but active too, to our owne destruc tion . . .”

Essentially, things haven’t changed as much as you might have supposed. We still die because we eat too much, or the wrong things, and exercise too little. Which of us has not had a patient who, on being told that he has such-and-such a disease, protested that he has always eaten healthily and in moderation, and walked 10 miles a day without fail, as if diseases were handed out as punishments by the great Epidemiologist in the sky?

One of Donne’s first prose works was a little essay entitled “Why Doth the Poxe So Much Affect to Undermine the Nose?” Donne does not seek a naturalistic explanation of the phenomenon, such as that the temperature of the mucosa is lower than elsewhere in the body, or some such: he is asking what the purpose lying behind the phenomenon is? “Is there so much mercy in this disease,” he asks, “that it provides that one should not smell his own stink?”

Or is it that, “being begot and bred in the obscurest and secretest places, because therefore his serpentine crawling and insinuation should not be suspected, he comes soonest into great place, and is more able to destroy the worthiest member, than a Disease better born?”

No: the explanation is simpler. “. . . it is reasonable that this Disease in particular should affect the most eminent and perspicuous part, which in general doth affect to take hold of the most eminent and conspicuous men.”

Dislike of the successful is nothing new, then, but a constant of human nature. Theodore Dalrymple is a writer and retired doctor

BETWEEN THE LINES

Theodore Dalrymple

Man for Donne is a great self destroyer . . . We still die because we eat too much, or the wrong things, and exercise too little

MEDICAL CLASSICS

Memoirs of a Physician By Vikenty Veresaev

First published 1901

Vikenty Vikentievich Smidovich (Veresaev was his pen name) was born in 1867 in Tula, a provincial city 200 km south of Moscow, into a doctor’s family. On qualifying Veresaev worked as a resident doctor in St Petersburg and joined a Marxist literary circle. In 1901 he was fired from his hospital job by order of the city governor, and by decree of the minister of internal affairs he was prohibited from living in St Petersburg or Moscow for two years. That year Veresaev published his Zapiski vracha (Memoirs of a Physician) in a popular literary magazine, immediately making him famous. In the early decades of the 20th century the book had 16 Russian editions and was translated into many languages, including German (eight editions), French, English, and Japanese.

Veresaev describes his experience of working among the poor. He writes about the unsatisfactory medical education system and discusses medical errors, autopsies and vivisection, private practice, and philanthropy. A separate chapter is dedicated to experimentation on humans, mostly in venereology, because “many questions which, in other branches of medicine, find their answer in experiments on animals can, in venereology, only be decided through human inoculation, and venereologists have not hesitated to take the plunge: crime stains every step made by their science.” Veresaev provides numerous cases of inoculation of gonorrhoea, soft ulcer, and syphilis in men, women, and children in the 19th century.

Although Veresaev’s book was highly praised in the popular press, many doctors criticised it harshly. The UK edition (published as The Confessions of a Physician in 1904) was critically reviewed in the BMJ. The US edition (Memoirs of a Physician, New York, Alfred Knopf, 1916) can now be downloaded for free from www.archive.org. The editor wrote, “Public spirited men and women all over the country are working for the advancement of our profession. Will it alter their view point if they know that ten or fifteen years ago certain science-mad individuals on the other side of the Atlantic inoculated healthy children with syphilis to prove whether or not the disease was contagious in the secondary stage? No.”

In reply to his critics Veresaev wrote, “Ethical problems of our profession will not be settled by a tiny code of professional ethics […] that just regulates the relationship between doctors and public and between doctors themselves. Ethics in a broad, philosophical sense is needed.” He viewed the problem of establishing a threshold beyond which an individual’s interests might be sacrificed to the interests of science, as a “great, eternal, fundamental problem of the relationship between personality and higher categories such as politics, science, law, etc.” This problem was not solved for a century after the publication of the Memoirs and will always be with us.

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**OBITUARIES**

**Diana Margaret Riley (née Dean)**

**Innovator in perinatal mental health**

Diana Riley was a key figure in obstetric liaison psychiatry and perinatal mental health. She researched and published widely over 36 years, including works for health professionals and lay readers on postnatal depression and drug addiction in pregnancy.

Diana instituted one of the first mother and baby mental health units in the country, at St John's Hospital, Stone, to care for mothers with postnatal depression without separating them from their babies—a revolutionary idea at the time. She established and supervised psychotherapy groups for mothers with postnatal depression in Buckinghamshire, and developed expertise in drug addiction in pregnancy while working and teaching at University College Hospital, London.

She was also a prime mover in one of the earliest dedicated pre-senile dementia units in the country, leading a multidisciplinary team at St John's Hospital, Stone.

Brought up in a deprived area of London, Diana was influenced by seeing people unable to afford proper medical treatment. Her conviction that one must add to the sum of human health and happiness informed her work and her relationships with family, friends, and the wider community.

After qualifying and marrying, she was a locum in general practice during 1956-60, producing a child a year. She cared for the families of the Royal Air Force at RAF Halton in Aylesbury during 1960-4 and then worked in child health clinics across Buckinghamshire until 1970, producing two more children.

In 1970 Diana retrained in psychiatry in the married women's retraining scheme. She also trained in psychotherapy, including at the Tavistock Institute. She worked as a consultant psychiatrist from 1974 until she retired in 1995, thereafter continuing as an expert witness in medicolegal work and seeing patients for private psychotherapy, often without accepting payment, and throwing herself into community activities.

Diana was a woman of great taste and refinement, as well as a silversmith with her own trefoil hallmark. Her often wicked sense of humour led her to design and make a pair of cufflinks in the likeness of breasts for the surgeon who operated on her earlier breast cancer. She leaves a husband, Colin, six children, and 12 grandchildren.

**Teresa Riley**

Diana Margaret Riley (née Dean), consultant psychiatrist Aylesbury and High Wycombe (b 1929; q University College Hospital, London, 1953; FRCPsych), died of ovarian cancer on 1 April 2007.

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**Daniel Turnberg**

**Promising renal researcher**

Daniel Turnberg was a leading young researcher on renal disease at the Royal Free Hospital. He was researching the immunological mechanisms underlying kidney disease, particularly in HIV nephropathy and Sjögren’s syndrome. He published on the immunology of adriamycin nephropathy, the role of complement in immunological glomerulonephritis, ischaemia-reperfusion injury, and nephrotoxic nephritis, and reviewed the regulation of the complement system and its role in glomerulonephritis. He had plans to work on AIDS in Africa.

Daniel took an intercalated BSc in psychology. He did his house jobs in Bradford and Wakefield, followed by six months as a senior house officer in the accident and emergency department at University College Hospital, London, and two years in various posts at Hemel Hempstead Hospital. From there he went to St Helier and St George’s Hospitals as senior house officer and registrar in renal medicine. He then spent two years in renal medicine on the north London rotation at the Royal Free and North Middlesex hospitals.

A National Kidney Research Fund fellowship with Mark Walport and Marina Botto enabled him to take his PhD. He went back to the Royal Free to the choice of two jobs.

The son of Lord Turnberg, a former president of the Royal College of Physicians, Daniel was modest and unassuming, had a great sense of fun, and did many acts of kindness to patients, colleagues, and friends. He was a voracious reader and keen sportsman, particularly mountain biking, rock and ice climbing, and playing squash.

On the day before he left for a cycling holiday in Malawi he spent three hours successfully persuading the family of a terminally ill patient to take their relative home. On the holiday, with two friends and two other people, he took a trip in a light aircraft to a game reserve. The plane crashed, killing everyone.

Tributes to Dan have poured in to his family and colleagues, speaking of his curiosity, enthusiasm, sense of fun, kindness, humanitarian outlook, supportiveness to colleagues, and the way he always had time for people. His post is to be renamed the Daniel Turnberg lectureship in nephrology. His former colleagues at the Hammersmith and Royal Free are organising a scientific meeting in his honour.

**Caroline Richmond**

Daniel Turnberg, researcher in nephrology Royal Free Hospital, London (b 1970; q Leeds 1994; BSc, PhD), died in a plane crash in Malawi on 16 June 2007.
Tarsem Lal Garg

General practitioner Manchester (b 1946; q Rohtak Medical College, Haryana, India, 1969; DCH), died from a subarachnoid haemorrhage on 15 June 2007. Tarsem Lal Garg did his initial medical training in Scotland before moving to Jersey as a medical registrar. In 1985 he trained in general practice, becoming a single-handed general practitioner in 1993. Outside of general practice he was interested in alternative medical treatment for atherosclerosis. He was one of only a few UK doctors trained in chelation therapy and, as a graduate of the American College for Advancement in Medicine, helped to train many doctors from around the world in this therapy. Outside of medicine he loved to travel, particularly on cruises; he fell ill on his final cruise in Italy. He leaves a wife, Usha, and a son. 

Scot Garg

James Crawford Little of Morton Rig

Former director of clinical research and consultant psychiatrist Chirton Royal Hospital, Dumfries (b 1922; q Bristol 1966; MD, FRCP Ed, FRCPych), died from a heart attack on 27 April 2007. James Crawford Little (“Johnnie”) trained under Martin Roth. He was consultant psychiatrist at St James’s Hospital, Leeds, from 1959 to 1966 before moving to Dumfries. He took early retirement in 1981, partly to care for his wife. Johnnie’s early research focused on the vulnerability of “athletic neurotics.” He also advocated a shift from mental hospital to general hospital and community based psychiatry. As secretary of the Society of Clinical Psychiatrists, he campaigned for more democracy in psychiatry and publicised the plight of all consultants subjected to prolonged suspension. In retirement he founded the Clan Little Society, and was proud to become Dr J C Little of Morton Rig. Predeceased by his wife, Catherine, he leaves two children.

Alan Kerr

Edward Lawson McDonald

Former consultant cardiologist National Heart Hospital, and senior lecturer Institute of Cardiology, London (b 1918; q Cambridge/Middlesex Hospital 1942; MD (Cantab), FRCP, FACC), d 13 January 2007. After junior appointments Edward Lawson McDonald (“Lawson”) served as surgeon lieutenant in the Royal Naval Volunteer Reserve on HMS Glasgow. Awarded a Rockefeller travelling fellowship in medicine in 1952, he worked in Boston and at Harvard on valvar heart disease. After returning to England and starting research on platelets and fibrinogen in heart disease in 1953, he eventually became consultant cardiologist at the National Heart Hospital, as well as to King Edward VII Hospitals in London and Midhurst (1968-9). Lawson was a member or chairman of many committees and travelled world wide. He was made a member of the Most Honourable Order of the Crown of Johore in 1980. He leaves a son and Patricia, a companion of many years.

Hazel M Baker

Sadie Bessie (“Bess”) Michaels

Former general practitioner Hove, Sussex (b 1918; q Royal Free Hospital 1947), died from carcinomatosis on 26 May 2007. Bess Michaels took an unconventional route into medicine, having previously worked in tailoring. She married shortly after qualification and gave up medicine for 16 years to look after her family. By ingenuity and persistence when there was no obvious route to return to medicine, she secured the necessary experience to practise as a general practitioner, initially in an all female group practice in Hove and latterly as senior partner in her own practice. For her, medicine was a calling and reflected her innate compassion. Non-judgmental of others, her approach was one of quiet determination, and she achieved all the more because of it. Predeceased by her husband, Lew Coleman, she leaves a son.

Andrew Coleman

Robert MacGregor (“Rab”) Milne

General practitioner Kirkliston, West Lothian (b 1941; q Edinburgh 1965; BAO, FRCS Ed, FRCP), died from injuries sustained in a car crash on 19 May 2007. Robert Milne (“Rab”) was in general practice in Kirkliston for over 30 years and still working when he died. His was one of the first Scottish practices to develop total purchasing, and he was much in demand as a spokesman for general practice with Lothian Health Board. His surgical skills were well used in the vasectomy service of West Lothian. He appraised colleagues for the Royal College of General Practitioners, bringing to the task great understanding and tact. Rab learnt to fly and passed his pilot’s licence while a general practitioner/surgeon in rural New South Wales shortly before returning to Scotland and the initially single handed practice in Kirkliston. He leaves a wife, Judith; three sons; and six grandchildren.

Alex Cargill

Patrick Joseph Evanson Smyth

Former general practitioner Newbury (b 1948; q Guy’s Hospital 1971; DA), died from metastatic malignant melanoma on 3 April 2007. As a junior doctor in and around Brighton, Patrick Joseph Evanson Smyth became interested in anaesthesia. This took him back to Guy’s, where he became a registrar rotating between London and East Grinstead. After the birth of his second child, he moved to primary care, providing anaesthetic services to Newbury and Reading Hospitals in addition to his duties as a general practitioner. He was a keen member and secretary of the Newbury Medical Society. After 25 years in primary care he took early retirement, working part time for a medicolegal firm until his final illness. Outside work he was an enthusiastic gardener and golfer. He leaves a wife, Libby, and two sons.

Elizabeth Smyth

Edward Smyth

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
Written material about what a research study is investigating and the risks and benefits of involvement is often presented to adults and children alike. Unsurprisingly, when the same material is modified to reflect the age of the reader and the reading and cognitive abilities of children, there’s much greater understanding and acceptance. Most children find the modified version to be “friendlier” and “easier to read” (Anesthesia and Analgesia 2007;105:358-64). The use of a larger font and pictures was particularly popular.

Tendon injuries located at osteotendinous junctions are commonly seen in general practice, and anti-inflammatory agents are often recommended. But when the effect of these drugs was tested on the healing strength at the bone-tendon junction in rats, anti-inflammatory agents, with the exception of ibuprofen, had a detrimental effect (American Journal of Sports Medicine 2007;35:1326-33). Paracetamol had no effect on healing strength. The adverse effect of these agents may be mediated by reducing the collagen content at the injury site.

Gay and bisexual men may get more out of their local primary care services by going to a new section on the Terrence Higgins Trust website (www.tht.org.uk/gpsandgaymen). General practitioners, nurses, and all other healthcare workers can also find information that they might not have known they needed. As well as providing a checklist of specific health problems relevant to this group of patients, the site helps service providers to audit the quality of their services.

Repair of the Achilles tendon using a percutaneous approach is limited by a high risk of injury to the sural nerve. Irish surgeons have devised a method for detecting and mapping the nerve, which they have validated using ultrasonography (Injury 2007;38:845-7). With the patient lying prone, the knee is flexed to 90°, the ankle is dorsiflexed, and the hindfoot is inverted by supinating the foot. This complicated sounding manoeuvre results in the sural nerve being pulled taut so that it can be palpated along its path and mapped on the skin, avoiding the need for surgical exposure.

According to Clinical Risk no published randomised trials compare the outcome of vaginal deliveries after previous caesarean section with elective repeated caesarean section (2007;13:127-30). As the number of caesarean section deliveries rises, there’s an unmet need for doctors to provide sufficient information to women faced with making the choice of how to deliver their baby. Among other important matters, doctors are duty bound to explain that the use of prostaglandins to induce labour in women who’ve had a previous caesarean section is off licence.

A 79 year old non-smoking white woman presented with six weeks of progressive malaise and a one week history of difficulty eating because of a swollen, tender tongue. Her left visual acuity had suddenly dropped, which prompted emergency assessment. Examination showed bilateral swollen optic discs and a necrotic tongue lesion. Her erythrocyte sedimentation rate was 98 mm in the first hour. She was urgently treated with pulsed intravenous and oral corticosteroids. Her symptoms improved and the focal lesion resolved within a week. Extracranial features of giant cell arteritis, such as ischaemia of the tongue secondary to involvement of the lingual artery, are uncommon but valuable signs that help diagnosis.

Susan P Mollan (soozmollan@doctors.org.uk), specialist registrar, Deepen Gosnari, senior house officer, Andrew B Callow, consultant, department of ophthalmology, Royal Shrewsbury Hospital, Shrewsbury SY3 8XQ

A 16 month old boy who presented with sexual precocity—with the development of pubic hair and an enlarged penis—was put through many tests before his parents admitted that he had been unintentionally exposed to androgen gel used by his father (Clinical Pediatrics 2007;46:540-3). The child slept in his parents’ bed with frequent contact between bare skin, and his father had been applying testosterone gel twice a day to his own shoulders, chest, and back area, prescribed by his doctor for decreased libido secondary to depression.

“Disease mongering”—widening the boundaries of treatable illness to expand markets for those who profit from treatments—may be a logical business strategy but can be unhealthy for patients and for healthcare systems with limited resources. Writers in the British Journal of Clinical Pharmacology say it’s the responsibility of everyone to limit its adverse effects, including journalists who often “omit” to divulge that their source is a drug company (2007;64:122-4).

A cup of coffee and a jog around the park may go some way to deflect the effect of damaging sunrays and protect against non-melanoma skin cancers, according to experiments in mice (Proceedings of the National Academy of Sciences USA 2007;104:12936-41). The combination of coffee and exercise kills more cells that have been damaged by ultraviolet B waves than either coffee or exercise alone. It’s not clear whether the scientists are suggesting drinking and running at the same time.

More people kill themselves in hot weather. Each one degree rise in temperature above 18°C results in a 3.8% rise in suicides and a 5% rise in violent suicide. But, interestingly, although the 1995 heat wave in the United Kingdom was associated with a 46.9% rise in suicide, the 2003 heat wave had no such influence (British Journal of Psychiatry 2007;191:106-12). Minerva wonders what will be the effect of non-stop rain and flooding.

Embarrassment is putting our lives at risk, according to research commissioned by the Family Planning Association (www.fpa.org). Almost two thirds of people asked admitted that they found it difficult to have a conversation about condoms with a new partner, and 42% said it was a turn-off to raise the subject. People aged 30 or older didn’t find it any easier than younger people.

Middle aged people who drink at least one soft drink a day have a higher prevalence and incidence of metabolic syndrome than people who consume less (odds ratio 1.48, 95% confidence interval 1.30 to 1.69; Circulation 2007;116:480-8). The data come from the Framingham heart study. The syndrome includes an expanding waistline, high cholesterol concentrations, falling high density lipoprotein cholesterol concentrations, and greater than normal blood pressure.

MINERVA