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Shortcuts from other journals: Common genetic polymorphisms linked to macular degeneration
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Shortcuts from other journals: Antidepressants ineffective in bipolar depression
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BMJ 2007;334:928, doi:10.1136/bmj.39191.635637.AD

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Complementary medicine: **Mapping the alternative route**

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Should patient groups accept money from drug companies? **Yes**

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Should patient groups accept money from drug companies? **No**

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**Tonsillectomy versus watchful waiting in recurrent streptococcal pharyngitis in adults: randomised controlled trial**
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**Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis**
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**Psoriasis**
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A Barker
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**Melville Robert ("Peter") Fell**
P M S Gillam
BMJ 2007;334:959, doi:10.1136/bmj.39183.458981.BE

**William George Grenville Loyn**
Hugh Herbert
BMJ 2007;334:959, doi:10.1136/bmj.39190.764618.BE

**Henry Gemmell Morgan**
Jim Shepherd, Alan Shenkin
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**Robert Roaf**
Roger Croston
BMJ 2007;334:959, doi:10.1136/bmj.39196.761713.BE

**Carl John Williams**
Simon Carley, Gary Boland
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### Minerva

Minerva

BMJ 2007;334:960, doi:10.1136/bmj.39199.505486.79

**Minerva**
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### Corrections

**Obituary: William Ian McDonald**

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### Career focus

Read this week’s articles on

**Website extra**

NHS: the Blair years
Recurrent pharyngo-tonsillitis

Tonsillectomy has some benefits over watchful waiting, but the net benefit is unclear and research into longer term outcomes is needed

In this week’s BJM, a randomised controlled trial by Alho and colleagues assesses the effectiveness and safety of tonsillectomy compared with watchful waiting in adults with recurrent streptococcal pharyngo-tonsillitis (three episodes of pharyngitis in six months or four in 12 months). Although the minority of patients presenting to general practitioners with tonsillitis have recurrent tonsillitis, about 12% of the population has recurrent tonsillitis at some stage, and a substantial familial element exists. The trial found that tonsillectomy significantly reduced the recurrence of the principal outcome, streptococcal pharyngitis, at 90 days (1/36 (3%) v 8/34 (21%); adjusted relative risk 21%, 95% confidence interval 6% to 36%; number needed to treat 5, 3 to 16). A systematic review of tonsillectomy for chronic tonsillitis found limited data to support tonsillectomy in children and no data in adults, so the trial is the first to provide evidence to help doctors and patients decide on the best course of action.

Despite these promising results, the trial does have limitations that make it difficult to apply the results to a clinical setting. The main problem is that the follow-up period of six months is relatively short, and people in the watchful waiting group reported considerable improvement during the trial period—after six months the mean number of sore throats was 0.4, and patients had on average had 2.5 days of sore throat. This begs the question of whether the benefit of immediate tonsillectomy would be reduced if the follow-up was longer. Secondly, because of the small size of the trial, the effect sizes were imprecise and confidence intervals were wide. Thus the trial is consistent with as small a benefit as a 3% reduction in episodes of sore throat (number needed to treat 34). A third limitation is that we do not know how severe the episodes of pharyngitis were. The authors provide some data on the number of days with a sore throat, but because patients were encouraged to consult to have swabs taken, it is difficult to judge severity on the basis of consultation data. The episodes of sore throat lasted six days, which suggests that they were shorter than normal episodes presenting to general practitioners (where on average patients have had symptoms for three days before they present and symptoms last for a further five days). Another issue relates to the chosen primary outcome measure of a reduction in streptococcal pharyngitis confirmed by culture, which is perhaps of limited clinical use as patients do not complain of streptococcal pharyngitis but of sore throats. More useful to clinicians and patients, is that the authors documented a reduction of 25% in episodes of sore throat (56% v 31%), and a sore throat for nine days less in the first 90 days of the follow-up period.

Any benefits of the operation must be balanced against potential disadvantages. The major disadvantage documented in the trial is the 13 days of sore throat after tonsillectomy, which can be severe in many patients. Other disadvantages include the risks associated with an anaesthetic, otalgia, dehydration, dental injuries, burns, and soft tissue injuries, and a risk of life threatening complications, such as major haemorrhage or sepsis (mortality rates range from one in 16 000 to one in 35 000). The trial is underpowered to quantify the risk of these complications accurately, and although only minor bleeding was seen after tonsillectomy, more severe but rarer complications are probably of greater concern to patients.

What is the take home message for clinicians? Until the longer term outcomes in people who do not have surgery are available, and we have more precise estimates of the benefit in terms of the severity of the episodes prevented by surgery, it is difficult to provide firm advice to patients. Until such evidence is available, I would advise patients who have had four episodes of sore throat in one year or three in six months that they are likely to have on average two and a half days of sore throat in the next six months if they decide not to have the operation; if they decide to have the operation they are likely to have about 13 days of severe pain immediately after surgery, and then on average half a day of sore throat in the next six months. I would also make them aware that they might have minor postoperative complications and very rarely life threatening complications.

Telephone interventions for disease management in heart failure

Such support for patients at home cuts admissions to hospital for heart failure

Several randomised trials have established that disease management programmes offering, for example, home visits, heart failure clinics, and telephone interventions result in better adherence to treatment and reduced admissions to hospital for heart failure than standard care for people with heart failure.1-4 Current evidence is unclear, however, on the impact of such programmes on mortality, all cause admissions, quality of life, and cost reduction. The most effective components of the interventions and the benefits to different subgroups are also unknown. Moreover, such evidence comes from small trials with short follow-up, performed at single centres, that applied complex strategies to selected high risk populations. These characteristics might affect both the internal and external validity of the trials’ findings. In this week’s *BMJ*, Clark and colleagues present a meta-analysis that includes 14 trials of telephone interventions in heart failure; it shows an overall 21% reduction in admissions for heart failure (but not in total admissions) and a 20% reduction in total mortality.5 The authors also report a benefit of these interventions on quality of life and cost reduction. The two types of intervention—structured telephone support and telemonitoring—were similarly effective.

In this new systematic review by Clark and colleagues only one trial included more than 1000 patients and only two trials had more than 12 months’ follow-up.6-7 But previous meta-analyses of heart failure programmes included fewer, smaller trials and did not show a beneficial effect of telephone interventions.8-9

Clark and colleagues reported a reduction in mortality, but this effect was seen in only one structured telephone study (TEN-HMS).7 Conversely, in the largest trial done so far, the DIAL trial, in which we were both investigators, mortality was not reduced, although admissions for heart failure were significantly reduced (relative risk reduction 29%, P=0.005).5 The DIAL trial randomised ambulatory stable patients with previously optimised drug treatment (95% used angiotensin converting enzyme inhibitors or angiotensin receptor blockers and 70% used β-blockers) to education and monitoring by nurses by telephone, and all patients were followed up by cardiologists. The reduced mortality seen in the TEN-HMS trial might have been explained by a more effective intervention or by a higher effect because it included sicker patients.

Evaluations of complex interventions with multiple and simultaneous strategies should aim to answer questions about how the interventions work and which of their components are essential. Available evidence suggests that disease management interventions in heart failure should incorporate education on self care and adherence to diet and medicines; monitoring and surveillance to detect early signs of decompensation; people trained in heart failure to provide the interventions; and facilitated access to specialised care for any clinical deterioration.

The impact of these interventions might be attributed at least in part to the ability to detect early signs of pulmonary and systemic congestion and to allow early consultation with medical specialists before severe decompensation occurs. Other mechanisms might include the effect of education and behavioural advice, as we found in the DIAL trial—patients with improved knowledge of medical treatment and early compliance with diet, daily weighing, and drug treatment (from baseline to the first 45 days) benefited most from the intervention.9

Telephone interventions usually need fewer resources than more complex interventions and transcend geographical and transport barriers, allowing wide scale implementation in clinical practice. More complex interventions might be needed in certain situations, such as advanced heart failure or in frail elderly patients. These might still be provided by telephone—for example, through transfer of patient data and other technologies—but such systems are more resource intensive and perhaps less feasible.

Overall, the evidence supports telephone interventions in the management of heart failure. But, as there have been no head to head comparisons of different disease management strategies, any intervention that includes education, monitoring, facilitated access, and trained personnel may be effective, no matter how it is delivered. And, despite these promising data about telephone based programmes in heart failure, we must bear in mind that these interventions cannot substitute for medical assistance for these patients; they simply provide support to the clinician-patient relationship and offer a better way to provide medical care in heart failure.

6. GESICA Investigators. Randomised trial of telephone intervention...
Onset of action of antidepressants
Most benefit is evident in the first two weeks, not six, as conventional wisdom says

Recent guidance from the National Institute for Health and Clinical Excellence (NICE) says that antidepressant drugs should be offered routinely to all patients with depression of at least moderate severity and recommends a selective serotonin reuptake inhibitor as first line treatment.1 The NICE guidance goes on to state that “Patients started on antidepressants should be informed about the delay in onset of effect.” This reflects conventional wisdom, but is it time to revisit this idea?

Speed of onset of the actions of antidepressants is clinically important for several reasons. Delayed onset means that depression, its associated disability, and for some patients the potential risk of suicide continue. Early onset of effects may improve future compliance and thus outcomes.

When tricyclic antidepressants were first introduced in the 1950s delays in antidepressant effects were not reported. Indeed, researchers on early tricyclic antidepressants asserted that they usually started to work within the first few days of treatment.2 3 Later clinical experience suggested, however, that the drugs did not act immediately. The ensuing debate continued into the 1970s. By the mid-1970s, animal models suggested that the dissociation of acute biochemical changes induced by antidepressant treatment and the therapeutic action were due to the development of subsensitivity in the postsynaptic monoamine receptor.4 5 In animal models, these changes became apparent only after dosing with antidepressants over a similar period to that taken for clinical efficacy to develop.5 Since then, increasingly refined neurobiological theories of the action of antidepressants have incorporated this delay.6

This message is largely unchanged, despite the development of newer antidepressants, such as the selective serotonin reuptake inhibitors, and even though newer antidepressants can often be started at a therapeutic dose, rather than titrated upwards over two to three weeks, as is necessary with the older tricyclic antidepressants to minimise adverse effects.

Research on this question is hampered by lack of an agreed definition of onset of action.8 This is particularly true in clinical practice, where it may be difficult to distinguish between signs of response and side effects. For example, sedation may relieve symptoms but it is not directly related to the medicine’s antidepressant properties. Recently, however, several studies have challenged the assumption of a delay in the onset of antidepressant action.9 10 11

A meta-analysis of 76 double blind placebo controlled trials of antidepressant treatment for depression in 2005 found that 60% of overall improvement occurred during the first two weeks and that half of all patients who respond to a six week trial respond in the same period.9 More recently, a meta-analysis of placebo controlled trials of selective serotonin reuptake inhibitors suggested that therapeutic response is greatest in the first week, with a gradual decline in the size of benefit over successive weeks of treatment.11 One third of the total effect seen at six weeks was apparent in the first week.12 As the studies were placebo controlled trials, this improvement was unlikely to be a placebo effect.

These recent findings raise further questions. Is speed of therapeutic benefit with antidepressants a class effect, and do differences occur within classes? Do some symptoms respond quicker than others? Does early response predict future response and, if so, should we routinely review response earlier and change treatment if no response occurs in the first week or two? Does this phenomenon apply only to a subset of the population and is it genetically determined? Should we be encouraging patients to anticipate early relief from symptoms and, if so, is there a risk of disappointment if benefit is delayed?

Until studies are specifically designed to measure the onset of action of antidepressants, results from meta-analyses of studies not designed for this purpose should be treated with caution. We suggest that future studies should look for subsets of symptoms that may be ameliorated earlier than others and seek to discover how this is mediated. In the meantime, if these findings are correct it is good news for many patients with depression treated with antidepressants. But these results are unlikely to alter clinical practice until these additional questions are answered.
Euthanasia in neonates
Should it be available?

Euthanasia for newborn babies with lethal and disabling conditions is illegal worldwide. However, in reality its acceptance and practice vary between different countries. In the Netherlands, about 200,000 live births occur annually; of these, 10-20 babies—mostly with severe congenital malformations—are thought to be actively killed, yet between 1997 and 2004 only 22 such deaths were reported to the authorities.

To regulate neonatal euthanasia, clinicians in the Netherlands have argued that all cases should be reported. In collaboration with lawyers, they have developed and subsequently published guidance, which defines criteria that must be fulfilled before euthanasia can be considered and which would subsequently be examined by the statutory legal authorities (see box). Doctors who follow this guidance are not guaranteed freedom from prosecution, but to date no paediatrician in the Netherlands has been prosecuted.

In 2006 it was reported in the national press in the United Kingdom that, in response to a consultation undertaken by the Nuffield Council on Bioethics on the ethics of prolonging life in fetuses and the newborn, the Royal College of Obstetricians and Gynaecologists (RCOG) had proposed considering “active euthanasia” in UK practice. Recurrent themes run through any debate about neonatal euthanasia. One is the tension seemingly felt by some clinicians as a result of the fact that in UK law the fetus becomes a legal entity only at the moment of birth. Because of this, the RCOG can recommend that late termination of pregnancy for fetal anomaly should be preceded by feticide, but any clinician who injected a similar severely malformed newborn baby with potassium chloride moments after birth would be guilty of murder. Another theme is the fine line between the practices of withholding life support, actively withdrawing life support, and intervening to deliberately kill the baby. The first two options, when undertaken because of apparent unbearable suffering or because treatment is futile, are seen as acceptable practice and are widespread; the last option is active euthanasia and anyone undertaking such an act should expect to be prosecuted.

The only babies for whom active euthanasia might be considered are those destined to survive and able to support their own ventilation, but who will have a very poor quality of life with no prospect of improvement. This group includes children with malformations such as some severe forms of spina bifida and a smaller group of preterm babies, whose extensive disabilities become apparent only after recovery from early respiratory problems. Extrapolation of the experience in the Netherlands indicates that there would be around 50 such cases each year in the UK.

The report of the Nuffield Council of Bioethics on “Critical care decisions in fetal and neonatal medicine,” published after widespread consultation in November 2006, “unreservedly” rejected the possibility of neonatal euthanasia in the context of UK practice even when life is intolerable. Why was this, and why was it apparently received with relief by most paediatricians in the UK?

Parents entrust their newborn babies to intensive care services, often for many weeks—the length of stay is typically much longer than that for adult or paediatric intensive care. They do this because they are confident that clinical decisions, often made in response to unpredictable life threatening emergencies, will be made in the child’s best interest and based...
on the principle that, within reason, the main objective of care is to preserve life.

One of the reasons the UK is resistant to adopting the Dutch recommendations is that active killing as a therapeutic option is seen as a “slippery slope” towards its wider use, although some reject this argument.2 Another reason is the fear that active killing may have a negative impact on the psychology of professional staff, and that parents may feel pressured to accept the option of euthanasia so that they do not become a burden on medical and social services.

Euthanasia can only be an option if the futility of continued treatment is certain. While this may be clear for some congenital malformations and genetic conditions it is often unclear for preterm infants. Older patients may decide themselves that their life is intolerable and request euthanasia or assisted suicide, whereas carers and family must judge the quality of life of a baby. This decision is extremely difficult because indicators that a very preterm baby is likely to be severely disabled are not foolproof. Clinicians who have led discussions that have resulted in active withdrawal of care have to live with the probability that they have occasionally allowed a baby to die who would have thrived.

Health professionals are frequently challenged by the press with deluding themselves by drawing a distinction between the withdrawal of active life support (euthanasia by omission) and active killing of a baby. In practice, experienced neonatologists and neonatal nurses feel comfortable with this distinction; they can discuss it openly with families and help them to understand, for example, the acceptability of infusing opiates at a dose that controls pain and distress but the impossibility of increasing the dose further with the primary intention of hastening death. Neonatal nurses have great expertise in assessing suffering in tiny babies and in providing palliative care.

Acts by neonatologists in the UK undertaken with the purpose of ending life seem to be rare.1 Guidance provided by the Royal College of Paediatrics and Child Health3 around end of life decisions has provided a framework within which UK neonatologists feel comfortable. We have a service that has become progressively more transparent, with parents increasingly involved in making clinical decisions.

The availability of active euthanasia as a therapeutic option would undermine this progress and be a step backwards. However, we must look at how to provide for babies who might be candidates for euthanasia elsewhere in the world—to control their pain and to support their families. Sadly, too often, parents have to battle for essential services that ensure the best outcome for their disabled child, and that also make their own lives more tolerable.


Health and welfare of older people in care homes

Improvements will depend more on reform of the whole system rather than on commissioners and champions

The welfare of older people who live in care homes has raised concern for decades in many countries.1 Scandals surface on a depressingly regular basis, and although these enter the public consciousness, none provokes the outcry caused by reports of abuse of vulnerable people at the opposite end of the age range—children.

Two recent campaigns by the charity Age Concern England and partners focused on lack of respect for the dignity of older people. “Hungry to be heard” examined the problem of malnutrition in older people in hospital,2 and it called for more help for those needing assistance with eating and drinking. But protecting patients’ meal times from interruption will prove a difficult goal for frazzled staff in many acute hospital units. “Behind closed doors” campaigned for people to be able to use the toilet in private in all care settings and argued that this was a general marker of whether human rights and dignity were being respected.3

Both reports bring fresh impetus to important topics but deal with issues that have been around for a discouragingly long time. The landmark study on malnutrition in hospital was published in the BMJ as long ago as 1994, yet problems persist and solutions remain elusive.4 Of course, both illness and dependency pose threats to dignity, but people of all ages have a fundamental right to be respected. So why is dignified respectful care for older people still lacking, and what might restore it?5

Legislation, regulation, and standard setting are widespread in the health and care home sectors, and more of the same seems unlikely to alter attitudes and prejudices. There is a current vogue to appoint champions and commissioners for older people. Such appointments may allow a degree of self congratulation
that something is being done for older people, but risk simply being a way of avoiding the difficult business of system change. Older people are the core business of the care sector; thus, what is needed is not just individual advocates but rather a long overdue and major change in culture and practice to reflect the central position of older people in systems of care.

How might this be achieved in care homes? Firstly, we need to stop blaming individual practitioners and care homes. Good people working in poor environments with poor systems of care will inevitably produce poor quality care, as has been shown in health care. A whole systems approach is much more likely to succeed; for example, changing infrastructure, procedures, management techniques, and staff training. Such an approach is beginning to reap dividends in terms of patient safety in health care. Frontline care staff should not be made scapegoats; instead, their dignity should also be assured. Being valued (in financial and non-financial terms) and able to work in a system, atmosphere, and culture that recognises and rewards good quality, informed, thoughtful care is much more likely to be effective than merely providing more training.

Secondly, access to good quality medical care should be readily available. Older people in care often have complex medical problems, yet their care is mostly provided by general practitioners, rather than specialists in the medicine of old age. Most older people in care are unable to initiate a referral for a medical review. They depend utterly on care in a system, atmosphere, and culture that recognises and rewards good quality, informed, thoughtful care is much more likely to be effective than merely providing more training.

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Secondly, access to good quality medical care should be readily available. Older people in care often have complex medical problems, yet their care is mostly provided by general practitioners, rather than specialists in the medicine of old age. Most older people in care are unable to initiate a referral for a medical review. They depend utterly on care staff to recognise that any abrupt change in their condition—for example, a sudden loss of mobility—is likely to be a marker of underlying illness, which should be assessed, diagnosed, and managed. While some general practitioners relish the challenges of their role in care homes, others lack the skills, support, or inclination to fulfil this unsought but demanding role. Primary care teams need to be supported by secondary care specialists and should be given time, money, incentives, and training in comprehensive geriatric assessment. Such an approach would improve the quality of care for people in institutional care. It would also enable more elderly people to live successfully in the community without the need for institutional care.

Older people have an important part to play too. The political impact of older people as a lobbying force is weak in many, but not all, countries. When older people become politically organised they are a large and formidable force that has real power to campaign for change, as has been shown by the American Association of Retired Persons. Older people need to demand that carers are paid a decent wage and are well trained, that managers are responsive to their needs, that buildings are fit for purpose, and that vulnerable older people are not denied the expert health care that they are entitled to. All of this costs money, and those of us in affluent countries need to pay more to ensure that care for older people is of a standard that we ourselves would be happy to receive.

8 Health Foundation. 20 hospitals join pioneering safety improvement initiative. Media Centre release, 20 Nov 2006.
Marcus R. Should you tell patients about beneficial treatments that they cannot have? Yes. BMJ 2007;334:826. (21 April.)


CANDOUR ON UNFUNDED TREATMENTS

Ignorance is a public health issue

Marcus indicates the importance of candour in outlining the choices available to individuals.1 However, there is also the effect on wider issues of public health and the availability of treatment options from which patients can choose.

Unacceptable radiotherapy waiting times have been highlighted by the Royal College of Radiologists for over a decade.2 They have now started to improve, but the last audit in September 2005 still showed that over half our patients wait longer than one month for curative treatment. What is probably not made clear to patients is the impact that this can have on their prognosis. A systematic review has shown that for breast cancer a wait of longer than eight weeks carries a 60% increase in the risk of local recurrence over five years.3 For postoperative radiotherapy of head and neck cancer, a delay of six weeks increases the risk of local recurrence 2.6-fold.3

Worse than this, delay may render patients untreatable. An audit of waiting times in lung cancer patients showed that 20% progressed so that they were unsuitable for radical radiotherapy while on a waiting list.4 An update in 2007 showed no change.5

These are serious risks to patients. Our failure to communicate them or to bring them into the public arena has contributed to the current lamentable state of our radiotherapy services. The report of the National Radiotherapy Advisory Group, which is currently with ministers, proposes a plan to tackle these issues.

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Competing interests: MWW holds a joint lymphoma clinic with Dr Marcus.

Patients do not live in an information vacuum

Firth has done his best with a very short straw and moved the debate from the general question to a very specific patient.1 Mr Brown is that rarity in today’s society: a person disinterested in his medical condition and bereft of sources of information or indeed of friends, relatives, or campaigners who will give him information he may not want.

My concern would be that when (not if) he receives the information, and then appreciates that the doctor failed to inform him, his trust in that doctor and the profession in general will be undermined.

People with ill health have to face many uncomfortable and distressing changes in their lives, and, although doctors have a duty to comfort, this cannot mean protecting patients from information that is both empowering and uncomfortable. Doctors cannot know what resources their patients may have or be able to rally.

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Competing interests: None declared.

1 Firth J. Should you tell patients about beneficial treatments that they cannot have? No. BMJ 2007;334:827. (21 April.)

ROYAL COLLEGES AND MMC/MTAS

We are alive and kicking and have upped our game

Hawks focuses on the role of the royal colleges in Modernising Medical Careers (MMC) and the Medical Training Application Service (MTAS).1 On MTAS, the royal colleges were permitted very little influence on its development.

As to upping our game, the colleges have over recent years developed new roles and responsibilities, have modernised their organisations, and have instigated new initiatives to advance medical practice in line with the continued development of healthcare reform. Such work has transformed the agenda of the colleges into one of proactive engagement with policy makers, of innovation, and of providing patient focused healthcare delivery.

The Academy of Royal Colleges, well placed to bring a unified medical professional view of issues that should be addressed, is developing a broad agenda that reflects continuing change in the nature and delivery of better health and health care, both generally in the UK and abroad, and in the context of the reformed NHS. The colleges, either working individually or together through the academy, are already influencing 21st century medicine, in a variety of alliances with other bodies—indepedent and statutory—that have interests and responsibilities in health. Examples are the highly acclaimed work on medical professionalism by the Royal

All that is needed is for good men to say nothing

I am sure Firth is a committed, caring, and competent doctor, but on this occasion he has failed his patient, Mr Brown.1 His actions are supporting the political lies and administrative sleight of hand which deny patients life enhancing treatments.

He should read the General Medical Council’s guidance further; after telling his employer of inadequate resources, he should seek independent advice on how best to put matters right.

A primary care trust that refuses to fund treatments recommended by the National Institute for Health and Clinical Excellence should be reported to the secretary of state for health, with a copy to the press.

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Competing interests: Remuneration from pharmaceutical industry for advice and lectures on ethical and legal aspects of off-label treatments for macular degeneration.

1 Firth J. Should you tell patients about beneficial treatments that they cannot have? No. BMJ 2007;334:827. (21 April.)
College of Physicians, the development of accreditation of radiological services currently being piloted by the Royal College of Radiologists, and the work currently being undertaken by the academy on reconfiguration of acute services. Finally, the academy and the individual colleges welcome their new and central role in helping implement a robust system of recertification or “revalidation” of doctors.

Such new roles and initiatives demonstrate that colleges are championing change and helping to direct modern trends in the development of health care. Representing a living and very important profession, the colleges are very much alive.

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Competing interests: None declared.

1 Hawks N. The royal colleges must use their game—or die. BMJ 2007;334:724. (7 April.)

IT AND PATIENT SAFETY

Software must be robust

De Wildt et al concentrate on the shortcomings of Excel but ignore other inadequacies.1 Using Excel or other spreadsheets for dose checking (with or without the locking facility) is inappropriate. The problem is not just data going in the wrong place—it is essential that the concepts of strength and dose are not confused, which seems to have occurred in this case, and that every entry is clear, follows accepted standards, and its purpose is clear.

Writing robust software for handling dose calculations is straightforward, but this is not a job just for the computer programmer. The first requirement is to assemble the knowledge domain of the application—in this case, all drug products (and all their details in standardised format) that would ever be needed in paediatrics and the medical information domain for their use (indications, contraindications, side effects, interactions, dosage, and so on). Next the knowledge concepts and related terminology need to be organised, preferably into some form of hierarchical thesaurus and put into a database. Now the algorithm to do the dose checking can be written and checked. Finally the programmer can write the program. This program makes calls to the knowledge domain database on the basis of the strictly controlled entries of the user. The drugs required are selected from the database, ensuring that real products are chosen by the user, as are the weight, age, and medical conditions. The knowledge database must contain all the drugs and other treatments including strengths, formulations, dose per kg body weight, dose for specific indications, and routes and rates of administration.

The whole job could be done by a team of one doctor or pharmacist with the necessary knowledge, one database expert, and one programmer—in one year or in standardised units three man years.

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Competing interests: RW is the managing director of SafeScript Ltd and co-author of its product: the World Standard Drug Database.


NEW CARE AFTER SURGERY

How new is new?

I was very excited when I read the headline “New approach to surgical care aims to improve recovery.”2 Like many surgeons I have been interested in improving recovery of patients after elective surgery for quite a while. However, the only thing new I was able to find in this “new approach” was a new acronym (enhanced surgical treatment and recovery programme, ESTREP).

Surgeons, anaesthetists, and other doctors interested in enhancing postoperative recovery have known the multimodal approach allegedly developed at University College London Hospitals NHS Foundation Trust for more than a decade under the acronym ERAS (enhanced recovery after surgery) or “fast track.” Except for intraoperative oesophageal Doppler guided fluid management (in some hospitals already a part of fast track surgery), the “new approach” does not seem to offer anything new.

The BMJ did publish a clinical review on this topic more than five years ago,2 while the first series of fast track rehabilitation for elective colorectal resection by Henrik Kehlet and coworkers from Hvidovre Hospital in Copenhagen, Denmark is as old as 12 years.2 Not only is the “new approach” not really new, but also the potential of fast track or ERAS or ESTREP is underestimated in this article—to reduce the average stay in hospital for patients undergoing complex colorectal surgery from 12 days to eight days. In the Copenhagen group postoperative hospital stay was decreased to two to three days after elective colectomy, postoperative hospital stay was five days in a recent international study,4 and postoperative hospital stay decreased from 12 to five days after introduction of fast track rehabilitation in my hospital.

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Competing interests: None declared.

1 Mayor S. New approach to surgical care aims to improve recovery and reduce length of hospital stay. BMJ 2007;334:816-7. (21 April.)


ASYLUM SEEKERS

Detained asylum seekers may be being re-traumatised

Bisson’s review does not mention torture, a common cause of post-traumatic stress disorder (PTSD), or the risk of re-traumatisation in such patients. UK doctors are most likely to encounter these problems among asylum seekers, especially those who have been detained in removal centres after being “failed” by the Home Office and immigration judges.5 The number of such cases probably exceeds 5000 per year.

It was accepted in the drafting of the detention centre rules6 and underlying statutory instruments that detention of torture survivors was unduly likely to cause severe psychological harm and should occur only under “exceptional circumstances.”

Doctors working in detention centres are required to report to the Immigration and Nationality Department (IND) about anyone whose health is likely to be harmed by detention, which can be of indefinite duration, exceeding one year without any conviction in some cases. Sadly, receipt of such reports (when sent) has resulted in inaction and significant misrepresentation by the department.

In a report on Harmondsworth Detention
Centre, Her Majesty’s Chief Inspector of Prisons identified 57 such “torture reports” sent to the immigration department over the first half of 2006. Not one of these is known to have resulted in any action by the department to investigate the accuracy of such reports.

In the past 18 months, colleagues in the Medical Justice Network and I have seen at least 25 detained asylum seekers with strong physical evidence of torture (including cigarette burn scars and stigmata of falaka (beating of the feet)) as well as fulfilling all necessary criteria for a diagnosis of post traumatic stress disorder. In some cases, we have been able to provide medicolegal reports that have helped their release by judicial decision. This has usually been resisted by the Home Office.

Doctors, especially general practitioners, whose asylum seeking patients have evidence they were tortured before coming to the United Kingdom, who have PTSD as a result and who are at risk of detention, may wish to supply them with a letter (or full medicolegal report) outlining evidence that detention would be unduly harmful. This would go some way to reducing the very substantial numbers who suffer re-traumatisation while seeking refuge.

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Competing interests: FWA helped to found the Medical Justice Network. www.medicalljustice.org.uk. For helping detained hunger strikers to obtain adequate medical care, he was reported to the GMC by the management of a detention centre, against the wishes of the patients concerned. He is occasionally paid, under legal aid, for medicolegal reports.

1 Bisson J. Post-traumatic stress disorder. BMJ 2007;334:789-93. (14 April.)
2 Detention Centre Rules 2001 (item 39). http://www.ukdetention.org.uk/uk/default.html

**Highest attainable standard of health is a human right**

Since my editorial explaining how the denial of failed asylum seekers’ access to free hospital care violates their fundamental human rights was published, there has been a deafening silence from the BMA.1 Yet the BMA has a proud record of promoting human rights—its website claims that “Action by medical associations ... to ensure that resources [reach] the most vulnerable populations, have played an important role in supporting the realisation of the right to health.”2 Not for over 400 000 failed asylum seekers living in the UK, it hasn’t.

In contrast, the parliamentary Joint Committee on Human Rights recently recommended that free secondary health care be provided “to comply with the laws of common humanity and the UK’s international human rights obligations,” and an innovative Department of Health policy document that requires health professionals to respect human rights acknowledges the government’s responsibility to comply with international treaties.3,4 The BMA’s reticence, given its influence and reputation on human rights, means that it has become part of the problem.

In 1984 the BMA withdrew from the World Medical Association (WMA) in protest at the reinstatement of a white dominated Medical Association of South Africa that supported apartheid. The protest was prompted by a representative organisation following government policy which violated international human rights law—a practice the BMA now seems to be emulating. In an ironic twist, the current South African government’s deliberate obfuscation of the cause of AIDS violates the same international covenant and may ultimately be responsible for more suffering and death than apartheid.5 Now human rights are to be engaged as best practice,6 doctors will have to understand that international human rights law is there to be respected not cherry picked.

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Competing interests: PH played a part in developing the General Comment 14 of the International Covenant on Economic, Social and Cultural Rights.


**BMA’s response**

The plight of failed asylum seekers in the United Kingdom is a matter of serious humanitarian concern. The BMA’s medical ethics department receives regular inquiries about the rights of extremely ill individuals to vital health services where legal entitlement is in doubt. We did not respond immediately to Hall’s thoughtful comments (previous letter), but this is not the same as silence. The BMA is a membership organisation, and its overall policy is decided at its annual representative meeting (ARM). This year, for example, we understand a motion is being taken to the ARM calling on the BMA to lobby the government to ensure the provision of appropriate health services for failed asylum seekers. If the motion is passed then we have a mandate to lobby directly. In the absence of such a mandate, our job is to interpret so far as possible existing policy and apply it to emergent circumstances.

Hall is right, the BMA does have a record of promoting human rights in health, and it is out of this background that we have shaped our policy. The medical ethics department has, for example, published guidance on rights of access to health care.1 Largely as a result of Hall’s vigilance, we have clarified that general practitioners have the discretion to register failed asylum seekers for routine primary care, although they are not obliged to do so.

In secondary care failed asylum seekers, who are not “ordinarily resident” in the UK, are entitled to free care only when it is “immediately necessary.” Despite these legal restrictions, the BMA has met with representatives of the Department of Health and the Home Office and established that what constitutes “immediately necessary” is a matter of medical judgment and, therefore, medical discretion. The government also undertook to set up a working party, with BMA representation, to look at broader questions of access to health care among migrants without entitlement, but despite our efforts, the group has yet to convene.

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Competing interests: JS is the BMA’s lead on health and human rights.


**DEPENDENCE ON OTC DRUGS**

Over the counter drugs can be highly addictive

The development of dependency on over the counter (OTC) drugs is often forgotten.1 In the past three months we have seen three patients with addictions to Nurofen plus (ibuprofen and codeine phosphate). All three had started using the product for
its approved indications, but their use had escalated as they became tolerant to the codeine element. Each patient presented with side effects related to ibuprofen.

Codeine phosphate is now only available on prescription but has been available over the counter in combination with aspirin, paracetamol, or ibuprofen for many years.

A Medline search found no research into addiction to OTC drug dependence in the UK. Numerous websites are, however, documenting cases of addiction and offering support to those people trying to withdraw from these drugs. Websites such as over-count.org.uk and codeinefree.me.uk tell many personal stories, often remarkably similar and usually starting with appropriate use of analgesia for pain such as back injury or menstrual cramps. Postings on the over-count website illustrate the most common addiction is to Solpadeine (paracetamol and codeine) and suggest more than 4000 people registered there currently have this problem.

There are no official statistics documenting the extent of dependence on legal non-prescription drugs. We need large scale research to assess and monitor the extent of the problem.

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Competing interests: None declared.
1 Zarocostas J. Misuse of prescription drugs could soon exceed that of illicit narcotics, UN panel warns. BMJ 2007;334:444. (3 March.)

Blinding is better than masking

We agree with Morris et al that “blinding” terminology is probably inappropriate in ophthalmological settings.1 However, we disagree that these settings should ordain terminology for all randomised trials. They describe “masking” done in 1784 and provide dictionary definitions of masking and blinding to buttress their argument for using masking terminology. The techniques used in 1784, however, were not termed masking, and regular dictionaries do not adequately define methodological terms for clinical trials.

Blinding in clinical research enjoys a splendid history spanning over two centuries.2 Over the years it became entrenched in the tenets of medical research, and most researchers and readers grasp its meaning, although they have more difficulty understanding the different types of blinding.3 Evidently, “blinding” terminology surfaced when Antoine Lavoisier and Benjamin Franklin actually blindfolded (not masked) participants to shelter them from knowledge in their evaluations of the therapeutic claims made for mesmerism.4 The visual imagery of blindfolding, a complete covering of the eyes, conveys stronger bias avoidance than masking, where eye openings allow extensive viewing.5 Moreover, the International Conference on Harmonization (ICH) guidance primarily uses “blinding” terminology.6 The long history, pervasive general understanding, strong visual imagery, and adoption by the ICH lead us to suggest that “blinding” should remain the predominant terminology.

However, we encourage authors to be more descriptive when describing the blinding used in the conduct of their randomised trial. For example, reporting that “participants and care providers were blinded” is more informative than simply stating “double blinding was used.” Moreover, with global electronic access to articles, if authors use “masking” they jeopardise communication. Medical researchers in Africa and Asia, for example, have little familiarity with masking terminology. Totally discarding blinding terminology seems imprudent.

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Competing interests: None declared.
1 Morris D, Fraser S, Wormald R. Masking is better than blinding. BMJ 2007;334:799. (14 April.)

TRANSAPRENCY OF NICE

NICE was explicit in constructing guideline

Fahey questions the transparency of the model used in the 2006 update of the NICE (National Institute for Health and Clinical Excellence) hypertension guideline and of the process of stakeholder consultation.1 The 2006 NICE hypertension guideline brought together NICE and the British Hypertension Society in developing a single guideline, using robust methods to consider both clinical and cost effectiveness.2

The fact that Fahey was able to contribute detailed, constructive criticism of the guideline model’s assumptions illustrates the transparency with which the model was laid bare for public consultation. His comments on behalf of the Royal College of General Practitioners were considered by the guideline development group, along with many others, and influenced the final model and recommendations. For example, many stakeholders asked for heart failure to be given more prominence as an adverse outcome in the model, and this was done. All comments from registered stakeholders are available, together with the developers’ responses, in a 126 page document available on NICE’s website (http://guidance.nice.org.uk/page.aspx?o=394279). We are unclear why Fahey should contrast NICE with SIGN’s (Scottish Intercollegiate Guidelines Network) methods, as SIGN does not routinely undertake economic modelling.

Fahey’s criticisms of the transparency of arrangements for stakeholder involvement is in contrast to the view expressed by the World Health Organization when it reviewed NICE’s clinical guidelines programme in 2006. Its independent report says that collaboration with stakeholders in the development of the guidelines through the consultation and feedback mechanisms available was in general very effective.3

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Competing interests: None declared.
1 Fahey T. Transparency in NICE: Construction and assumptions of models should be explicit. BMJ 2007;334:814. (21 April.)
Benefits of contract may not be known for years

Adrian O’Dowd  LONDON
The government has admitted that it will have to wait years before it discovers whether there are real productivity gains from the new consultants’ contract.

NHS leaders also told the House of Commons Committee of Public Accounts last week that lessons had been learnt from mistakes made when the contract was introduced, such as not piloting it before implementation. They were giving evidence as part of the committee’s inquiry into the consultants’ contract.

The session was prompted by the publication earlier this month of a report from the government’s spending watchdog, the National Audit Office (BMJ 2007;334:865, 28 Apr).

Edward Leigh, the Conservative MP for Gainsborough and the committee’s chairman, said that that report had been damning, and he asked why the contract cost £715m (€1.1bn; $1.4bn) in the first three years—£150m more than estimated—“without any discernable increase in productivity.”

Giving evidence, David Nicholson, chief executive of the NHS, said that the negotiations over the contract were complex and that the Department of Health had underestimated the cost.

“I don’t accept that it’s a mess,” he said. “This was a new contract that we tried to implement over a relatively short space of time. The key thing about it is the potential it gives local management to connect consultant workload with what patients need.”

“It is too early to tell yet whether we are going to get many of the productivity gains that we wanted,” he said. “This is a long term solution to something that has been going on for many years.”

The National Audit Office’s report can be seen at the publications section of www.nao.org.uk.

Blair trumpets Labour’s investment in NHS

Lynn Eaton  LONDON
Prime Minister Tony Blair has trumpeted his government’s investment in the NHS over the 10 years since he came into power and has hit out at the media for always focusing on the negative.

“The single most difficult thing is to get a sense of balance,” he told an invited audience of health service managers, doctors, nurses, and NHS leaders at a breakfast meeting on Monday at the health charity the King’s Fund in London. His comments came days before he was due to announce the date of his handover to his successor, Gordon Brown, the current chancellor of the Exchequer.

The prime minister was speaking almost 10 years to the day since he won the election in 1997 and set in train a series of reforms, including the introduction of the private and independent sector as alternative healthcare providers to the NHS and giving patients a choice of provider.

“We’ve obviously got a great deal of work to do to take people with us on these reforms,” he said. “However, I personally think that [these reforms] will stay in place. I can’t see any government turning their back on that.”

Mr Blair spoke after various speakers, including James Johnson, chairman of the BMA, gave a brief overview of the state of the NHS in the last decade. All speakers acknowledged the investment in the NHS over that period. Annual growth over the decade has averaged 6.6%, whereas for the whole of the period 1949-50 to 1999-2000 average growth was 3.4%.

“There is not a single person [who has spoken] who hasn’t acknowledged the improvements,” said Mr Blair as he began his speech. He cited the “real improvement” in waiting times, which, he said, had been the main problem when Labour came into power.

He raised his concerns at proposals, mooted by Gordon Brown among others, of an independent board for the NHS that might enable the NHS to distance itself from political interference.

“I would be very worried if it became a means to avoid taking decisions,” he said.

In response to questions, he admitted that it might have been better to have had fewer reorganisations.
Number on UK transplant waiting list reaches new high

Roger Dobson ABERGAVENNY
The number of people in the United Kingdom waiting for an organ transplantation reached an all-time high of 7234 in March this year.

But although the number of patients waiting for an organ has never been higher, the number of transplantations being carried out has also reached a record level. In the 12 months to March this year a total of 3074 transplantations had been carried out, 10% more than in 2005-6.

The UK Transplant Authority says that more organ donors are urgently needed to keep pace with the rising number of people awaiting a transplantation.

“The number of patients waiting a transplant is greater than ever before, and it is vital that if people wish to help others live after their death they make their intentions known by talking to their families and joining the NHS organ donor register,” said Chris Rudge, the authority’s managing director.

He said the record number of patients getting organs showed that the authority’s policy of investing in programmes to increase the number of donors is working. Some 1.1 million more people joined the register during the year, taking the total to more than 14 million.

The latest figures from the authority, for 2006-7, show that transplantations of almost all types of organ were up on the previous year, although the 2400 cornea transplantations were 100 fewer than in 2005-6.

Since 2001 the total number of transplantations has risen by 16%, but over the same period the number of patients on waiting lists has risen by 30%. The authority says that the greater demand for transplantations is due to an ageing population, an increase in kidney failure, and scientific advances that allow more patients to benefit from a transplant.

The figures also show that although the number of non-heart beating donors has risen by 280% since 2001, the number of heart beating donors—the main source of organs—has fallen by 10%. The authority defines heart beating donors as those who die on a ventilator in a hospital intensive care unit, and it says that this group of patients is more affected by improvements in road safety, advances...
in treatment, and the prevention of strokes in younger people.

Over the last six years the authority has invested £14m (€21m; $28m) in hospital based programmes to increase opportunities for donation and widen access to transplants. The programmes include 25 living kidney donor schemes, which enable a patient to receive an organ from a living friend or relative.

See www.uktransplant.org.uk.

Health secretary should resign over job applications debacle

Lynn Eaton LONDON

Angry junior doctors called for the resignation of the health secretary, Patricia Hewitt, and the minister of state for quality in the health department, Lord Hunt, after what the BMA’s chairman described as a “difficult” meeting of the association’s Junior Doctors Committee in London on Saturday.

Delegates were so angry and frustrated that they were turning on each other, James Johnson told the audience at a breakfast briefing on Monday at the health charity the King’s Fund.

But the BMA leaders managed to fend off a vote of no confidence at the Saturday meeting. Instead the anger was turned on government ministers, who, said the committee’s deputy chairman, Tom Dolphin, had been warned of the pending disaster over the medical training application service (MTAS).

Dr Dolphin, who proposed the motion calling for the two ministers’ resignation, said it was important that the ministers accepted responsibility for the situation that had developed. “The government was warned,” he said. “They need to accept responsibility and to resign.”

The more than 200 delegates at the meeting mandated their representatives to continue to attend talks with the MTAS review group, led by Neil Douglas, president of the Royal College of Physicians of Edinburgh. They also agreed that the chairwoman of the Junior Doctors Committee, Jo Hilborne, should argue for all doctors throughout the UK to be interviewed for each of their four chosen posts, so they are treated the same as those in Scotland, Wales, and Northern Ireland.

They also want all training under the Modernising Medical Careers (MMC) scheme to be postponed for a year until the MTAS problem was sorted out.

For up to date news on MTAS go to http://blogs.bmj.com/category/comment/mtas/.

US health experts consider a centre for effectiveness

Bob Roehr WASHINGTON, DC

The possibility of setting up a centre to evaluate the effectiveness of health care in the United States was discussed at a Capitol Hill policy forum in Washington, DC, last week.

The participants at the forum, which was organised by the Alliance for Health Reform and the Commonwealth Fund, thought that such a centre could be useful because of the escalation in spending on health care—in absolute terms and relative to the economy—and because health outcomes in the US were often poorer than those in other industrialised democracies that spent far less on health.

The forum’s moderator, Stuart Guterman, from the Commonwealth Fund, said that the forum’s consensus was that better information and better decisions were needed.

The health economist Gail Wilensky, a senior fellow at the international charity Project Hope, said that other countries are ahead of the US when it comes to evaluating comparative effectiveness. But they tended to focus on drugs and to review existing literature, not conduct their own research.

For a US centre Dr Wilensky envisages “a model that is quite different,” focusing on medical conditions, not on specific interventions, and including the full spectrum of preventive and treatment options. It would also conduct its own research into efficiency, directly and through grants and contracts.

She said that such a centre “should be close to government, but maybe not too close.” Both the political left and right have concerns about vulnerability to political pressures.

Unlike most European single payer health care systems, the US has many players making healthcare policy decisions—and that was not likely to change any time soon, she said. The new entity should include all stakeholders in its governing and advisory boards, and ideally it would be funded through a variety of mechanisms and sources.

Steven Pearson, director of the Institute for Clinical and Economic Review at Harvard University, drew on his experience during a sabbatical year he spent at the UK National Institute for Health and Clinical Excellence to illustrate the importance of including all stakeholders in setting the standards for evaluating an intervention.
Nearly all English practices are set to run their own budgets

Zosia Kmietowicz LONDON

Almost all general practices in England have signed up to practice based commissioning and are preparing to draw up plans to take control of their own budgets.

Figures from the Department of Health show that as of March this year 96% of practices have been receiving incentive payments—a nationally negotiated “directly enhanced services payment” or a local alternative—which commits them to practice based commissioning by 2008.

The government believes that widespread use of the system will reduce admissions to hospital, because under the scheme GPs are able to keep at least 70% of the savings they make by directly commissioning services. They can then use the savings to develop specialist services within their own practices by investing in diagnostics, equipment, specialist care, or staff.

Uptake of the incentive payments has been increasing steadily since the scheme was launched in April 2005. In May last year uptake was only 40%.

Evidence from early adopters of practice based commissioning shows that practices have cut the number of patients referred for hospital treatment by between 25% and 33%. A 25% reduction in referrals across the country would mean 2.5 million fewer hospital appointments.

Cost effectiveness of heart drugs varies widely, study says

Roger Dobson ABERGAVENNY

The cost effectiveness of treatments for coronary heart disease varies more than 100-fold, a new study shows.

It found that the cost for each life year gained of aspirin and β blockers (pictured) for secondary prevention after a heart attack worked out at less than £1000 (€1500; $2000), whereas the cost of statins used for primary prevention in men aged 35–44 was around £70 000 (Quarterly Journal of Medicine 2007;100:277-80).

“Large amounts of NHS funding are being spent on relatively less cost effective interventions, such as statins for primary prevention, angioplasty, and coronary artery bypass graft surgery. This merits debate,” say the authors, from the University of Liverpool and Liverpool School of Tropical Medicine.

They estimated that, in 2000, medical and surgical treatments prevented or postponed 25 888 deaths in patients with coronary heart disease aged 25-84 years, generating 194 929 extra life years between 2000 and 2010 (range 143 131 to 260 167).

In the study the authors worked out the number of life years gained from 2000 to 2010 for individual treatment categories, including acute myocardial infarction, secondary prevention after acute myocardial infarction or revascularisation, unstable angina, chronic angina, heart failure in hospital and in the community, and primary prevention using statins.

Their results show that aspirin and β blockers for secondary prevention after myocardial infarction or revascularisation for angina and for heart failure were highly cost effective at less than £1000 per life year gained.

Other secondary prevention treatments, including cardiac rehabilitation, ACE inhibitors, and statins, were reasonably cost effective (at £1957, £3398, and £4246 per life year gained, respectively), as were coronary artery bypass graft surgery (£3239 to £4601) and angioplasty (£3845 to £5889).

Primary angioplasty for myocardial infarction was intermediate (£6054 to £12 057, depending on age), and statins in primary prevention were much less cost effective (£27 828, but as much as £69 373 in men aged 35–44).

Publicly available performance tables do not make surgeons

Susan Mayor LONDON

A new study shows that the introduction of publicly available performance tables in the United Kingdom showing mortality after major cardiac surgery by individual surgeons did not result in fewer procedures being performed on high risk patients, as critics had predicted. The study also shows an association between the introduction of the tables and a decrease in mortality.

The study, published online in Heart (http://heart.bmj.com; doi: 10.1136/hrt.2006.106393), analysed data that were collected prospectively from all NHS centres in northwest England that undertake cardiac surgery. The data covered 25 730 patients undergoing coronary artery bypass grafting for the first time between April 1997 and March 2005. Figures were for 30 different surgeons in four major NHS sites.

The researchers compared surgery carried out before and after individual cardiac surgeons’ outcomes became public in 2001, to determine whether some surgeons had become more averse to risk, operating only on patients with a lower risk of complications or death. They also assessed the effect of the introduction of the tables on patients’ mortality.

They used the EuroSCORE risk scoring system for patients undergoing cardiac surgery to divide them into low risk (EuroSCORE 0-5), high risk (6-10), and very high risk (11) patients. Analysis of data before and after public disclosure of surgeons’ performance showed that the number of high risk patients undergoing cardiac surgery rose rather than fell—from 449 (14% of all patients who underwent surgery) before public disclosure to 547 (17%) afterwards (P<0.001). The number of patients at very high risk who underwent surgery also rose slightly, from 41 (1.3%) to 47 (1.4%). The proportion of patients aged over 80 and of
Abortion does not raise risk of breast cancer, US study finds

Janice Hopkins Tanne

Neither induced abortion nor miscarriage increases the risk of breast cancer, a large prospective US study has found.

Results of previous case-control and retrospective studies have been inconsistent. Anti-abortion groups in the United States have claimed that having an abortion increased a woman’s risk of breast cancer by 30%, and anti-abortion counsellors used the argument to dissuade women from having an abortion.

The researchers, from Harvard University, say that about a quarter of US women aged under 45 years have had at least one induced abortion (Archives of Internal Medicine 2007;167:814-20).

They wrote, “In this cohort of young women, we found no association between induced abortion and breast cancer incidence.” They found no relation between the incidence of breast cancer and number of abortions, age at which the woman had an abortion, whether she had had a previous pregnancy, and the time between a previous pregnancy and an abortion.

The researchers found that among women who had had one or more induced abortions the hazard ratio for having breast cancer was 1 (95% confidence interval 0.9 to 1.2), after they adjusted for known risk factors for breast cancer. Among women who had had one or more spontaneous abortions the hazard ratio for breast cancer was 0.9 (0.8 to 1). Breast cancers in the study group were mostly in premenopausal women.

The study looked at the association between breast cancer and induced or spontaneous abortions in 105 716 registered nurses who were aged 25 to 42 at the beginning of the study and were free of cancer.

Previous studies had retrospectively asked women with breast cancer if they had had an abortion. The current study’s lead author, Karen Michels of Brigham and Women’s Hospital, said they had “selected women with breast cancer whose records could be confirmed for 99% of the women reporting an abortion. The panel concluded that no link between induced abortion and breast cancer was significant. In the study 1458 (about 1.4%) developed breast cancer. The researchers reviewed medical records and found that breast cancer was histologically confirmed for 99% of the women reporting breast cancer whose records could be found.

The authors say that a full term pregnancy before the age of 35 reduces a woman’s lifetime risk of breast cancer, perhaps by speeding up breast cell differentiation. They wrote, “An incomplete pregnancy may not result in sufficient differentiation to counter the high levels of pregnancy hormones that may foster proliferation. However, the biological mechanisms are uncertain, and a prematurely terminated pregnancy may not affect breast cancer risk at all.”

In 2003 the US National Cancer Institute convened an expert panel to review the evidence for an association between induced or spontaneous abortion and the risk of breast cancer. The panel concluded that no link existed.

avoid high risk cases

Those with kidney disease, a recent heart attack, or peripheral vascular disease all increased significantly. In contrast, the number of patients at low risk who underwent surgery fell slightly, from 2694 (85%) to 2664 (82%).

Observed mortality fell from 2.4% in 1997-8, before disclosure, to 1.8% in 2004-5 (P=0.014)—even though the expected mortality (based on EuroSCORE) rose from 3.0 to 3.5 (P=0.001), indicating that more complicated cases or more elderly people were being taken on. Overall, the ratio of observed to expected mortality decreased from 0.8 to 0.5 (P=0.05).
**C difficile infections rise—but MRSA rates drop**

**Michael Day** LONDON

The number of infections of *Clostridium difficile* in the NHS in England rose again last year. Hospitals saw 55,681 cases among patients aged over 65 years—up 8% on the 2005 figure, says the Health Protection Agency.

The latest figures come two months after it was revealed that *C difficile* and methicillin-resistant *Staphylococcus aureus* (MRSA) had killed record numbers of patients in 2005. In that year *C difficile* was mentioned on 3,807 death certificates—up 69% on the 2004 figure, the Office for National Statistics said. MRSA was a factor in 1,629 deaths, a rise of 39%

The Health Protection Agency noted that the latest increase in the number of *C difficile* cases was smaller than the 17% jump seen in 2005. And there was also evidence of the tide turning against MRSA bacteraemia. A total of 1,542 MRSA bloodstream infections from October to December 2006 represented a 7% fall from the figure for the previous quarter.

However, Katherine Murphy, director of communications at the Patients Association, said: “This is no reason for celebration. The number of deaths from *C difficile* is equivalent to a packed jumbo jet crashing every month.

“When is a [NHS] chief executive actually going to lose his or her job over this?”

The government’s chief nursing officer, Chris Beasley, said: “Many trusts that have received help from MRSA improvement teams have seen significant reduction in infection. We are determined to see these national reductions replicated for *C difficile*.

The Conservative party blamed the continuing rise in the number of *C difficile* infections on the thousands of job losses in the NHS in the past 12 months, particularly among nursing staff.

The Liberal Democrats’ health spokesman, Norman Lamb, said that tougher action was needed “to deal with the many hospitals that are not meeting acceptable hygiene standards.”

From May the Healthcare Commission will start sending “hygiene hit squads” into NHS trusts. Trusts found to be in breach of good practice “will be issued with improvement notices to ensure that they take the appropriate remedial action.”

In a *BMJ* editorial last month, however, John Starr, reader in geriatric medicine at the University of Edinburgh, questioned whether *C difficile* should be thought of as purely a hospital acquired infection and suggested that other infection control measures might be needed, such as screening people in the community before they were admitted (*BMJ* 2007;334:708).

Quarterly MRSA and *C difficile* figures are available at [www.hpa.org.uk](http://www.hpa.org.uk).

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**US health insurance firm settles lawsuit brought by 900 000 doctors**

**Fred Charatan** FLORIDA

The biggest health insurance company in the United States, Blue Cross Blue Shield, has been forced to settle a class action lawsuit brought by 900,000 doctors who claimed that they were not being fairly paid for treating patients.

The lawsuit, filed in the Southern District of Florida in Miami in May 2003, alleged that numerous insurance plans run by Blue Cross Blue Shield, which covered 77 million patients, “had conspired in a massive scheme to defraud doctors in violation of the [1970] federal Racketeer Influenced and Corrupt Organization Act (RICO).”

The Tennessee Medical Association, which filed the original class action lawsuit in 2002 against Blue Cross Blue Shield of Tennessee in Tennessee State Court, said in a statement, “The provisions of the settlement call for BCBST [Blue Cross Blue Shield of Tennessee] and other plans to pay more than $128m [£64m; €94], but more importantly to physicians the settlement will set into motion a series of important business practice changes that bring the estimated value of the entire settlement consideration to well over $1bn.”

The changes called for are in the health insurers’ systems for processing reimbursement claims from the doctors. These systems look at doctors’ claims and often reduce them by combining or rejecting charges. Insurers maintain that such systems check for redundant or excessive billing so as to cap medical costs. The doctors and their medical societies say that the insurers conspired to systematically cheat them out of full payment.

The Blue Cross Blue Shield group has promised to change certain practices and among other points has agreed to:

- Implement a definition of medical necessity, which ensures that patients are entitled to receive medically necessary care as determined by a doctor in accordance with generally accepted standards of medical practice, and
- Use clinical guidelines that are based on credible scientific evidence published in peer reviewed medical literature.
Access to health care in Afghanistan is improving

Tessa Richards BMJ
An independent evaluation of health services in Afghanistan carried out by Johns Hopkins University has shown that access to care and key health indicators have improved over the last three years.

Speaking at a press conference in Kabul last week to draw attention to the study, Mohammad Amin Fatimi, the country’s minister of public health, said that the data provided “clear signs of health sector recovery.” Access to health care is markedly better in secure provinces than in insecure areas, such as Helmand (above).

Further evidence of this recovery came from a conference on health research held earlier in the week to mark the opening of Afghanistan’s first public health institute.

“This was a landmark event,” said Egbert Sondorp, senior lecturer at the London School of Hygiene and Tropical Medicine, who has been working in Afghanistan for several years. “It’s the first time since 2001 that health researchers and others concerned with service provision have been able to come together to share results and exchange expertise.”

The conference also debated the smuggling of drugs. Currently brand name formulations of antibiotics and a range of basic drugs, including paracetamol, are being smuggled into the country illegally because obtaining them in generic formulations through the normal government channels is slow and cumbersome.

One of the major challenges for Afghanistan’s health sector is providing primary care services at a cost that poor people can afford. Currently, Dr Sondorp said, an estimated 30% of the population have to sell assets to pay for their medical care.

The establishment and roll-out of a basic package of health care in Afghanistan, delivered primarily by non-governmental organisations, began in 2004 (BMJ 2006;332:718-21).

The Johns Hopkins survey of 600 publicly financed health facilities between 2004 and 2006 shows that this package has improved access to care for most of the population but that it is still not reaching people in remote rural areas and provinces where security is poor. The survey found that infant mortality fell from 165 deaths per 1000 in 2001 to 135 in 2006; and provision of antenatal care increased from 5% of women in 2003 to 30% in 2006.

Nations support stockpile of H5N1 vaccine by WHO

John Zarocostas GENEVA
Rich and developing countries—and vaccine manufacturers—have backed calls by the World Health Organization to try to establish a stockpile of vaccine against the H5N1 strain of influenza in humans. They also want to see a mechanism to ensure wider access to a vaccine by poor nations in the event of a flu pandemic.

At a one day meeting at WHO headquarters in Geneva last week, stakeholders also agreed to the setting up of expert groups to focus on how to create, maintain, fund, and use an H5N1 vaccine stockpile. WHO said that it would continue to consult with appropriate partners and member states on developing a mechanism for access to a vaccine.

“I think it is a very important step in the process towards shoring [up] better access for poorer countries to vaccines that will be required in the event that they are affected by or at risk of an influenza pandemic,” said David Nabarro, the UN’s global coordinator for pandemic preparedness.

Although no target figure for the stockpile of H5N1 vaccine has so far been agreed, during a WHO meeting in Indonesia in March officials from developing countries said that they were looking at coverage of roughly 1% of their populations—enough to cover health workers, police, and other essential staff.

Margaret Chan, WHO’s director general, noted: “We have taken another crucial step forward in ensuring that all countries have access to the benefits of international influenza virus sharing and pandemic vaccine production.”

But Dr Chan earlier warned delegates at the meeting that current vaccine manufacturing capacity “is woefully inadequate to meet worldwide demand.” She added: “The issue of access to vaccines has acquired an urgency that we cannot fail to address.

“For a trivalent pandemic vaccine, annual manufacturing capacity is about 500 million doses. For a monovalent vaccine this figure increases to 1.5 billion doses. This is still not enough.”
Older people get weaker during bed rest

Older people lose substantial amounts of skeletal muscle when they stay in bed for more than a week, according to an experiment in healthy volunteers. Twelve men and women with a mean age of 67 had a series of tests before and after being confined to bed for 10 days. They ate a standard diet containing the recommended daily amount of protein. Muscle protein synthesis decreased by 30% during the experiment (95% CI 7% to 54%) and they lost a mean of 1.5 kg of lean body mass (0.62 to 2.48). Most of the loss was from their legs, which became significantly weaker as a result. The volunteers’ nitrogen balance was negative even before the experiment started, but it fell further during bed rest, despite the balanced diet. These volunteers were healthy and reasonably active, say the researchers. The adverse effects of 10 days in bed are probably even greater for older people in hospital who have the added disadvantages of physiological stress and poor diet. Loss of muscle mass could help explain why many older people experience functional decline when in hospital. In this experiment, healthy older people lost more lean tissue in 10 days than younger people would be expected to lose in a month. 

JAMA 2007;297:1772-3

New antifungal looks safer than liposomal amphotericin B

Micafungin is the newest in a class of antifungal agents called echinocandins. A recent trial showed that it works as well as liposomal amphotericin B, but has a significantly better safety profile when used to treat patients with invasive Candida infections.

The trial, which was sponsored by the manufacturers of micafungin, compared both drugs in 531 adults, most of whom had Candida in their bloodstream. The infection cleared or partially cleared in almost 90% of patients given either drug (181/202 (89.6%) vs 170/190 (89.5%)). But those given micafungin had better preserved renal function during treatment than controls. They also had less back pain during infusions (1/264 (0.4%) vs 12/267 (4.5%); P=0.003) and fewer electrolyte disturbances. Patients given micafungin were less likely to stop treatment because of serious side effects, although the difference wasn’t statistically significant (13/264 (4.9%) vs 24/267 (9.0%); P=0.087). Death rates were high in both groups, but most deaths were due to the underlying disease, not the invasive fungal infection. 


Common genetic polymorphisms linked to macular degeneration

Researchers have found two common genetic variants that help predict which patients with age related macular degeneration will progress to the sight threatening form of the disease. Polymorphisms of the CFH and LOC387715 genes were both significantly and independently associated with progression in an analysis of data from a randomised trial of vitamin and mineral supplements. The odds ratios were 2.6 (95% CI 1.7 to 3.9) for the CFH risk genotype and 4.1 (2.7 to 6.3) for LOC387715 risk genotype after adjusting for other risk factors and for the treatment arm of the randomised trial.

Half (48%) of those patients who were homozygous for the risk alleles of both genes progressed to severe macular degeneration during a mean follow-up of six years. Only 5% of patients with neither risk genotype progressed. Smokers with both risk genotypes who were also overweight were 19 times more likely to develop severe disease than people with none of these three risk factors. 

JAMA 2007;297:1793-800

US doctors still have strong ties with drug industry

Relationships between the medical profession and the drug industry are often highly visible these days, thanks to sustained attention from the medical and scientific media. Despite the critical spotlight, such relationships are almost universal among American doctors, according to a large survey.

Out of 1662 respondents (1662/3167), 94% reported associations with the drug industry, usually related to free food, drink, or drug samples. Some had also received expenses for attending meetings (35%) or payments for consulting, lecturing, or enrolling patients in trials (28%). Cardiologists were significantly more likely than other hospital specialists or primary care doctors to receive payments for professional services, possibly because drug companies target doctors whose prescribing habits are likely to influence others, say the researchers.


Antidepressants ineffective in bipolar depression

The antidepressants bupropion and paroxetine don’t work for patients with major depression associated with bipolar disorder, report researchers from the United States. In the largest trial to date, neither drug helped patients achieve a durable remission when used in conjunction with a mood stabiliser such as lithium.

Only about a quarter of participants got better from their depression and stayed well for at least eight weeks—23.5% (42/179) of those given a mood stabiliser and an antidepressant, and 27.3% (51/187) of those who had a mood stabiliser and placebo.
Antiretroviral agents associated with heart attack

Researchers investigating the cardiovascular effects of antiretroviral drugs have found a significant association between protease inhibitors and myocardial infarction in 23,437 adults with HIV. The risk was modest—an increase of 16% (95% CI 10% to 23%) each year—and was partly explained by worsening serum lipids, a known side effect of protease inhibitors. Non-nucleoside reverse transcriptase inhibitors were not associated with myocardial infarctions in this cohort, although the researchers warn that this finding isn’t particularly reliable (relative rate per year of exposure 1.05, 0.98 to 1.13).

These data come from an international collaboration of 11 different cohorts from Europe, the United States, and Australia. The participants were followed up for more than four years and had been taking antiretrovirals for a median of seven years.

It’s impossible to know from this kind of study whether protease inhibitors actually cause cardiovascular disease or whether non-nucleoside reverse transcriptase inhibitors are indeed safer. A linked editorial (pp 1773-5) says doctors should note the reported associations but remember that uncontrolled viraemia is considerably more dangerous than either class of drug. And so is smoking, which is common among adults with HIV. Doctors should concentrate on aggressive treatment of HIV infection and tackle traditional cardiovascular risk factors first, it says.


New recreational drug has its first casualty in UK

Piperazines were developed to treat worm infestations in animals. But they’ve become a popular recreational drug because in the right blend they mimic the high induced by ecstasy (methyleneoxymethamfetamine). An 18 year old girl became the first reported casualty of this new drug in the United Kingdom when she collapsed in a London nightclub. She fitted for 10 minutes but made a full recovery after treatment with benzodiazepines. Toxicological analysis of her blood found benzylpiperazine, and nothing else. She had bought the tablets from a dealer thinking they were amphetamines or ecstasy.

The piperazines have an undeserved reputation for safety, writes one commentator (pp 1411-3). This case report may be the first in the UK, but many other cases have probably been misdiagnosed. Doctors have yet to catch up with the new recreational drugs and could easily mistake piperazine poisoning for the more familiar amphetamine poisoning. The symptoms are similar and include vomiting, hypertension, agitation, and seizures.

Benzylpiperazine became illegal in the UK in March this year. Other piperazines are widely sold as legal alternatives to controlled drugs. Doctors should expect more cases of poisoning. They should also be aware that routine toxicological screens don’t detect piperazines.

Lancet 2007;369:1490, 1411-3

Disease resurgence threatens success of pneumococcal vaccine

The native children of Alaska have always been vulnerable to pneumococcal diseases such as pneumonia and meningitis, despite the apparent success of a heptavalent childhood vaccine introduced in 2001. The vaccine all but wiped out invasive disease caused by seven specific serotypes, but other serotypes have emerged to take their place, say researchers.

Ongoing surveillance shows that rates of invasive disease among native Alaskan children under 2 years increased by 82% between the two surveillance periods 2001-3 and 2004-6. Most cases were of the pneumococcal serotypes not covered by the vaccine. Serotype 19A was the most common. Rates of disease among non-native Alaskan children remained low.

Experts worried about the prospect of serotype replacement even before the original seven valent vaccine was licensed, says an editorial (pp 1825-6). The resurgence of these serious infections in native Alaskan children could signal similar problems for less vulnerable populations elsewhere and ultimately threaten the otherwise “spectacular” success of the national vaccination programme.

New 13 valent vaccines are already in the pipeline, says the editorial. But they may have to be modified every five to 10 years until scientists develop a vaccine that protects children from all known serotypes of Streptococcus pneumoniae.

JAMA 2007;297:1784-92, 1825-6

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JAMA 2007;297:1784-92, 1825-6
SHORT CUTS EXTRA

WHAT’S NEW IN BMJ JOURNALS

Harvey Marcovitch, BMJ syndication editor h.marcovitch@btinternet.com

Carpal tunnel syndrome rarely predicts underlying disease

When researchers screened for raised blood glucose, thyroid stimulating hormone, and erythrocyte sedimentation rate in 386 of 516 consecutive patients retrospectively identified to have carpal tunnel syndrome, they found that only four patients had positive results; 130 patients had been excluded from the screening because of a previous diagnosis of diabetes mellitus, hypothyroidism, or connective tissue disorder.

Two patients were found to have diabetes mellitus (a positive predictive value for screening of 0.5%; 95% confidence interval 0.1% to 1.7%); two were hypothyroid (0.4%; 0.1% to 1.5%), and none had connective tissue disorder. Despite these largely negative findings, the authors say that some might consider that the €1468 (£1000; $2000) cost per diagnosis of hypothyroidism (and fourfold lower cost for diabetes mellitus) is a worthwhile expenditure.

J Neurol Neurosurg Psychiatry 2006; doi: 10.1136/jnnp.2006.102145

Road traffic noise linked to hypertension

A linear exposure-response relation was found between road traffic noise and self-reported diagnosis of hypertension in 667/1000 residents of Stockholm, Sweden, who responded to a questionnaire.

About half the subjects lived within 100 metres of a highway or other main road, and the rest acted as controls. Noise exposures were measured, modelled, or assessed by a noise specialist. The odds ratio for reported hypertension in those who had lived in their house for >10 years, whose house was built before 1976, and whose bedroom windows faced the street or had no triple glazing. Occ Environ Med 2007;64:122-6

Chondroitin sulphate may help knee osteoarthritis a little

A randomised controlled trial of 1000 mg/day of chondroitin sulfate versus placebo for six months showed a minor advantage of the drug in relieving pain. This result, however, was regarded by the investigators as of questionable clinical import, with no significant difference in function over placebo. Both groups (just over 150 patients in each) with symptomatic knee osteoarthritis were permitted to take rescue medication, and no difference was seen in their use of analgesics or non-steroidal anti-inflammatory drugs. Similarly, no difference was found in relevant biochemical markers of joint metabolism, but chondroitin was rated “slightly more effective” than placebo with regard to quality of life and as an overall assessment by the investigators.

Ann Rheum Dis 2007; doi: 10.1136/ard.2006.059899

Better interaction on prescribing needed between GPs and hospitals

Medical staff at a Copenhagen university hospital are apparently unaware of a fifth of medications used by newly admitted patients and fail to inform general practitioners about nearly 60% of medications being taken at discharge.

Two hundred patients were interviewed at home soon after hospital discharge: they were storing 1189 prescription-only medicines and using 955. Only 444 medicines were mentioned in the discharge letters to the general practitioners, while a further 305 were documented in hospital notes but not recorded in the discharge letters, despite 47 of the medications being newly prescribed. For 66 patients who were taking at least one prescription-only medicine, the discharge letter contained no record of any medication.

Ten patients interviewed were not taking a drug newly prescribed while they were in hospital, and 12 had resumed taking a medication that had seemingly been discontinued during their hospital stay, with most of these patients at risk of harmful effects. Forty prescription-only medicines were being used at a different dose or frequency from that documented on discharge.

The authors conclude that the hospital had not succeeded in producing an updated medication list nor did it successfully communicate the administration of prescription-only medicines to patients’ general practitioners. The inadequacy was especially apparent with surgical patients, 55 of 83 having no medications mentioned in the discharge letter.

Qual Saf Health Care 2007;16:34-9

“Superhero” boys live to tell the tale—just

One UK hospital reported that five boys sustained serious injury while dressed as Spiderman or Superman. At least three of them had tried to fly without a planned landing strategy. Four of the boys sustained fractures and one a minor head injury. Guidance for parents of putative superheroes is available from the American National Association for the Education of Young Children at www.naeyc.org/eece/1997/16.asp.

Arch Dis Child 2007;92:242-3

INR easily monitored at home

A portable coagulometer (CoaguChek XS, Roche Diagnostics Australia), which measures blood international normalised ratio (INR) on a fingerprick sample proved accurate and easy to use. Tasmanian patients received two training sessions and then had near synchronous tests performed with the device and by a standard laboratory method. Paired results were highly correlated (r = 0.91) and only three (5%) of the home tests differed from laboratory results by >20% or were discrepant by >0.5 INR units. Further tests are needed to evaluate its accuracy outside standard INR target ranges.

J Clin Path 2006;60:311-4
For a long time complementary medicine was seen, by the public at least, as the gentle alternative to conventional treatment. It might not work, but at least it didn’t carry the risks associated with synthetic drugs. That romantic notion was challenged more than a decade ago when nine women in previously good health developed end stage kidney disease months after receiving Chinese herbal treatment at a Belgium slimming clinic.1

But toxic herbs are not the only concern. A swift trawl through Google seems to back suggestions by the UK Health Professions Council, the regulatory body for 13 health care professions (box), that there are now over 100000 counsellors and therapists practising in the United Kingdom. In February, the council’s chief executive, Marc Seale, summed up the current situation: “At present you could come out of Wormwood Scrubs and set yourself up as a counsellor.”

One obvious solution is to regulate these professions. And nobody has been clamouring more loudly for statutory registers than some of the complementary practitioners themselves. “There are a lot of people who don’t have the necessary training and knowledge to protect the public, that’s why we need statutory registration,” says Amrit Ahluwalia, project director of the European Herbal Practitioners Association (box). “And we’re not just talking about knowing how to avoid interactions with other drugs. It’s about knowing when to refer patients to other professionals. If you’re going to be a professional dealing with the public then you need to know the limits of your competence.”

The House of Lords Science and Technology Committee put all these arguments in its report on complementary and alternative medicine in November 2000. The committee called for emerging health professions to come under statutory regulation.2 A series of working groups, consultation documents, and responses followed. But the shockwaves caused by Shipman have seen moves to regulate other health professions take a back seat, and it took until February this year for a white paper finally to emerge that looked to regulate acupuncture and Chinese and herbal medicines.3

The Health Professions Council seems likely to assume the responsibilities. It already regulates radiography, physiotherapy, occupational therapy, and biomedical scientists among others. It is preparing to take on the statutory registration of clinical psychologists within the next 12 months.

Further down the line, but ahead of herbal medicine and acupuncture, the statutory regulation of counsellors and therapists is now on the council’s growing “to do” list. Mike Pittilo, the vice chancellor of Robert Gordon University in Aberdeen, is chairing the Department of Health working group looking at how acupuncturists, herbalists, and Chinese medicine practitioners will be regulated. He is no doubt about the need for statutory regulation of these professions: “Given that around 42% of the British public access these treatments we should be regulating them and at the same time putting them under pressure to develop and show their evidence base,” he says. “If you look at other therapies, such as arts therapy or even physiotherapy or traditional medicine, the evidence base is sometimes pretty thin.

“But the difference is that I see a lot of alternative practitioners being completely indifferent to the need to get better evidence-based practice within the profession.”

The association was set up in 1994 as an umbrella body for professional associations across Europe wanting to benefit from joint working and to strengthen the role of the herbal profession. It represents practitioners from ayurveda, Chinese herbal medicine, traditional Chinese medicine, and Western herbal medicine. It aims to promote the availability of professional herbal treatment and to raise standards of training and practice within the profession. It also campaigns for the legalisation of professional herbal practice throughout the European Union as a specialty in its own right. A central aim is to encourage the creation of “appropriate European legislation that ensures the continuing right of professional herbal practitioners to access traditional herbal medicines.” It notes that this is likely to require statutory self regulation.
How can you regulate acupuncture and herbal medicine if we’re not sure if they’re effective?

Based practice. At least with arts therapy or medicine there’s a sense that practitioners are trying to build the evidence.”

Section 7.12 of the white paper says that practitioners would have to be assessed for competence before being admitted to a statutory register. But how will regulators assess competency in disciplines where the efficacy is not well established? Professor Pittilo says that the primary role of statutory regulation is one of protecting the public. “Statutory bodies are more about safety than efficacy. Under regulation they will have to understand the significance of how their treatments could interact with other things and of the potential harm they could cause.”

Professor Pittilo notes, however: “There’s not just the danger of adverse reactions to chemicals in herbs or the risks of infection from needles, there’s also the danger that patients might fail to seek appropriate established treatments that could save their life. There are still some terribly false claims being made by practitioners of Chinese or herbal medicines. It’s still going on with claims of cures and this kind of thing.”

Regulating the unknown

A leading critic of alternative medicine takes a tougher line on the need for measuring efficacy, however. Edzard Ernst, who is professor of alternative medicine at Exeter University, says herbal medicine and acupuncture should not be regulated until there is clearer evidence that they work.

One of his concerns is that statutory registration might be erroneously paraded as evidence of efficacy. “The evidence for the efficacy of chiropractic, for example, is very slim indeed. And since it has been regulated, research for establishing that it works has diminished. People are saying: ‘We are fully regulated so don’t ask us questions about whether this works or not’; and that is very worrying.

“And how can you regulate acupuncture and herbal medicine if we’re not sure if it’s effective? In the absence of an evidence base it seems ridiculous.”

He concedes there is evidence that acupuncture is effective for back pain and knee osteoarthritis. “However, for most uses the Cochrane Database shows that it is no better than placebo. So we’re effectively regulating placebo therapies.”

His most serious criticisms surround herbal and Chinese medicines, however, which he says “can kill.” He makes a distinction between the over the counter “phyto-medicines,” such as St John’s Wort, with reasonably well defined pharmaceutical properties, and the more arcane herbal mixtures prescribed on an individual basis.

Professor Ernst says that only three credible clinical trials of individualised herbal medicine have been done: in the UK, Australia, and Asia. “And the results suggest there are no benefits beyond that of placebo.”

He says that acupuncture can help relieve my symptoms of acid indigestion. He stresses that Eastern medicine uses products and treatments that are “more natural” and “less likely to cause addiction. This has been around for 3000 years, so it’s got to be doing something right.” He concedes that sticking lots of needles into someone’s body “isn’t exactly natural, but there’s evidence it works and the evidence shows that it’s one of the safest of all interventions.” And a BMJ editorial by medical safety expert Charles Vincent has confirmed this, he says. He too seems unconvinced about the need for statutory regulation of acupuncturists and herbalists. “I already am registered with British Acupuncture Council, so I’m not sure whether that’s necessary or not.”

Chinese medicine practitioner

I visit the Green Healer, a traditional Chinese medicine centre in south London, and ask about treatment for acid indigestion. The practitioner inquires about my diet and sleeping habits in a 15 minute consultation, during which she studies my tongue and feels my pulse in both wrists.

She diagnoses a stomach Ying deficiency, made worse by eating too late at night. “In Western medicine you give out a prescription, and the person takes the drugs and that’s it. In Chinese medicine we believe that it’s important to make lifestyle changes too,” she says.

She then makes up three bags each containing a mixture of around 15 herbs and tree bark taken from hundreds of boxes labelled in Chinese. I am told to boil them up and drink the solution three times a day. I’m assured the mixture is quite safe, if unpleasant to drink. I ask her if she thinks it’s a good idea for practitioners like her to come under statutory regulation. She’s unconvinced: “I already am a member of the register of Chinese Herbal Medicine.”

Acupuncturist

Anton Michael Rocke is an acupuncturist who consults at the Diagnostic Clinic in New Cavendish Street, London, and treats people in nearby Harley Street. He works with “Western practitioners” so patients “get the best of both worlds.”

He says that acupuncture can help relieve my symptoms of acid indigestion. He stresses that Eastern medicine uses products and treatments that are “more natural” and “less likely to cause addiction. This has been around for 3000 years, so it’s got to be doing something right.” He concedes that sticking lots of needles into someone’s body “isn’t exactly natural, but there’s evidence it works and the evidence shows that it’s one of the safest of all interventions.” And a BMJ editorial by medical safety expert Charles Vincent has confirmed this, he says. He too seems unconvinced about the need for statutory regulation of acupuncturists and herbalists. “I already am registered with British Acupuncture Council, so I’m not sure whether that’s necessary or not.”
However, the agency notes that in the large unlicensed sector things “vary considerably” with “evidence of poor or patchy standards.”

Michael McIntyre, a herbalist near Oxford and chairman of the European Herbal Practitioners Association, takes a different view: “There is a huge amount of evidence that herbal medicine works,” he says. “The reason that I’m busy here in this village in the middle of nowhere is that doctors know that I can help with irritable bowel syndrome and migraine—things that they’re not particularly good at treating. There are not going to be big, expensive clinical trials funded by drugs companies that show these things work, because the companies would not be able to patent herbs and therefore would not be able to get their money back. And Edzard Ernst is wrong when he says these professions should not be regulated until there’s an evidence base. Lots of good people would be deterred from entering the professions if they knew there was no immediate prospect of being able to join a proper register.”

Practical problems
But even the supporters of statutory registration can see some daunting logistical hurdles. And these practical problems have been brought more sharply into focus by a pressing deadline for the regulation of herbal medicine. Changes to section 12 of the Medicines Act that seek to protect people having one-to-one consultations with herbal medicine practitioners will mean that by 2011 practitioners must be part of a statutory register.

If a statutory register is not in place by then, “it will mean that no-one will be able to practise herbal medicine in the UK and the whole practice will be driven underground,” says Professor Pittilo. The omens for this deadline being met are not good.

Victoria Nash, a spokeswoman for the Health Professions Council, admits that her organisation is not even sure how it will measure the competence in professions such as counselling or therapy, which are ahead of acupuncture and herbal medicine in the queue for registration. “If you’re treating something like a broken leg, it’s fairly easy to see if there’s an improvement. But it’s hard to measure improvement with things like counselling,” she says.

She says the council has not even begun to work out how continuing education and re-accreditation—two key aspects of a statutory register—will be organised. And then there’s the sheer scale of the operation. She says that there are currently around 175000 practitioners of various sorts registered with the council. “It could rise to 350000 when we take on counsellors and therapists, and I just don’t know how that will work.”

Intriguing, to say the least, is her suggestion that the size of the workload might require revalidation to be done on a sample basis. So will it be possible to do all this and set up a register for acupuncturists and herbal medicine practitioners by 2011? “In my experience it takes a long, long time to do these things, so they’re probably being rather optimistic.” So if anything can be described as a consensus it might be that there’s an awful lot that needs to be done, and not much time in which to do it.

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Competing interests: None declared.


Given the choice, I’d have the miracle pill story

Complex problems have depressingly complex causes, and the solutions are often unsatisfactory.

Looking at popular culture, it seems there’s something very attractive about simple biomedical explanations—and solutions—for complex social and psychological problems.

Four weeks ago the BMJ published a large randomised controlled trial, with a positive result: it showed that one treatment for children at high risk of developing conduct disorder could significantly improve antisocial behaviour (BMJ 2007; 334: 678-82). It was a well conducted trial, at multiple sites, with a novel result, on a subject specifically called for by NICE, and it even had a compelling cost effectiveness analysis.

Was this miracle pill reported as front page news in the Daily Mail, natural home of miracle cures and sinister hidden scares? Was it followed up on the health pages, with an accompanying photo feature, describing one child’s miraculous recovery, and an interview with a relieved mum with whom we could all identify?

No. In fact, this story was completely ignored by the entire British news media, despite their preoccupation with both antisocial behaviour and miracle cures, for one simple reason: this was not a story about a pill. It was a cheap, practical parenting programme.

At the same time, for over two years now, the newspapers and television stations have gushed praise on an endless stream of largely unpublished and increasingly melodramatic claims made for fish oil pills in schoolchildren.

This represents an interesting disparity. These fish oil “miracle pill” claims are generally made on the basis of unpublished “studies,” with clear involvement of the multimillion pound pharmaceutical companies manufacturing the supplements, which are presented directly to the media with minimal corroborating evidence—no published paper, no statistics, and in essence no science at all. My attempts to get further information about the data behind various of these stories for my Guardian newspaper column have routinely been met with polite but firm obstructiveness.

This is in stark contravention of not just every published guideline on communicating research findings to the public, but also a clear challenge to common sense, since there is no meaningful opinion whatsoever, with the best will in the world, that anybody could sensibly hold about unpublished scientific research, reported only in the form of a press release and a tabloid news story.

Now there may yet turn out to be good evidence for significant benefits for children from fish oil tablets (although, in context, fish oil pills cost more per day than many councils spend on the entire school meal). That’s not my concern right here. What is interesting is where the attention of the media is drawn: weak and unpublished “scientific proof” for a miracle pill receives blanket coverage, while strong evidence for a parenting programme, from a rather prestigious academic journal, is deemed irrelevant.

Explanations abound. Firstly, of course, “pill solves complex social problem” feels more like a news story than a parenting programme does. And there is also the question of how stories are pushed: I’ve not met Hutchings et al, the authors of the parenting study, and if they want to persuade me, I’m perfectly prepared to believe that they are in Soho House until 2 am every night, schmoozing broadcast media journalists with champagne and nibbles, but in reality, I suspect they are modest academics.

Private companies, meanwhile, have top dollar public relations firepower, one single issue to promote, time to foster relationships with interested journalists, and a wily understanding of the desires of the public and the media. It is these wider cultural desires that are the key to exploiting our collective hopes and consumer dreams. Pharmaceutical companies have worked hard, let’s remember, in their direct to consumer advertisements and their lobbying, to push the serotonin hypothesis for depression, even though the scientific evidence for this theory is growing thinner every quarter, and the nutrition supplements industry, for its part, promotes dietary deficiencies as a treatable cause for low mood.

These crude biomedical mechanisms may well enhance the placebo benefits from medication. But I wonder if we also risk disempowering patients, and robbing ourselves of a deeper understanding, when we reframe complex social problems in such mechanistic terms.

The biomedical explanations may be so seductive precisely because of what they edit out. In the media coverage around the launch of pills for “female sexual dysfunction,” it wasn’t just the tablets that were being sold: stories on couples with relationship problems focused on biomedical interventions, and more than that, on hormone tests, or esoteric imaging studies of clitoral blood flow. We don’t want to talk about her feeling tired from over work, or him being exhausted by a new baby, any more than we want to talk about social inequality, the disintegration of local communities, the breakdown of the family, the impact of employment uncertainty, changing expectations and notions of personhood, or any of the other complex, difficult factors that play into the apparent rise of antisocial behaviour and depression.

In the past, medicalisation has been portrayed as something that doctors inflict on an unsuspecting world, and as an expansion of the medical empire: but in reality, biomedical narratives can appeal to us all, because complex problems have depressingly complex causes, and the solutions are often taxing and unsatisfactory. Given the choice, I’d have a miracle pill story, any day.

Ben Goldacre is a doctor and writer, London ben@badsceince.net
MEDICINE AND THE MEDIA

Thalidomide: the true story?

A legal battle in Germany over a TV drama about thalidomide has put the 50 year old tragedy back in the headlines.

Annette Tuffs reports

One of the worst tragedies in the history of drug therapy began almost 50 years ago, on 1 October 1957, when thalidomide was introduced as a sleeping pill by the firm Grünenthal onto the West German market. The drug, known as Contergan in West Germany, was launched in almost 50 other countries, including the United Kingdom and Canada, mostly under licence. It had sedating effects and seemed to be well tolerated and without toxic side effects, even in pregnancy. Two years later the link between the pill and serious malformations in newborn babies was discovered. Worldwide, about 12,000 children with limb deformations were born.

This anniversary should have been accompanied by the broadcasting of the television drama “Eine einzige Tablett” (“Just one pill”) in two 90 minute episodes on the German state television Westdeutscher Rundfunk, which had commissioned the programme from the award winning producer Michael Souvignier and his production firm Zeitsprung. However, legal battles are threatening the launch, and a fierce debate in the German media between Grünenthal, Westdeutscher Rundfunk, and Zeitsprung. However, legal battles are threatening the launch, and a fierce debate in the German media between Grünenthal, Westdeutscher Rundfunk, and Zeitsprung has recalled the events of the Contergan tragedy 50 years ago.

At the core of the legal dispute are two questions: how accurately should a fictional television drama based on real events report details of the events and the people involved, and, how far can artistic freedom go without hurting personal rights and feelings?

The film is the story of a young lawyer and his wife whose child is born with malformations after the wife took just one Contergan pill. With a doctor in Hamburg the lawyer uncovers the cause of the malformations and acts as a representative for the victims in the court case against Grünenthal. In the film as in reality, the firm withdrew the drug after experts’ suspicions were raised in Germany and Australia and published in the German press. Despite being found guilty, representatives of Grünenthal were not convicted of negligence, and the case was dropped when the firm established a DM100m compensation fund for the victims. The German government doubled this, and the fund now stands at €204m (£140m, $279m). It provides a monthly income of about €500 to about 2500 people in Germany who were severely affected by Contergan and have no other income.

The names of the protagonists in the television drama were invented and their personal details were changed considerably, but the pharmaceutical firm appears in the film as Grünenthal. After Grünenthal read the script, it instigated a court action against the film production company Zeitsprung to alter 15 key scenes. For example, Grünenthal challenged the statement in the script that the drug was not withdrawn until more than a year after the first suspicions were raised, stating that in reality this happened after just 12 days.

“We tried to convince Zeitsprung to alter these scenes. When they did not agree we had to take swift legal action to stop the broadcasting in the interest of our staff,” said Sebastian Hillen, on whom the lawyer in the film was modelled. He alleged that his personal rights were infringed, claiming that real events and personal details were tampered with, and reality and fiction mixed.

On the basis of the 2005 screenplay, the court decision by the Landgericht Hamburg in July 2006 was in favour of both these claims. Zeitsprung was not to release the film unless changes were made in 32 instances. But a higher court in Hamburg, the Oberlandesgericht, decided on 10 April that a version of the original film revised in just one of the 32 instances could be broadcast and that the other 31 should be dismissed. The Landgericht Hamburg will decide on 11 May whether changes should be made in two critical scenes involving Grünenthal.

Zeitsprung and Westdeutscher Rundfunk welcomed the court’s principal decision on broadcasting. “We are happy that almost all obstacles have been removed by this trend setting decision which allows us in the future to handle recent historical topics in an artistic way,” said WDR-TV director Ulrich Deppendorf. Mirek Nitsch, legal adviser at Zeitsprung, pointed out that the film had not been altered or recut, as Grünenthal states; revising is a natural process in filmmaking and the final version is never entirely true to the original script. He is hopeful that the final court decision will also be in favour of the film producers.

Grünenthal sees its original claims confirmed by the Oberlandesgericht’s decision, saying that many key scenes have now been changed. The firm points out that it is still considering an appeal to the German constitutional court and has warned international television companies about buying the film. Annette Tuffs is a freelance journalist, Heidelberg

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Should patient groups accept money from drug companies?

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YES

By accepting donations from drug companies, patient groups lay themselves open to allegations that they are losing their independence and becoming part of industry’s efforts to “sell more pills.” Not taking such money reduces the opportunity that patient groups have to advance their case for better services and support the individuals and families on whose behalf they speak. Damned if they do, and damned if they don’t; is there a way to steer through this dilemma?

There is nothing inherently wrong with patient groups taking money from the drug industry provided that it does not put them under pressure to adopt a position that they would otherwise not choose to take up. Patient groups and industry share some common objectives, so collaboration is reasonable when these mutual interests overlap. Industry can provide core funding, funding for projects or publications, or both. Providing the source is acknowledged and there are no hidden strings, industry funding can be an important boost to the viability of patient groups—particularly as public or charitable funding often does not cover core costs.

No giving is free

The idea that public money, or grants from charitable trusts, come without strings attached is a fiction. No person or group will be overly keen to support a campaigning organisation if they think that their money will be used to “buy a stick to beat them with.” Government grants often give the grant making department the control over outcomes. A Charity Commission survey of over 4000 charities delivering public services showed that only 26 “felt free to make decisions without pressure to conform to the wishes of the funders” that is, the public sector.

Nor is it the case that public sector bodies display higher standards of ethical conduct than private sector ones. The World Health Organization recently seemed to be trying to use a patient organisation to disguise a grant that is diversified. Without diversified funding, patient groups can find themselves exposed. Diversity also gives protection from the fear of undue influence being exerted. Although it may be painful to walk away from a funder, doing so will be much less of a problem if your portfolio is diversified.

Ensuring independence

Patient organisations should not take money from the drug industry if they feel that it would compromise their ability to achieve their objectives. Just as many patient groups will not accept tobacco money, or other ethically unacceptable sources of funding, so they should avoid becoming over-dependent on any one funder, whether public or private. Fashions in funding change and today’s funding priority may not attract instant public sympathy. Arguments about animal experimentation or the use of embryonic stem cells, for example, are difficult to communicate through sound bites to a mass audience.

Patient groups need to be principled, but they need to be pragmatic too

Although clumsy attempts have been made in the past to use money to manipulate patient groups, the Association of British Pharmaceutical Industry recently established a framework for industry funding of patient groups. A few simple precautions help deter inappropriate offers of help. Patient groups should ask themselves about the origins of an idea for a given project—was it their own or did a third party propose it? Do they retain control over the process and the outputs? Is there any desire to conceal the payer’s identity? If financial support is out in the open and any attached strings are clear and appropriate (for example, restricted to a specific project or publication) then industry money is as good as that from any other source. Neither patient groups nor the drug industry should be shy about a relationship that has the potential to benefit not just the participants but which can also improve effective patient advocacy. Indeed, it is surprising to many working for patient groups that the drug industry is not a more vociferous champion of its relationship with patient groups. Industry funding has been an enabler for many patient groups—just as it has for clinicians and academics.

Patient groups are not naïve. They value their independence fiercely and are quite capable of spotting the strings that may be attached to funding—whatever the source. If those strings are unacceptable then most will walk away. In the experience of many patient groups, industry money often comes with fewer strings than that from other sources.

Although it can feel ideologically fine to turn your back on drug industry money, out in the real world there is a job to be done. Patient groups need to be principled, but they need to be pragmatic too. Patients demand effective advocates, and if drug company money makes this possible then bring it on. Actions that change things for the better will be welcomed by patients irrespective of the funding source. Ideological purity at the cost of preserving the status quo will and should be rejected as a cop-out.

Competing interests: AK has received hononaries from GSK and Novartis and has travelled to speak at conferences paid for by Roche, EFPIA, and Genzyme. The Genetic Interest Group has received funding from various pharmaceutical and biotechnology companies in the past year (see www.gig.org.uk/gig1/docs/brnialreport0506/website.pdf for list).

References are in the full version on bmj.com
Patient groups provide valuable support and advocacy for vulnerable people but funding the work can be difficult. Alastair Kent argues that not accepting industry money will limit the groups’ effectiveness, but Barbara Mintzes believes that the money undermines their independence.
NICE appraisals should be everyone’s business

When Newbury and Community Primary Care Trust appealed against NICE’s decision on Herceptin, it was the first to do so. Jane Wells and Claire Cheong-Leen explain the process and why other trusts should make their voices heard in appraisals of new treatments.

Publicly funded health services should aim to provide the best possible health care within the available budget. With finite resources and demand for health care growing both in quantity and cost, they are faced with increasingly difficult decisions about the services they should provide. They must balance their responsibilities to the whole population and to individual patients; consider the need for preventive, therapeutic, and long term care; weigh the merits of new against established treatments; and deliver the services they wish to provide as well as those that are mandatory. In England, primary care trusts are mainly responsible for these decisions. Following the latest NHS reorganisation there are now 152 primary care trusts, each of which commissions health services for a population of up to about 600,000.

**NICE and the NHS**

NHS provision is fundamentally influenced by the National Institute for Health and Clinical Excellence (NICE), which produces national guidance on health technologies, public health, and clinical practice. NHS organisations in England and Wales are required to implement NICE guidance on new technologies within three months of issue.

A large proportion of the treatments that NICE appraises are drugs, many of them expensive, and most appraisals result in a recommendation that they should be used. NHS organisations must then give funding of these new treatments precedence over other interventions, which can affect their ability to provide other services.

NICE appraisals consider the cost effectiveness of each intervention, with a threshold of about £30,000 (€44 000; $60 000) per quality adjusted life year (QALY). However, the appraisals do not explicitly take into account the affordability of the technologies within the NHS, and NICE does not advise on what interventions should be stopped in order to implement the new guidance. This is crucial given the overriding requirement of primary care trusts to keep within budget.

Despite the potential effect of NICE guidance, NHS organisations have made little use of the opportunities to participate in NICE appraisals and consultations. In contrast, there has often been stronger representation from groups such as drug companies, advocacy or special interest groups (which may themselves be funded by the drug industry), and professional organisations.

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| Claire Cheong-Leen |
| head of public health policy and development, Thames Valley Priority Setting Unit, Oxford OX4 2GX |

**Box 1: The trastuzumab story**

- **March 2002:** NICE approved trastuzumab for metastatic breast cancer
- **May 2005:** Abstracts of preliminary results from trials of trastuzumab in early breast cancer presented at American Society for Clinical Oncology conference
- **October 2005:** A few women receive NHS funded treatment for early breast cancer as “exceptional” cases, some after high profile court actions
- **February 2006:** Roche applies for a European licence for the drug to be used “for the treatment of patients with HER2 positive early breast cancer following surgery, chemotherapy . . . and radiotherapy (if applicable)”
- **June 2006:** NICE publishes draft guidance on use in early stage breast cancer after a single technology appraisal
- **August 2006:** Final guidance published requiring NHS implementation within 3 months. In a primary care trust serving a population of 400,000, about 77 women will require treatment annually at a cost of around £30 000 each, totalling about £2.3m a year (Berkshire Priorities Committee, paper 18a/2006)

**Trastuzumab and beyond**

In July 2006, we submitted an appeal to NICE on behalf of Newbury and Community Primary Care Trust after the publication of draft guidance on the use of trastuzumab [Herceptin] in HER2 positive early stage breast cancer (box 1). This was the first time an NHS organisation had appealed against NICE guidance. Trastuzumab was also the first intervention to be appraised under the (then draft) single technology appraisal process, and our trust was one of two invited to participate as a stakeholder.

Single technology appraisal was established “for the appraisal of single products, with single indications . . . normally . . . close to their introduction into the UK market.”{7} It differs from standard appraisal in that the evidence comes from the manufacturer rather than an independent review by an academic unit. Although the evidence is reviewed by an independent evidence review group, the manufacturer is not required to include evidence that it does not consider appropriate. Another key difference is that stakeholders can comment at several stages during a standard appraisal whereas in the single technology appraisal we were not given the opportunity to comment during the appraisal process, only a right of appeal before the final guidance was issued.

When the draft guidance was published we had serious concerns about whether it would allow trastuzumab to be used to achieve the greatest benefit for
patients, and whether the requirement to implement the guidance would undermine primary care trusts’ ability to provide health care for the whole population. We received comments supporting this view, along with concerns about the appraisal process, from individuals and NHS organisations, and the trust’s board and executive agreed to support an appeal (box 2).

Although NICE dismissed the appeal, it responded to several of the points on which we had appealed, clarifying questions about when treatment should start and which women should receive it. We had also shown that it was possible for NHS organisations to have a greater role in the NICE appraisal process. The single technology appraisal process has since been reviewed to allow earlier involvement by primary care trusts.

Participation by primary care trusts in technology appraisals is important because they have responsibility for the whole population, rather than representing a particular professional, commercial, or special interest. Our trust was the only stakeholder organisation in the trastuzumab appeal with this perspective; the other stakeholders were three patient groups, Cancer Research UK, and nine professional groups including

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**Box 2: The primary care trust’s appeal**

Newbury and Community Primary Care Trust was invited to participate in the single technology appraisal of trastuzumab as a stakeholder organisation, one of two primary care trusts selected apparently at random. As a stakeholder the trust had the right to appeal against the guidance once it was published in draft. The process gave stakeholders 15 days to respond to the draft guidance, setting out the grounds for appeal within the conditions set by NICE. This required them to show that the guidance was “perverse in the light of the evidence submitted.”

The appeal did not aim to prevent the use of trastuzumab, but sought clarification on several points:

- Which HER2 positive women should receive trastuzumab—this was not specified, except in relation to cardiac function
- When treatment should start—women in the published trials started trastuzumab shortly after completing their initial treatment. Under the guidance women whose initial treatment had been completed years previously could receive trastuzumab, despite there being no evidence of benefit
- How long treatment should last—the guidance stated that treatment should be for one year despite evidence that the clinical rationale for this was open to question and evidence from a trial excluded from the submission by Roche that 3 months’ treatment might be as effective
- The effect on NHS resources and on patients whose treatment might be displaced by the treatment and monitoring of patients receiving trastuzumab
- The uncertainty about the long term risks and benefits of trastuzumab the main study on which assumptions about effectiveness were based had a median follow-up of only a year

A team of five from the trust presented the appeal to a public hearing of the NICE appeal committee. NICE dismissed the appeal, but the final guidance contained clarification of several of the above points.
make explicit decisions about healthcare priorities, considering all patient groups and including prevention and care as well as treatment. Robust and transparent systems for decision making and priority setting are therefore essential.

The lack of involvement of NHS organisations in NICE appraisals probably reflects their limited capacity for assessing effectiveness and prioritisation. Our trust’s ability to respond to the NICE draft guidance within the required 15 days was helped by support from the Thames Valley Priority Setting Unit, which had already considered the published evidence on trastuzumab. However, many areas do not have a similar resource to draw on. The new larger primary care trusts should have more scope to include such capacity or to share their skills across a wider area, but this needs to be recognised in their plans and resourced adequately.

We were also helped by the information, comments, and support we received from a large number of individuals and NHS organisations. Good informal networks and a readiness to share the outcomes of work and offer contributions to others’ work would help organisations make best use of their limited capacity. Forums such as email discussion groups offer excellent opportunities to do this. NHS organisations selected as stakeholders in NICE appraisals may then be able to contribute more by drawing on work done elsewhere.

NHS staff and organisations should take every opportunity to participate in consultation and debate about the services the NHS should provide. NICE has now identified 18 more topics that it will consider under the single technology appraisal process, in addition to the ongoing programme of health technology appraisals. NHS organisations are likely to be invited to participate as stakeholders and should contribute.

For example, NICE is currently appraising the use of ranibizumab and pegaptanib in age related macular degeneration, a common cause of blindness in older people. These drugs could benefit large numbers of patients but are extremely expensive. Pegaptanib could cost the NHS over £0.5bn annually, and ranibizumab even more than this. Studies suggest that bevacizumab, which is currently unlicensed for this indication, could be as effective at a fraction of the cost. Input from NHS organisations could ensure that NICE’s decision considers not only the effectiveness of individual drugs but also how effective treatment can be provided for the maximum number of patients with age related macular degeneration without imposing unaffordable costs.

NHS organisations should also continue to engage with NICE about how its appraisal systems work. NICE has changed its single technology appraisal process to allow NHS organisations to comment earlier in the appraisal. However, NHS organisations might have more confidence in appraisal decisions if consultation was to be the rule rather than the exception, and if other evidence could be considered apart from that submitted by the manufacturer. The NHS’s ability to implement new technologies would also be helped by clarity on how the appraisal process has considered the effect of implementation on other NHS services.

NICE could make it easier for NHS organisations to participate in appraisals through some relatively simple steps such as flexibility over meeting dates, realistic timescales (bearing in mind that most such organisations have limited capacity), and clarity over what is required. NICE has committed to keep the single appraisal process under review and NHS organisations should have the opportunity to contribute to this.

Conclusion

National policy decisions about treatment must consider affordability in the context of all healthcare provision, as well as the clinical and cost effectiveness of individual interventions. Without this, local providers with a fixed budget may be required to give higher priority to new treatments than to established services that are more cost effective.

A two way link is essential between the makers of national policy and those required to implement it. To achieve this, NHS organisations must build their skills and capacity to participate in policy development and NICE needs to make it easier for stakeholders to submit their views.

Competing interests: JW and CCL are both employed by NHS organisations that are required to implement NICE guidance.

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Accepted: 6 March 2007
Tonsillectomy versus watchful waiting in recurrent streptococcal pharyngitis in adults: randomised controlled trial

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ABSTRACT

Objective To determine the short term efficacy and safety of tonsillectomy for recurrent streptococcal pharyngitis in adults.

Design Randomised controlled trial.

Setting Academic referral centre in Finland.

Participants 70 adults with documented recurrent episodes of streptococcal group A pharyngitis.

Intervention Instant tonsillectomy (n=36) or remaining on waiting list as control (n=34).

Main outcome measures Percentage change in the risk of an episode of streptococcal pharyngitis at 90 days. Rates of all episodes of pharyngitis and days with symptoms and adverse effects.

Results The mean (SD) follow-up was 164 (63) days in the control group and 170 (12) days in the tonsillectomy group. At 90 days, streptococcal pharyngitis had recurred in 24% (8/34) in the control group and 3% (1/36) in the tonsillectomy group (difference 21%; 95% confidence interval 6% to 36%). The number needed to undergo tonsillectomy to prevent one recurrence was 5 (3 to 16). During the whole follow-up, the rates of other episodes of pharyngitis and days with throat pain and fever were significantly lower in the tonsillectomy group than in the control group. The most common morbidity related to tonsillectomy was postoperative throat pain (mean length 13 days, SD 4).

Conclusions Adults with a history of documented recurrent episodes of streptococcal pharyngitis were less likely to have further streptococcal or other throat infections or days with throat pain if they had their tonsils removed.

Trial registration Clinical Trials NCT00136877.

INTRODUCTION

Group A streptococcal pharyngitis is an acute infection, mainly of the oropharynx, caused by Streptococcus pyogenes.1 2 Recommended treatment is antibiotics to prevent rheumatic fever and supplicative complications and to ameliorate symptoms and decrease contagion.1 3 Some patients experience multiple episodes of acute pharyngitis with results of culture positive for group A streptococci. Possible explanations for these episodes are new infections with group A streptococci, a streptococcal carrier having non-streptococcal infections, and failures of treatment.3

Traditionally, tonsillectomy has been used to prevent recurrent streptococcal throat infections. Yet according to a recent Cochrane review, there is no empirical evidence to show that it is effective in adults.4 The exact role played by infection of the palatine tonsils (the tissue removed in tonsillectomy) in streptococcal pharyngitis is unknown, as other pharyngeal lymphoid and soft tissues are often also infected.4 5 We conducted a randomised controlled trial on adults with documented recurrent episodes of streptococcal pharyngitis to determine the effects of tonsillectomy.

METHODS

Participants

From October 2001 to May 2005, consecutive patients referred for tonsillectomy because of recurrent episodes of streptococcal pharyngitis were screened for enrolment at an ear, nose, and throat department of a university hospital. All patients provided written informed consent.

The clinical criterion for study entry was three or more episodes of pharyngitis in six months or four episodes in 12 months. The symptoms and signs during the episodes had to be typical of streptococcal pharyngitis.1 In addition, these episodes had to be severe enough for the patient to seek medical attention and at least one episode had to be group A streptococcal infection proved by culture or rapid antigen test. Exclusion criteria were age under 15 years, history of peritonsillar abscess, ongoing antibiotic treatment for other illness, recurrence probably caused by non-compliance with treatment, major heart or airway disorder or bleeding diatheses that would make same day surgery unfeasible,4 and residence outside the city of Oulu or the neighbouring eight communities.

Study design

We allocated patients to tonsillectomy or the waiting list (control). To avoid disparity between group sizes, we used replacement randomisation. If the disparity
exceeded the preset criterion of six, we generated another randomisation list using simple randomisation until we achieved a balanced group size.7 A research assistant not involved in the assignment or care of the trial patients generated the randomisation sequence with a computer random number generator. The assistant concealed the allocation sequence from the investigators who enrolled the participants by putting the assigned treatments in sequentially numbered, opaque, sealed envelopes. These were opened sequentially only after an eligible participant had been found and informed consent obtained, after which a study nurse attached a self fastening slip of paper containing the patient’s name to the official study logbook. A trial physician recorded the baseline data and status.

Outcomes
We tested the hypothesis that tonsillectomy in adults with recurrent streptococcal pharyngitis would reduce the short term risk of developing an episode of streptococcal pharyngitis, reduce the rate of all episodes and days with symptoms, and not cause excessive adverse effects.

The primary end point was the proportion of patients with an acute episode of group A streptococcal pharyngitis during the 90 days’ follow-up, as determined by signs and symptoms of acute pharyngitis with a positive result of throat culture. The secondary end points were the percentage change in the proportions of patients with all episodes of pharyngitis at 90 days, the times to episodes, and the difference in the mean rates of episodes and days with symptoms during the whole follow-up. Patients recorded episodes and days with symptoms in diaries. We considered an episode to be at least two consecutive days with a sore throat. We recorded data on adverse effects related to tonsillectomy from the diaries and the patients’ charts.

Intervention
After baseline data collection and randomisation, the participants were operated on as soon as possible (tonsillectomy group) or placed on the waiting list for tonsillectomy (control group). In the tonsillectomy group, the median time between the randomisation and the tonsillectomy was 13 days (interquartile range 8–21) for practical reasons. The operation was performed under general anaesthesia as day surgery. Four experienced ear, nose, and throat surgeons performed total extracapsular tonsillectomy using blunt or diathermy dissection. In the control group, the waiting times ranged from three to six months, during which time the patients did not receive any prophylactic treatment for their tonsillitis.

Surveillance protocol
We obtained background data and examined the patients at assignment. Both groups were followed up for at least 90 days after randomisation, but otherwise the time of the follow-up visit depended on the length of the waiting list for tonsillectomy in the control group (range 90–210 days) and was 150–180 days in the tonsillectomy group. At randomisation patients in the control group were given the first available date for the operation, the length of follow-up therefore being unrelated to the severity of symptoms.

The primary outcome was objective and based on the presence of group A β haemolytic streptococci in the throat culture during acute pharyngeal symptoms. Patients were given a prepaid microbiological postal package and the phone number of the study nurse with instructions to order a new package immediately after using one. The package included equipment for taking a specimen (Transpocult, Orion Diagnostica, Helsinki, Finland). All participants were advised to visit their own general practitioner whenever they had acute symptoms suggestive of pharyngitis. The general practitioner would then take a culture sample from the pharynx and send it to Oulu University Hospital for analysis. The patients were given written instructions for their general practitioner about the study and illustrated information on how to obtain the culture sample—namely, from the surface of both tonsils or tonsillar fossae in the patients who had undergone tonsillectomy and the posterior pharyngeal wall.3

The patients were told that it was important to seek medical advice for their symptoms during the trial in exactly the same way they had done before the trial and that it was possible to have streptococcal pharyngitis after tonsillectomy.

We plated the swab on sheep blood agar, selecting the growth of streptococci, and incubated them at 35°C for 18–24 hours before reading. The plates were examined again at 48 hours. We used latex agglutination tests (streptococcal grouping kit, Oxoid, Unipath, Hampshire) to differentiate group A streptococcus from the other β haemolytic streptococci. To identify streptococcal carriers, we obtained throat cultures at assignment when the patients were asymptomatic. We were able to serotype streptococcal isolates in case a carrier had a culture positive acute episode. All microbiological analyses were done blinded.

The secondary outcomes were based on the patients’ symptoms. Patients used diaries to record their acute symptoms (fever, throat pain, cough, and rhinitis), episodes of pharyngitis, and visits to a doctor. Individuals with acute pharyngitis and positive throat cultures received treatment as prescribed by their own general practitioner. Patients in the tonsillectomy group also documented the duration of postoperative throat pain. At the follow-up visit, we collected the diaries and checked them for completeness.

Statistical analysis
We estimated that we needed to enrol 70 patients for the study to have a statistical power of 80% to detect an absolute difference in streptococcal recurrence rates of 25%, given a 90 day recurrence rate of 25% in the control group and 0% in the tonsillectomy group.8 We considered a two sided P value of 0.05 to indicate significance. For the primary and secondary end
points, all participants were analysed on an intention to treat basis.

All data analyses were done according to a pre-established plan. Descriptive data are given as means (SD) or as medians with interquartile ranges. We used the Mann-Whitney U test to compare continuous variables. We constructed survival curves, as they related to the treatment group, according to the Kaplan-Meier method, starting from the date of the randomisation. The differences between the groups were tested with the log rank test. We calculated the absolute difference and the 95% confidence intervals in the proportions of recurrence between the groups and the respective number needed to treat at 90 days. In the tonsillectomy group, we excluded from the risk time the individual recovery times immediately after tonsillectomy during which the patient had continuous throat pain (mean 13 days, SD 4), as reported by patients in their diaries.

RESULTS

Patients

The first patient underwent randomisation in October 2001, and the last participant completed the study in December 2005. We screened 298 candidates, 226 of whom were excluded, and two declined to participate. Most of those excluded had too few episodes of pharyngitis or had undocumented or non-streptococcal episodes or chronic tonsilitis. Of the 70 remaining patients who we enrolled, 34 were randomly assigned to the control group and 36 to the tonsillectomy group. All patients were seen at follow-up visits and were followed up for at least the scheduled 90 days, the mean lengths of follow-up being 164 days (SD 63) in the control group and 170 days (SD 12) in the tonsillectomy group. In the control group, one patient did not want tonsillectomy because of a lack of symptoms, but all the others were operated on after their follow-up. Tonsillectomy was done at the scheduled date in all except two cases, where the operation was done before the limit of 90 days (fig 1). One patient was operated on the same day as his sibling, who had a peritonsillar abscess, and the other had unbearable throat pain. There were no clinically important differences between groups in the baseline characteristics (table 1).

Primary outcome

At 90 days, according to the intention to treat in all randomised patients, eight patients (from 20 samples taken) in the control group and one (from five samples taken) in the tonsillectomy group had had an episode of group A streptococcal sore throat (difference 21%, 95% confidence interval 6% to 36%; number needed to treat 5, 3 to 16) (table 2). None of these patients were streptococcal carriers. This difference between the two groups was also evident in the time to the first episode (fig 2).

Table 1 | Demographic and baseline characteristics of adults with recurrent streptococcal pharyngitis according to allocation to waiting list (control) or immediate tonsillectomy. Figures are numbers (percentages) unless otherwise indicated

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=34)</th>
<th>Tonsillectomy (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age (years)</td>
<td>27 (8)</td>
<td>25 (7)</td>
</tr>
<tr>
<td>Female</td>
<td>20 (59)</td>
<td>26 (72)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By patient</td>
<td>11 (33)</td>
<td>15 (43)</td>
</tr>
<tr>
<td>Someone else in the family</td>
<td>9 (27)</td>
<td>14 (40)</td>
</tr>
<tr>
<td>History of allergy</td>
<td>7 (21)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>Risk factors for pharyngitis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than four people in family</td>
<td>11 (32)</td>
<td>12 (33)</td>
</tr>
<tr>
<td>Similar infections in family</td>
<td>5 (15)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Untreated caries</td>
<td>4 (12)</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Symptoms of gingivitis</td>
<td>5 (15)</td>
<td>5 (14)</td>
</tr>
<tr>
<td>Use of same toothbrush &gt;3 months</td>
<td>11 (32)</td>
<td>11 (31)</td>
</tr>
<tr>
<td>Mean (SD) No of previous episodes of acute pharyngitis*:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>During past 6 months</td>
<td>3.3 (1.5)</td>
<td>3.5 (1.3)</td>
</tr>
<tr>
<td>During past 12 months</td>
<td>4.8 (2.1)</td>
<td>5.1 (1.9)</td>
</tr>
<tr>
<td>Frequent throat pain</td>
<td>20 (59)</td>
<td>23 (64)</td>
</tr>
<tr>
<td>Complications of pharyngitis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint symptoms</td>
<td>3 (9)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Rheumatic fever</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Tonsils at baseline according to clinical assessment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merely large</td>
<td>4 (13)</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Chronically infected</td>
<td>4 (13)</td>
<td>4 (14)</td>
</tr>
<tr>
<td>Scarred</td>
<td>22 (73)</td>
<td>21 (75)</td>
</tr>
<tr>
<td>Carrier of group A streptococcus</td>
<td>2 (6)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

* Exudative throat infection diagnosed by physician; according to inclusion criteria at least one episode had to be group A streptococcal infection proved by culture or rapid antigen test.
Secondary outcomes
At 90 days, compared with the tonsillectomy group, a significantly larger proportion of the control group had had acute episodes of pharyngitis, both with and without need for medical assessment (table 2). The times to these first episodes were significantly shorter in the control group than in the tonsillectomy group (fig 2). Similarly, the mean numbers of days with fever or throat pain, but not rhinitis or cough, during follow-up were significantly higher in the control group than in the tonsillectomy group (table 3).

Adverse effects of tonsillectomy
On average, the tonsillectomy operation required a one hour stay in the operating room, a one day stay in hospital, and a 13 days recovery period with postoperative throat pain (table 4). There were no serious adverse effects related to tonsillectomy. Two patients (6%) had mild secondary bleeding 9 and 11 days after the operation.

DISCUSSION
Principal findings
Our trial supports the surgical removal of palatine tonsils to prevent immediate further episodes of group A streptococcal pharyngitis in adults with a documented history of recurrent episodes. We estimate that performing tonsillectomy on such adults would lead to one extra patient avoiding streptococcal infection during the following months for every five patients treated. Tonsillectomy also significantly reduced the short term risk of other episodes of pharyngitis with or without need for medical intervention and the mean number of days with fever or throat pain, but not with rhinitis or cough. The most important morbidity related to the operation was postoperative throat pain and a small risk of bleeding after the operation. Our results support the theory that palatine tonsils have an important role in recurrent streptococcal pharyngitis.5

Comparison with other studies
A recent systematic review of randomised trials in children estimated that (adenoid)tonsillectomy reduced the

Table 2 | Primary outcomes at three months in adults with recurrent streptococcal A pharyngitis randomised to waiting list (control) or immediate tonsillectomy. Figures are numbers (percentages) of patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (n=34)</th>
<th>Tonsillectomy (n=36)</th>
<th>% difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experienced episode of group A streptococcal pharyngitis*</td>
<td>8 (24)</td>
<td>1 (3)</td>
<td>21 (6 to 36)</td>
</tr>
<tr>
<td>Experienced episode of pharyngitis with medical consultation</td>
<td>14 (41)</td>
<td>4 (11)</td>
<td>30 (11 to 49)</td>
</tr>
<tr>
<td>Experienced acute episode of pharyngitis of any kind</td>
<td>19 (56)</td>
<td>11 (31)</td>
<td>25 (3 to 48)</td>
</tr>
</tbody>
</table>

* Determined by signs and symptoms of acute pharyngitis with positive result of throat culture.

Table 3 | Secondary outcomes at end of whole follow-up* in adults with recurrent streptococcal A pharyngitis randomised to waiting list (control) or immediate tonsillectomy. Figures are means (SDs)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (n=34)</th>
<th>Tonsillectomy (n=36)</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical consultations for episodes of pharyngitis</td>
<td>0.9 (1.1)</td>
<td>0.1 (0.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>All episodes of pharyngitis</td>
<td>2.1 (2.3)</td>
<td>0.6 (0.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Days with sore throat‡</td>
<td>12.1 (14.1)</td>
<td>3.2 (5.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Days with fever</td>
<td>2.8 (3.9)</td>
<td>0.6 (1.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Days with rhinitis</td>
<td>7.6 (11.9)</td>
<td>6.3 (7.1)</td>
<td>0.55</td>
</tr>
<tr>
<td>Days with cough</td>
<td>2.6 (5.5)</td>
<td>2.6 (3.3)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

* Mean length of follow-up 164 days (SD 63) in control group and 170 days (SD 12) in tonsillectomy group.
† Mann-Whitney U test.
‡ Not including postoperative throat pain in tonsillectomy group.
incidence of episodes of sore throat by 1.2 episodes a year and reduced school absence associated with sore throat by 2.8 days a year, differences regarded by the authors as clinically insignificant. The respective decreases we found after tonsillectomy in adults were significantly higher at 3.3 episodes and 20 days with sore throat. The reduction in days with sore throat would have been smaller if we had included the days with postoperative throat pain. The reasons for the smaller effect size found in children may be that parents of the most severely affected children refused to participate in the trial, a high number of children entered the trial, we consider that our results are generalisable to the population seen in otolaryngological outpatient clinics in Finland. Extracapsular complete tonsillectomy is a clear cut procedure, and the use of several surgeons and surgical techniques further increase the generalisability of our results.

**Implications**

According to our results, tonsillectomy is an effective alternative for adults with a documented history of recurrent episodes of pharyngitis. Naturally, the morbidity and complications related to the operation must be considered. The most common postoperative complications were sore throat and mild bleeding. Several other factors, such as risks of anaesthesia, otalgia, fever, dehydration, dental injuries, burns, and soft tissue injuries, have been described. These complaints are usually mild, but a small risk of even life threatening complications exists (recent reported mortality ranging from 1 in 16 000 to 1 in 35 000). Physicians and

### Strengths and weaknesses

As we had waiting list controls we could not exceed our normal waiting time for tonsillectomy, which resulted in a relatively short follow-up period. However, we think that the immediate effect of tonsillectomy reflects its overall usefulness. Moreover, when we consider the

### Table 4 | Details and adverse effects of tonsillectomy and operative findings in adults with recurrent streptococcal A pharyngitis randomised to waiting list (control) or immediate tonsillectomy. Figures are numbers (percentages) unless otherwise indicated

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=34)</th>
<th>Tonsillectomy (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>—</td>
<td>34 (94)</td>
</tr>
<tr>
<td>Adenotonsillectomy</td>
<td>—</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Operative technique:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blunt dissection</td>
<td>—</td>
<td>12 (33)</td>
</tr>
<tr>
<td>Diathermy dissection</td>
<td>—</td>
<td>24 (67)</td>
</tr>
<tr>
<td>Mean (SD) times* (min):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In operating room</td>
<td>—</td>
<td>51 (15)</td>
</tr>
<tr>
<td>Under general anaesthesia</td>
<td>—</td>
<td>42 (12)</td>
</tr>
<tr>
<td>Operation</td>
<td>—</td>
<td>16 (8)</td>
</tr>
<tr>
<td>Median (IQR) blood loss (ml)</td>
<td>—</td>
<td>5 (5-31)</td>
</tr>
<tr>
<td>Mean (SD) time with postoperative throat pain (days)</td>
<td>—</td>
<td>13 (4)</td>
</tr>
<tr>
<td>Postoperative haemorrhage†</td>
<td>—</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Retained in hospital for postoperative pain</td>
<td>—</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Findings at operation‡:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scarred tonsils</td>
<td>26 (77)</td>
<td>30 (83)</td>
</tr>
<tr>
<td>Extracapsular microabscesses</td>
<td>5 (15)</td>
<td>5 (14)</td>
</tr>
<tr>
<td>Granulating infected tonsils</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Merely large tonsils</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

IQR=interquartile range.

*Data missing in one patient.
†Mild (no transfusion needed) secondary bleeding treated with electrocautery in outpatient clinic.
‡33 patients in control group underwent tonsillectomy at end of follow-up. There were no significant differences between groups in operative finding.
WHAT IS ALREADY KNOWN ON THIS TOPIC
Observational studies have suggested that tonsillectomy may be effective in preventing recurrent streptococcal throat infections in adults
Evidence from randomised controlled trials has been lacking

WHAT THIS STUDY ADDS
Adults who have documented recurrent episodes of streptococcal pharyngitis are less likely to have further streptococcal or other throat infections or days with throat pain during the months after tonsillectomy
The most important morbidity related to tonsillectomy was postoperative throat pain and a small risk of bleeding after the operation

patients must decide whether these clinical benefits outweigh the risk of further morbidity and the risks involved in the operation.

We thank Tuomas Holma for treating some of the patients, Tuula Gehör and Pirkko Kokko (trial nurses), and Raili Puhakka (research assistant).

Contributors: O-PA was primarily responsible for designing, initiating, and conducting the study and data analysis and drafting of the manuscript and is guarantor. TP and HT participated in conducting the study and critical review of the manuscript. PK, MK, and JL participated in the study design, conducting the study, data analysis, and critical review of the manuscript.

Funding: None.

Competing interests: None declared.

Ethical approval: Oulu University hospital ethics committee.

11 Altman DG, Andersen PK. Calculating the number needed to treat for trials where the outcome is time to an event. BMJ 1999;319:1492-5.

Accepted: 9 February 2007
ABSTRACT

Objective To determine whether remote monitoring (structured telephone support or telemonitoring) without regular clinic or home visits improves outcomes for patients with chronic heart failure.

Data sources 15 electronic databases, hand searches of previous studies, and contact with authors and experts.

Data extraction Two investigators independently screened the results.

Review methods Published randomised controlled trials comparing remote monitoring programmes with usual care in patients with chronic heart failure managed within the community.

Results 14 randomised controlled trials (4264 patients) of remote monitoring met the inclusion criteria: four evaluated telemonitoring, nine evaluated structured telephone support, and one evaluated both. Remote monitoring programmes reduced the rates of admission to hospital for chronic heart failure by 21% (95% confidence interval 11% to 31%) and all cause mortality by 20% (8% to 31%); of the six trials evaluating health related quality of life three reported significant benefits with remote monitoring, and of the four studies examining healthcare costs with structured telephone support three reported reduced cost and one no effect.

Conclusion Programmes for chronic heart failure that include remote monitoring have a positive effect on clinical outcomes in community dwelling patients with chronic heart failure.

INTRODUCTION

Chronic heart failure is a common diagnosis, carries a poor prognosis, and affected patients are major consumers of healthcare resources.1 As the prevalence of chronic heart failure is increasing this situation will deteriorate unless new management strategies are developed.2 The effectiveness of multidisciplinary non-pharmacological approaches for improving outcomes in patients with chronic heart failure has been well established in over 30 randomised trials.3-7 As most of these trials have tested multifaceted approaches, however, it has been difficult to identify the incremental benefits of the components of each intervention.6 Nevertheless, it is clear that within most populations access to these programmes is limited as a result of barriers related to funding or geography.8 As a result interest is increasing in remote monitoring models for delivering care, which incorporate information communication technology either as telemonitoring (transfer of physiological data such as blood pressure, weight, electrocardiographic details, and oxygen saturation through telephone or digital cable from home to healthcare provider) or as regular structured telephone contacts between patients and healthcare providers, which may or may not include the transfer of physiological data.6

Earlier reviews of multidisciplinary programmes for chronic heart failure have been unable to make definitive conclusions about the value of remote monitoring strategies given the paucity of relevant studies and patient numbers at the time of these analyses.6,16 However, several studies with relatively large numbers of patients have since been published, permitting a more detailed analysis. We evaluated the effect of remote monitoring strategies in patients with chronic heart failure and whether the effect differed by the type of technology used for the communication of information.

METHODS

We updated two earlier systematic reviews that dealt with telemonitoring5,6 by searching 15 electronic databases using search methods recommended by the Cochrane Heart Review Group.9 All randomised trials evaluating remote monitoring programmes published between 1 January 2002 and 6 May 2006 were included. Databases searched included the Cochrane library and the Cochrane CENTRAL register of controlled trials, Medline (1 January 2002 to 6 May 2006), Embase, CINAHL (1 January 2002 to 6 May 2006), AMED, ISI web of knowledge, HSTAT, Ingenta, Zetoc, Lilacs, and science citation index expanded (to search forward to detect studies citing the original reviews), DARE, national research register, Psych Info, and web of science. We also hand searched the reference lists in 21 published systematic reviews of disease management programmes in chronic heart failure,3-7 10-26 149 review articles on telephone support...
programmes in chronic disease, and those studies identified in our electronic searches that met the inclusion criteria. Unpublished conference proceedings were reviewed and published abstracts were included if the authors replied to our request and sufficient details and outcomes of studies were retrieved. Finally, we communicated with the principal investigators of the identified trials and with national and international experts in the specialty to identify any studies we had potentially missed. We did not restrict study inclusion by language but did limit our review to only randomised controlled trials.

We applied the highly sensitive search strategy from the Cochrane Collaboration. Keywords for searches of the database included heart failure (exp), cardiac failure (exp), telemedicine (exp), telecare (exp), telemonitoring (exp), teleconsultation (exp), teleconference (exp), telecommunications (exp), case management (exp), comprehensive health care (exp), disease management (exp), health services research (exp), home care services (exp), clinical protocols (exp), patient care planning (exp), nurse led clinics and special clinics (exp), randomised controlled trial (s), controlled clinical trial, random allocation, double blind method, single blind method, clinical trial(s), research design, comparative study, follow-up study, and prospective study.

Search strategies were written for each database and double checked by the second reviewer, under the direction and supervision of a medical librarian.

Types of interventions
Remote monitoring programmes started by a health professional (medical, nursing, social work, pharmacists) for patients with chronic heart failure living at home were eligible for inclusion if the monitoring was carried out at least once in the first month after hospital discharge, was targeted towards the patient (that is, the patient had to be the person on the telephone), was structured (as opposed to offering telephone follow-up on an “as needed” basis), and was to be delivered as the only aftercare intervention without home visits or more than usual clinic follow-up. We excluded studies in which the remote monitoring was intended primarily to deal with the problems of caregivers rather than of patients. We a priori classified programmes as being structured telephone support if they consisted of standardised telephone contact of patients with chronic heart failure and relied on reporting of symptoms alone, or telemonitoring if they consisted of telephone contact for eliciting symptoms and transmission of physiological data.

Our primary outcomes were all cause mortality, all cause rate of admission to hospital (proportion of patients readmitted to hospital at least once during follow-up), and rate of admission to hospital as a result of chronic heart failure (proportion of patients readmitted to hospital at least once during follow-up). Our secondary outcomes were health related quality of life, cost, and acceptability.

Validity assessment and data abstraction
Two investigators (RAC, SCI) independently reviewed the results of the searches for study inclusion and extracted data. We excluded any studies in which additional home or clinic visits (more than usual care) were offered to patients in the intervention or control arms. Study quality (particularly method), randomisation, and intervention, were judged using accepted criteria and compared with the review protocol.

Disagreements between the two reviewers were resolved by a third reviewer (SS, FAMcA, or JGFC). Data abstraction was carried out independently and blinded by RAC and SCI, with FAMcA checking extracted data. Overall the inter-rater reliability on key inclusion criteria (randomisation and intervention) was strong ($k$ score 0.73, 95% confidence interval 0.54 to 0.92).

Study characteristics and data synthesis
Owing to the expected differences in patient populations, programme characteristics, and length of follow-up, we carried out our primary analyses using the Der-Simonian and Laird random effects model. Analyses were carried out using RevMan 4.2 (Nordic Cochrane Centre). As the outcomes of interest were relatively common we calculated risk ratios and 95% confidence intervals. The risk difference (difference between observed proportion of the event in the treatment and usual care groups) was calculated by subtracting the risk of the event in the usual care group from that of the treatment group. These data are presented with 95% confidence intervals.

We carried out intention to treat analyses—that is, all patients and their outcomes were analysed in the groups to which they were allocated, regardless of whether they received the treatment. We examined for statistical heterogeneity in each outcome of interest using Cochran’s $Q$ test and $I^2$ statistic. Secondary outcomes (expected to be reported less often) were described and tabulated.
RESULTS

Overall 234 of 499 citations were reviewed in detail. Of these, 14\textsuperscript{w1–w11} randomised controlled trials (4264 patients) were eligible for inclusion (fig 1). One trial was three armed\textsuperscript{w1; to avoid double counting of the control patients the results for the control arm were shared between the two comparisons for the pooled analysis of all remote monitoring programmes, but all patients in the control arms were counted in each of the sub-analyses (telephone support v usual care, telemonitoring v usual care). Four trials evaluated telemonitoring, \textsuperscript{w11–w14} nine evaluated structured telephone support, \textsuperscript{w2–w10} and one\textsuperscript{w11} evaluated both. Ninety five per cent of the included trials were captured by the Medline search, 2\% from CINAHL, and 3\% from hand searching and contact with experts.

The length of follow-up of these trials ranged from three to 16 months, the mean ages of participants ranged from 57 to 75 years, and all trials enrolled patients with symptoms (New York Heart Association classification range II–IV, left ventricular ejection fraction <40\%). Structured telephone support programmes included monitoring of symptoms, medicine management, and education and counselling on lifestyle. All the telemonitoring programmes included transfer of daily data on weight, pulse, blood pressure, and electrocardiographic findings.

The quality of the studies was evaluated using Cochrane recommendations.\textsuperscript{9} The 14 included studies were rated as adequate, reporting 61\% of the recommended quality variables. Six (42\%) described concealment and some level of blinding of patient or outcome assessors, and seven (50\%) reported completeness of follow-up (table 1).

Quantitative data synthesis

All cause mortality

All 14 trials reported all cause mortality (15 comparisons, 581 deaths, fig 2) and the pooled estimates showed a statistically significant 20\% reduction (95\% confidence interval 8\% to 31\%) with remote monitoring programmes. The benefits were greater with telemonitoring (risk ratio 0.62, 0.45 to 0.85, \textit{P}=0.003, based on 127 deaths in 807 patients) than with structured telephone support (0.85, 0.72 to 1.01, \textit{P}=0.06, based on 482 deaths in 3542 patients), although this difference did not

Table 2 Effect of remote monitoring on chronic heart failure related quality of life, cost, and acceptability to patients

<table>
<thead>
<tr>
<th>Study</th>
<th>End point (months)</th>
<th>Health related quality of life\textsuperscript{a} and depression</th>
<th>Effect on cost or patient</th>
<th>Cost of intervention</th>
<th>Acceptability of intervention to patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleland et al 2005 (TEN-HMS study)\textsuperscript{w1}</td>
<td>400 days\textsuperscript{f}</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>4.1% of patients refused to accept technology in their homes, 2.9% of patients asked for equipment to be removed, and 1.8% discontinued recording. Overall patient acceptance was 91.2%. 96% of patients were well satisfied with the system and 97% found the telemonitoring devices easy to use</td>
</tr>
<tr>
<td>Barth 2001\textsuperscript{w4}</td>
<td>2</td>
<td>Increase in scores on MLHFQ (P≤0.005)</td>
<td>—</td>
<td>$23.60/patient</td>
<td>—</td>
</tr>
<tr>
<td>Riegel et al 2002\textsuperscript{w9}</td>
<td>6</td>
<td>46% reduction in inpatient costs (P=0.04)</td>
<td>$443/patient</td>
<td>Patient satisfaction was significantly higher among people assigned to intervention group compared with usual care group (P=0.01)</td>
<td></td>
</tr>
<tr>
<td>Laramee et al 2003\textsuperscript{w6}</td>
<td>3</td>
<td>—</td>
<td>$2482/patient (average) reduction</td>
<td>$228.52/patient (average)</td>
<td>—</td>
</tr>
<tr>
<td>Tsuyuki et al 2004\textsuperscript{w8}</td>
<td>6</td>
<td>—</td>
<td>$2531/patient reduction</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>GESICA investigators 2005\textsuperscript{w9} (DIAL trial)</td>
<td>16 (mean)</td>
<td>Increase in scores on MLHFQ, mean total score, intervention v control 30.6 v 35.0, mean difference 4.4, 95% CI 1.8 to 6.9, \textit{P}=0.001</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Riegel et al 2006\textsuperscript{w10}</td>
<td>6</td>
<td>MLHFQ (NS), EQ-5D (NS), depression by PHQ-9 (NS) No effect on cost of care for heart failure or all cause acute care cost</td>
<td>—</td>
<td>—</td>
<td>Video link over standard telephone lines was not found to be useful by participants</td>
</tr>
<tr>
<td>De Lusignan et al 2001\textsuperscript{w11}</td>
<td>12</td>
<td>GHQ, CHFSQ (NS)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Goldberg et al 2003 (WHARF trial)\textsuperscript{w13}</td>
<td>6</td>
<td>MLHFQ (\textit{P}=0.22), SF-12 (physical score \textit{P}=0.15, mental score \textit{P}=0.73), HDS (\textit{P}=0.57)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Woodend et al 2003\textsuperscript{w13}</td>
<td>3</td>
<td>Increase in scores on MLHFQ (\textit{P}=0.025)</td>
<td>—</td>
<td>—</td>
<td>Very highly satisfied</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Variance between baseline and study end point, details provided as included in study. \textsuperscript{f}Patient acceptability measured at 400 days.
achieve significance (P=0.18) using the adjusted indirect comparison method described by Song et al.\textsuperscript{28} Mortality data from these 14 trials showed little heterogeneity (P=0.56, I\textsuperscript{2}=0%).

\textbf{All cause admission to hospital}  
Of the eight trials (nine comparisons) that reported rates of all cause admission to hospital (fig 3), none reported a statistically significant result. Even the pooled estimates did not show a significant benefit on this end point with remote monitoring programmes (0.95, 0.89 to 1.02).

\textbf{Hospital admissions as a result of chronic heart failure}  
Nine trials (10 comparisons) reported rates of admission to hospital as a result of chronic heart failure, and although only one reported a statistically significant benefit, all trials showed similar relative reductions (P for heterogeneity 0.76, I\textsuperscript{2}=0%) and the pooled results showed a reduction of 21\% (11\% to 31\%) with remote monitoring programmes (fig 4). Although no appreciable difference was found between the relative reductions seen with telemonitoring and telephone support programmes, evidence from randomised trials was insufficient to conclusively state that telemonitoring programmes reduce admissions to hospital since only one of these trials reported this outcome.

\textbf{Quality of life, cost, adherence, and patient acceptability}  
Only six trials examined the effect of the intervention on health related quality of life (table 2). Of these trials, three reported a significant and substantial improvement in quality of life between the intervention and control groups at the end of follow-up. The effect of the intervention on healthcare costs was reported in only four of these trials (all of structured telephone support); however, three of the four trials reported lower healthcare costs for patients randomised to the intervention (table 2). The cost of the intervention was infrequently reported and variation existed between programmes (table 2). None of the trials on telemonitoring reported the cost of the intervention or its effect on healthcare costs. Acceptability of the intervention to the patient was under-reported, with only four trials reporting this outcome (table 2). Three of these trials reported that the intervention was acceptable to patients, with patients from one trial of telemonitoring considering the video link not useful.\textsuperscript{11}

An analysis of publication bias using funnel plots showed an unlikely possibility of bias within studies showing a reduction in mortality after remote monitoring.

\textbf{DISCUSSION}  
This systematic review found that remote monitoring programmes for patients with chronic heart failure...
living in the community reduced admissions to hospital and all cause mortality by nearly one fifth while improving health related quality of life, but had no significant effect on all cause admission to hospital. Although few studies have examined economic outcomes, the three studies on structured telephone support suggested that the interventions were economically cost effective. Thus, this systematic review builds on earlier ones of multidisciplinary interventions for chronic heart failure by tackling key issues and uncertainties relating to the specific effect of telephone based programmes. This review is particularly important as remote monitoring programmes provide a potentially feasible option for dealing with the expanding population of patients with chronic heart failure that cannot be accommodated within existing multidisciplinary chronic heart failure clinics owing to constraints caused by geography or resources.

The significant effect of structured telephone support on the risk of admissions to hospital for chronic heart failure (risk differences ranged between 2% and 33%) can be attributed in part to the triage of patients by telemonitoring nurse at the first sign of clinical deterioration, and the consequent immediate intervention of a primary care doctor. Similarly, all trials on telemonitoring in this review involved daily transmission of vital signs, weight, and symptoms at various time points to healthcare providers, thus potentially leading to earlier detection and management of clinical deterioration by the patient or managing health professional. A recent study of rapid up-titration of beta blockers in 49 patients with chronic heart failure reported that deterioration in symptoms, including weight gain, oedema of the legs, and increasing dyspnoea, were usually present eight to 12 days before admission to hospital.

The lack of effect of remote monitoring programmes on all cause admissions to hospital may require further exploration. This observation is consistent with an earlier meta-analysis. Importantly this result does not simply reflect a paucity of data as there were more events for this end point (1561 admissions in 3586 patients) than for deaths and admissions to hospital. Reduced mortality will increase the duration of exposure to the risk of admission and will reduce the effect of intervention on this outcome. However, telemonitoring is likely to produce false alarms and pre-emptive admissions in patients who are deteriorating but not yet in crisis and also to lead to early discharge because the patient still has a high level of monitoring at home. Consequently, telemonitoring may be more effective at shortening hospital stay than at reducing admissions. Increased survival and admissions for common comorbid conditions (for example, chronic respiratory disease, fractures from falls, and cancer among participants who were typically elderly) may also prevent a reduction in the frequency of admissions associated with telemonitoring. Finally, remote monitoring in patients with chronic heart failure focuses on indices specific to that disease and treatment; it may have little effect on other reasons for admission. Whether extending the range of monitoring to provide more comprehensive support will result in a further improvement in health outcomes is yet to be determined.

### Table: Effect of remote monitoring on risk of all cause admission to hospital

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment group</th>
<th>Control group</th>
<th>Relative risk (random) (95% CI)</th>
<th>Weight (%)</th>
<th>Relative risk (random) (95% CI)</th>
<th>Risk difference (random) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structured telephone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleland et al 2005(^{11})</td>
<td>73/110</td>
<td>40/55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riegel et al 2002(^{55})</td>
<td>56/130</td>
<td>114/228</td>
<td>0.91 (0.74 to 1.13)</td>
<td>0.01</td>
<td>0.98 (0.84 to 1.15)</td>
<td>-0.06 (-0.21 to 0.08)</td>
</tr>
<tr>
<td>Laramee et al 2003(^{96})</td>
<td>49/141</td>
<td>46/146</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeBusk et al 2004(^{97})</td>
<td>116/228</td>
<td>117/234</td>
<td>0.98 (0.84 to 1.15)</td>
<td>0.01</td>
<td>1.00 (0.78 to 1.28)</td>
<td>0.00 (-0.12 to 0.12)</td>
</tr>
<tr>
<td>Tsuyuki et al 2004(^{98})</td>
<td>59/140</td>
<td>51/136</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GESICA Investigators 2005(^{99})</td>
<td>261/760</td>
<td>296/758</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riegel et al 2006(^{10})</td>
<td>39/69</td>
<td>37/65</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1578</td>
<td>1622</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2=4.78, df=6, P=0.57, I^2=0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $z=1.44, P=0.15$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Telemonitoring</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleland et al 2005(^{11})</td>
<td>75/106</td>
<td>40/55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goldberg et al 2002(^{112})</td>
<td>65/138</td>
<td>67/142</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>244</td>
<td>197</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2=0.03, df=1, P=0.87, I^2=0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $z=0.21, P=0.83$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fig 3**: Effect of remote monitoring on risk of all cause admission to hospital.

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Quality of life, acceptability, and cost benefits were infrequently reported in these trials. Although those reporting these outcomes showed significant improvements with remote monitoring, future studies of telemonitoring or structured telephone support programmes should be encouraged to incorporate such measures and outcomes in their reporting. The same caveats and recommendations apply to cost data arising from these studies.

Limitations of the study
A limitation of this review is the relatively small number of studies (n=14) and participants (n=4264). In addition, few trials had follow-up beyond six months. Thus our observations on the positive, short term benefits of remote monitoring programmes may not extend to longer term outcomes. However, the hazard ratio for admission to hospital in patients with chronic heart failure is not linear as the greatest risk of readmission in such patients occurs in three to six months. Nevertheless, it is expected that the body of evidence on remote monitoring for chronic heart failure will expand considerably in the next decade as strategies on communicating information become normalised into medical practice and a better understanding is gained of the content of care provided by remote monitoring.

Furthermore, it is anticipated that the following studies will add to the evidence base in this specialty: the as yet unpublished reports on the home or hospital in heart failure trial, which showed an overall neutral effect on mortality and admissions to hospital; the recent work by the Scalvini et al team in Italy, which showed a significant reduction in risk of readmission [risk ratio 0.50, 95% confidence interval 0.34 to 0.73; P=0.01]; and Riegel et al’s most recent paper, which questions the effect of this type of intervention in non-Caucasian ethnic groups.

Conclusion
Although we have shown substantial and statistically significant benefits with remote monitoring for patients with chronic heart failure, monitoring is not a treatment but rather a different way of systematically organising effective care. Thus programmes that include remote monitoring should not be seen as a replacement for specialist care or multidisciplinary chronic heart failure clinics (two interventions that improve outcomes). However, remote monitoring may be of particular benefit to patients who have difficulty accessing specialised care because of geography, transport, or infirmity.
We thank librarian Margaret Goodhart (University of South Australia) for her knowledge and skill in navigating bibliographies and electronic sources, and the following investigators for further data and information from their studies:

WA Gattis, LR Goldberg, A Laramée, B Riegel, RT Tsuyuki, A Woodend, and S Scalvini.

Contributors: RAC conceived and designed the study. RAC and SCI reviewed the literature, developed the study protocol, and searched for and abstracted the data. RAC, SCI, SS, and JGF analyzed and interpreted the data. FAMcA assessed the quality of extracted data and was responsible for synthesis and analysis of the data. He will act as guarantor. JGF hand searched the literature and referred experts to RAC and SCI. All authors contributed to the drafting of the article and revising it for important intellectual content.

Funding: RAC is supported by the National Institute of Clinical Studies and the National Heart Foundation of Australia. SCI and SS are supported by the National Health and Medical Research Council and the National Heart Foundation of Australia. FAMcA receives salary support from the Alberta Heritage Foundation for Medical Research, and has received honorariums from Phillips for speaking on telemonitoring. JGF is a consultant to the EU sponsored My-Heart project which is part funded by Phillips and other manufacturers of telehealth devices.

Ethical approval: Not required.


27 Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.


34 Cleland JGF. Patients with treatable malignant disease—including heart failure—are entitled to specialist care. CMAJ 2005;172:207-9.

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<table>
<thead>
<tr>
<th>Study</th>
<th>Participants (location)</th>
<th>Interventions and usual care</th>
<th>Reported outcomes (study end point)</th>
<th>Randomisation</th>
<th>Allocation concealment</th>
<th>Blinding of patients and assessors</th>
<th>Complete- ness of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleland et al 2005 (TEN-HM study)**</td>
<td>426 patients (mean age 67 years) with a recent admission for heart failure and left ventricular ejection fraction &lt;40% (Germany, Netherlands, United Kingdom)</td>
<td>Patients assigned to nurse telephone support arm received a telephone call each month by a heart failure specialist nurse to telemonitoring received nurse telephone support and had their weight, blood pressure, and electrocardiogram monitored twice daily. Usual care consisted of a management plan forwarded to patient’s primary care physician, who was asked to implement it. If the practice involved nurse titration of drugs this was allowed. Patients were assessed at a research clinic every four months; contact with clinic was discouraged between visits.</td>
<td>Mortality, readmission to hospital, compliance with intervention (15 months)</td>
<td>Random permuted blocks</td>
<td>After consent and collection of baseline data an independent statistical centre was contacted</td>
<td>NS</td>
<td>1% lost to follow up</td>
</tr>
<tr>
<td>Gattis et al 1999 (PHARM study)**</td>
<td>181 patients (mean age 67 years) with heart failure being evaluated in cardiology clinic (United States)</td>
<td>Clinical pharmacist led drug review and patient education. Regularly scheduled telephone contact (at 2, 12, and 24 weeks) to detect clinical deterioration early. Control group received usual care that did not include pharmacist providing recommendations on drug therapy to attending physician or providing education to patient. Patient assessment and education were provided by attending physician, physician assistant, or nurse practitioner. Patient was contacted by pharmacist by telephone to identify patients.</td>
<td>Mortality, readmission to hospital, drug prescription (6 months)</td>
<td>Computer generated</td>
<td>Assignment revealed after provision of consent</td>
<td>Yes ; NS</td>
<td>NS</td>
</tr>
<tr>
<td>Rainville 1999**</td>
<td>34 patients aged 50 years (mean age 70 years) discharged from hospital with heart failure (United States)</td>
<td>Usual care plus pharmacist led drug review, patient education, drug management before discharge and at days 3, 7, 30, and 90, and 12 months. Usual care consisted of routine care and preparation for discharge, including written prescriptions, physician discharge instructions, and nurse review of diet, treatment plans, and drugs. Nurses provided patient with computer generated drug information sheets. Patients were contacted by a pharmacist at 30 days, 90 days, and 12 months to determine readmissions.</td>
<td>Mortality, readmission to hospital, functional assessment score (12 months)</td>
<td>Method not stated</td>
<td>Unclear</td>
<td>Yes ; NS</td>
<td>2.9% lost to follow up</td>
</tr>
<tr>
<td>Barth et al 2001**</td>
<td>34 patients (mean age 75 years) discharged from acute care to home with primary diagnosis of chronic heart failure (United States)</td>
<td>Structured nurse managed telephonic post-discharge programme involving predischarge education plus post-discharge telephone follow-up. Structured interaction at 72 hours, 144 hours, and then fortnightly. Control group received routine discharge teaching at time of discharge as per hospital procedure. Patients were contacted at 2 months for collection of data.</td>
<td>Mortality, readmission to hospital, physician and emergency department visits, quality of life, cost of intervention (3 months)</td>
<td>Method not stated</td>
<td>Unclear</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Riegel et al 2002**</td>
<td>358 patients (mean age 74 years) discharged from hospital with heart failure (United States)</td>
<td>Telephonic case management by registered nurse using decision support software, involving patient education and counselling and liaison with primary care physician. Patients were telephoned within 5 days of discharge and thereafter at a frequency guided by software and case manager (mean 17 calls). Usual care was not standardised, and no formal telephonic case management was in existence at these institutions. These patients presumably received some education on heart failure management before hospital discharge.</td>
<td>Mortality, readmission to hospital, physician and emergency department visits, inpatient costs, patient satisfaction (6 months)</td>
<td>Physicians were unit of randomisation; method not stated</td>
<td>Unclear</td>
<td>Physicians blinded ; NS</td>
<td>NS</td>
</tr>
<tr>
<td>Laramee et al 2003**</td>
<td>287 patients (mean age 72 years) admitted to hospital with primary or secondary diagnosis of chronic heart failure, left ventricular systolic dysfunction &lt;40% or radiological evidence of pulmonary oedema (United States)</td>
<td>Telephonic case management carried out by one nurse case manager for chronic heart failure, involving four major components: early discharge planning, patient and family education on chronic heart failure, promotion of optimal drugs for chronic heart failure and 12 weeks of telephone follow-up. Usual care consisted of standard care typical of a tertiary care hospital. It included inpatient social service evaluation (25%), dietary consultation (15%), physiotherapy or occupational therapy (17%), and education on drugs and chronic heart failure by nurses. Post-discharge was carried out by the patient’s local physician (44% received some home care services).</td>
<td>Mortality, readmission to hospital, outpatient costs, drug prescription and adherence (3 months)</td>
<td>Simple randomisation of first 42 patients, followed by randomisation in blocks of eight</td>
<td>Unclear</td>
<td>NS</td>
<td>5.2% lost to follow up</td>
</tr>
<tr>
<td>Delius et al 2004**</td>
<td>462 patients (mean age 72 years) admitted to hospital with provisional diagnosis of chronic heart failure from Kaiser Permanente (United States)</td>
<td>Standardised telephonic physician directed nurse managed care management, involving lifestyle education and drug management for chronic heart failure. Patients contacted weekly for 6 weeks, biweekly for 8 weeks, and then monthly and bimonthly. Usual care not clearly defined, but was provided by participating Kaiser Permanente medical centres, seemed to involve a high frequency of all of kinds of follow-up clinic visits (13 in 12 months after admission to hospital).</td>
<td>Mortality, readmission to hospital, emergency and outpatient department visits, prescription of recommended pharmacotherapy (12 months)</td>
<td>Sealed assignment using ENF procedure</td>
<td>Research staff not associated with delivering intervention provided sealed assignment</td>
<td>NS ; Yes</td>
<td>NS</td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Intervention Details</td>
<td>Outcomes</td>
<td>Method</td>
<td>Losses to Follow-up</td>
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<td>Tsuuki et al 2004&lt;sup&gt;18&lt;/sup&gt;</td>
<td>276 patients (mean age 72 years) discharged from hospital with heart failure (Canada)</td>
<td>Early discharge planning with provision of adherence aids, patient education, regularly scheduled telephone contact with local research coordinator at 2 and 4 weeks then monthly thereafter for 6 months. Recommendations to see primary care physician if not receiving target dose of angiotensin converting enzyme inhibitor or diuretic. Patients assigned to usual care received a pamphlet on general heart disease before discharge, but no formal counselling beyond what was routine at the hospital. Patients were contacted monthly for 6 months to ascertain clinical events</td>
<td>Mortality, readmission to hospital, drug adherence, physician and emergency department visits, cost analysis (6 months)</td>
<td>Computer generated sequence using block randomisation stratified by study site</td>
<td>Randomised by a telephone call to project office</td>
<td>NS</td>
<td>2.5% lost to follow-up</td>
</tr>
<tr>
<td>GESICA Investigators 2005 (DIAL trial)&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1518 outpatients (mean age 65 years) with stable chronic heart failure (Argentina)</td>
<td>Nurses trained in management of patients with chronic heart failure carried out structured telephone follow-up involving adherence to diet and treatment, monitoring of symptoms, control of fluid retention, and daily physical activity. Patients were contacted four times in the first fortnight and then as needed. Patients in control group were followed by their attending cardiologists and received care similar to the intervention group</td>
<td>Mortality, readmission to hospital, quality of life (mean 16 months)</td>
<td>Permuted block randomisation using concealed randomisation lists, stratified according to patient's cardiologist</td>
<td>After provision of consent, patient's cardiologist contacted study centre</td>
<td>NS ; Yes</td>
<td>0.5% lost to follow-up</td>
</tr>
<tr>
<td>Riegel et al 2006&lt;sup&gt;20&lt;/sup&gt;</td>
<td>134 Hispanic patients (mean age 72 years) admitted to hospital with chronic heart failure (United States)</td>
<td>Education, monitoring, and guidance by bilingual-bicultural Mexican-American registered nurses by telephone case management standardised using decision support software. Patients were contacted on average within 5 days of discharge and thereafter at a frequency guided by the software and nurse case manager over a 6 month period (mean 13.5 calls to patients and 8.4 additional calls to families). Printed educational material was provided monthly and on request in relevant language. Usual care was not standardised and no formal printed management programme existed at these institutions. Standard of usual care was that patients were educated about heart failure management before discharge, assuming that nurse spoke patient’s language or someone bilingual was available to translate. In reality, only a small portion of staff were bilingual so much of the discharge instruction was provided in writing. Typical discharge instructions included a drug list and institution specific discharge instruction sheet with handwritten notes to follow a low sodium diet and contact the physician if symptoms occur</td>
<td>Mortality, readmission to hospital, cost of care, self reported health related quality of life and depression (6 months)</td>
<td>Sealed envelopes attached to sequential data forms</td>
<td>Sealed envelopes opened after collection of baseline data</td>
<td>NS ; Yes</td>
<td>No losses to follow-up</td>
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</tbody>
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**Telemonitoring (on basis of symptom and sign monitoring):**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Intervention Details</th>
<th>Outcomes</th>
<th>Method</th>
<th>Losses to Follow-up</th>
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<tr>
<td>De Lusignan et al 2001&lt;sup&gt;21&lt;/sup&gt;</td>
<td>20 patients (mean age 75 years) with heart failure confirmed by cardiologist, identified from database of academic general practice (United Kingdom)</td>
<td>Telemonitoring of vital signs (pulse, blood pressure, weight) and clinical status assessed daily by nurses along with video consultations with a nurse weekly for 3 months, fortnightly for 3 months, then monthly. Usual care consisted of standard general practice treatment; in addition they had pulse, blood pressure, and weight measured quarterly. They were evaluated in the same manner as the intervention group</td>
<td>Mortality, compliance with intervention and drugs, patient satisfaction, quality of life (12 months)</td>
<td>Random table allocation</td>
<td>Unclear</td>
</tr>
<tr>
<td>Goldberg et al 2002 (WHARP trial)&lt;sup&gt;22&lt;/sup&gt;</td>
<td>280 patients (mean age 59 years) admitted to hospital with NYHA class III-IV, with left ventricular ejection fraction ≤35% (United States)</td>
<td>Daily transmission of weight and symptoms using a customised monitor; data were reviewed daily by nurses and concerns reported to physician. Patients in control group were instructed to contact their physician for weight increases of more than a prespecified amount or if their symptoms of heart failure worsened. They had a weight log to bring to visits. Follow-up visits, other than study visits, were at the discretion of the treating physician. Telephone contacts were permitted at the discretion of the treating physician or nurse</td>
<td>Mortality, readmission to hospital, emergency department visits, quality of life, patient satisfaction, compliance with intervention (mean 6 months)</td>
<td>Method not stated</td>
<td>Unclear</td>
</tr>
<tr>
<td>Woodend et al 2009&lt;sup&gt;23&lt;/sup&gt;</td>
<td>121 patients (mean age 68 years) with symptomatic heart failure (NYHA class II or greater) (Canada)</td>
<td>Daily transmission of weight and periodic transmission of electrocardiogram and blood pressure. Weekly video conferences by telephone care nurse. Video conferences more frequent in first few weeks and tapered over 3 months. Usual care was not described</td>
<td>Mortality, readmission to hospital, quality of life, emergency department visits, patient satisfaction (3 months)</td>
<td>Method not stated</td>
<td>Unclear</td>
</tr>
<tr>
<td>Capomolla et al 2004&lt;sup&gt;24&lt;/sup&gt;</td>
<td>133 patients (mean age 57 years) discharged from specialist chronic heart failure unit to home (Italy)</td>
<td>Daily communication of vital signs (including weight, systolic blood pressure, heart rate) and symptoms with review by nurses and physicians. Access to medical staff by phone as needed was available. Usual care consisted of referral to patient’s primary care physician or cardiologist department at discharge. Post-discharge care was governed by care provider</td>
<td>Mortality, readmission to hospital, emergency department visits, compliance with intervention (12 months)</td>
<td>Method not stated</td>
<td>Unclear</td>
</tr>
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NYHA=New York Heart Association. NS=Not stated.
PREGNANCY PLUS

HIV and pregnancy

Glenda E Gray, James A McIntyre

The management of HIV infection during pregnancy is complex, and the scenario box on this page illustrates the complexities involved. In 2005, UNAIDS (the Joint United Nations Programme on HIV/AIDS) estimated that 38.6 million people had HIV, of whom 17.3 million were women (with most being in their reproductive years). At least 3.28 million pregnant women infected with HIV are estimated to give birth each year, with more than 75% of these in sub-Saharan Africa; this is where most of the annual 700 000 new infections of HIV in children occur.

Timing of and factors affecting mother to child transmission

Perinatal transmission of HIV can occur in utero, during labour and delivery, or postnatally through breastfeeding.\(^1\) Most transmission occurs during the intrapartum period.\(^1\) Transmission will vary from less than 2% in the developed world (with its access to antiretroviral therapy, caesarian section, and formula milk) to more than 30% in the developing world (where access to therapy is limited and breastfeeding is prolonged).\(^2\) Observational studies have shown that the risk of perinatal transmission is affected by maternal stage of disease; duration of rupture of membranes; increased genital secretion of HIV associated with sexually transmitted infections such as herpes simplex virus; and other factors such as prematurity. Large randomised controlled studies have shown that mother to child transmission can be reduced by the use of antiretroviral therapy, elective caesarean section, and exclusive formula feeding.\(^2\)

How does pregnancy affect progression of HIV disease?

Pregnancy does not adversely affect HIV progression or survival.\(^3\) \(w1\) Dual infection with HIV and malaria has been associated with increased risk of maternal, perinatal, and early infant death.\(^4\) \(w8\) Improved access to care, treatment, and nutritional support in resource limited settings may help to reduce poor pregnancy outcomes. The decline in the CD4 cell count during pregnancy normally resolves in the postpartum period and is attributed to haemodilution.\(^5\) \(w9\) \(w10\) Although HIV RNA levels seem to remain stable during pregnancy, some studies have shown an increase in viral load in the postpartum period.\(^6\) \(w11\) In developed countries, with easy access to specialist care, HIV infection is a rare cause of maternal mortality. In contrast, HIV infection has become an important contributing cause of maternal mortality in Africa.\(^7\) \(w12\) In areas of high HIV prevalence, the infection has become a leading cause of maternal mortality. Several reports from southern African countries have shown this trend, including maternal mortality rates...
Box 1 | Antiretroviral regimens for preventing mother to child transmission of HIV-1 (adapted from the British HIV Association)

Zidovudine monotherapy
• From 18 weeks of pregnancy
• If viral load <6000-10 000 HIV RNA copies/ml plasma
• If virus is wild-type
• If highly active antiretroviral therapy (HAART) is not required for maternal health
• If mother does not wish to take HAART during pregnancy
• If mother is willing to deliver by elective caesarean section

Effective (≥3 drug) combination therapy
• Indicated for maternal health as per adult guidelines
• If baseline maternal viremia ≥10 000 copies/ml
• If baseline maternal viremia <10 000 copies/ml if an alternative is required to zidovudine monotherapy plus pre-labour caesarean section
• If drug resistance is detected on genotype/phenotype
• Avoid nevirapine as part of combination therapy if CD4 count ≥250

Short term HAART for prevention of mother to child transmission
• Discontinue this after delivery when viral load <50 copies/ml
• Carefully consider the half-life of each component to avoid unplanned monotherapy after stopping, especially drugs with a low genetic barrier to resistance

Stavudine plus didanosine
• Avoid stavudine plus didanosine whenever possible

HAART started before conception
• Usually this should be continued throughout pregnancy

Detailed anomaly ultrasound
• Consider a detailed anomaly ultrasound examination at 21 weeks for all fetuses exposed to antiretrovirals during the first trimester

How does HIV affect pregnancy and pregnancy outcomes?
Observational studies have shown that HIV infection is associated with varying rates of adverse pregnancy outcomes, such as increased spontaneous abortion, stillbirth, perinatal and infant mortality, intrauterine growth retardation, low birth weight, and chorioamnionitis. In South Africa’s confidential inquiry into maternal deaths for 2002-4, HIV/AIDS was reported to be the leading cause of death, responsible for 20.1% of all deaths, higher than any direct obstetric cause. This figure may underestimate the problem as HIV status was only known for about half of the maternal deaths.

Clinical management of labour and delivery
The British HIV Association recommends an elective caesarean section for women receiving zidovudine alone; those receiving combination therapy with detectable viraemia; and those with HIV and hepatitis C co-infection. Observational data have shown that caesarean section may be associated with a slightly higher risk of postoperative complications in women with HIV than in uninfected women and that frequent complications such as postpartum fever, endometritis, and minimise adverse outcomes.

In many resource poor areas, tuberculosis is a common opportunistic infection in pregnant women with HIV, so it should be excluded in these settings or in women who have recently arrived in a developed country from a developing one. Laboratory investigations, in addition to routine tests in pregnancy, should include liver function tests, complete blood count (including platelet count and lymphocyte subsets), plasma HIV RNA viral load, and screening for sexually transmitted infections. Where hepatitis screening is not one of the routine investigations, then hepatitis B testing should be offered to women from areas with a high prevalence of HIV infection, and hepatitis C screening should be considered if intravenous drug use is common.

Antiretroviral therapy can be used in pregnancy (according to a country’s guidelines) when indicated as an ongoing treatment for maternal health; when not needed for this indication, it can be provided for preventing mother to child transmission. If antiretrovirals are indicated for maternal health, the choice of regimen should ensure that maternal side effects and risks to the infants are minimised. Dosage modification is not required for nucleoside reverse transcriptase inhibitors and nevirapine. Efavirenz should be avoided during early pregnancy because of teratogenic neural tube defects seen in both primates and humans. The combination of didanosine and stavudine should be avoided in pregnancy because of lactic acidosis. Nevirapine should be avoided in women with CD4 counts >250×10^6 cells/l. When antiretroviral therapy is used for preventing mother to child transmission, regimens range from the use of triple antiretroviral therapy to zidovudine started antenatally, with or without peripartum nevirapine (box 1). Post-exposure prophylaxis should be started at birth (box 2).

How can HIV be managed in pregnancy?
Antenatal care provides an opportunity to counsel pregnant women about HIV risk and offer HIV testing. The management of a pregnant woman with HIV infection will depend on the resources available and the individual needs of the woman; a multidisciplinary team of clinicians, psychologists, and social workers will optimise care. In women who know their HIV status, prepregnancy counselling may optimise medical care and minimise adverse outcomes.

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wound infection, and pneumonia occur significantly more often in infected women.\textsuperscript{19-21}

Although the use of elective caesarean section has been a major factor in reducing the rates of mother to child transmission in well resourced settings, it may not be a feasible option in many less resourced areas of high HIV prevalence. In these areas, some cases might merit a lowered threshold for caesarean section; such cases would include any pregnancies where labour is expected to be prolonged or where other obstetric complications may be associated with increased transmission risk (such as abruptio placentae and preterm rupture of membranes). Depending on the available facilities, this may also apply to women who had had previous caesarean sections or breech presentations.

When caesarean section is not performed, care in labour should focus on minimising the risk of mother to child transmission. This risk is increased with increased duration of rupture of membranes. As artificial rupture of membranes has little obstetric benefit in normal labour, it should not be done routinely in women who are known to be HIV positive or in areas of high HIV prevalence. In the case of premature rupture of membranes, with or without labour, the risk of HIV transmission must be balanced against the risk of premature delivery.

Invasive fetal monitoring techniques such as penetrating or spiral scalp electrodes and fetal scalp blood sampling may create a portal of entry for the virus and ought to be avoided. Epiisolomy may increase the exposure of the infant to HIV during delivery and increase the risk of transmission. Routine episiotomy is not recommended, and it should be reserved for those cases with a clear obstetric indication. Assisted delivery by forceps or vacuum extraction carries a theoretical possibility of increasing the risk of transmission through damage to the baby’s skin. Little information exists on the contribution of obstetric procedures to the risk of transmission in the presence of antiretroviral therapy.

**Postpartum complications**
In most HIV positive women the postnatal course will be uncomplicated and no special medical care will be needed. Postpartum complications encountered more often in HIV positive women include puerperal sepsis, infected episiotomies, massive condylomata acuminata, urinary tract infections, pneumonia, fever, tuberculosis, and unusual infections.

**What about breast feeding?**
Breast feeding is an important route of transmission. In the United Kingdom, where safe infant feeding alternatives are available, HIV infected women are advised to refrain from breast feeding. In resource poor settings where breast feeding is essential for infant survival, exclusive breast feeding for four to six months may be justified.

**Diagnosis in infants**
In non-breastfed infants, HIV infection can be diagnosed definitively at age 6-12 weeks using DNA polymerase chain reaction. In some settings, such testing is done at birth to exclude in utero transmission of HIV-1, and this test is repeated at age 6 weeks and 12 weeks to exclude transmission that may have occurred in the intrapartum and postpartum period. If the mother is breast feeding her infant, HIV testing can start one month after weaning, with a second test eight weeks later.\textsuperscript{20}

**Conclusion**
Preventing HIV infection in children has become possible in the past decade. Interventions exist for minimising mother to child transmission of HIV, both in the developed and the developing world. If these are widely implemented in the next decade, they will result in a substantial decline in the number of children acquiring this devastating disease from their mothers.

**ADDITIONAL EDUCATIONAL RESOURCES**

- World Health Organization. HIV-infected women and their families: psychosocial support and related issues. A literature review. 2003. [www.who.int/reproductive-health/publications/hr_03_07/]
A PATIENT’S JOURNEY
Psoriasis

Ray Jobling

In 1955, I was 14 years old and just diagnosed with psoriasis. I didn’t know it then of course, but it would never go away. Psoriasis and its treatment were to be part of my life for the next 50 years and more.

My general practitioner gave it no name, but said it was common and could just go away. He said I might “grow out of it” and that I should get used to it, “learn to live with it.” This attitude scarcely promoted confidence in his prescribed tar ointments and baths—as noxious and loathsome in use as they were ineffective in action. He seemed unsurprised that I returned worse rather than better. By now the pink patches were large, numerous, and widespread. My body looked like an old map of the British Empire. The lesions grew fiery, scaling profusely, and crumbled messily. They bled; I looked and felt a mess.

I was dispatched to a dermatologist. I had psoriasis—no more information let alone an explanation was forthcoming. I was to redouble my ointmenting efforts. Perhaps, it was alleged, my (the family’s) compliance had not been strict enough, a ludicrous accusation for we were dutifully dedicated to the demanding daily rituals of topical treatment. We pressed on for months. Tar gave way to anthralin (dithranol), which stained me black and all but invisible as much as my clothing and bed linen. Life was punctuated by endless clinic encounters with a bewildering succession of skin doctors. I was repeatedly, rather routinely, told that I was not ill and must not think of myself as such. I had to live a normal life. It was after all no more than a “benign” condition. Later, I heard a dermatologist tell his students as I departed the consultation, “Not very interesting that one, just another very ordinary psoriasis.” If there was any awareness of the practical, psychological, and social complexities involved, no explicit interest was shown, and neither assistance nor advice was offered.

Not ill then, but obviously a permanent patient, I found myself in a strange and perplexingly ambiguous position. For someone who was not ill—I was otherwise in robust rugby playing good health in fact—I spent a puzzling amount of time in consulting rooms or clinics and labouring away at treatment. The demanding treatment regimens, which at times took more than 20 hours a week, brought scant reward. “Clearance” seemed to be the goal, but even improvement was only ever partial and dispiritingly temporary—remission was impossible. I was engaged in a relentless physical assault on my symptoms, at war with my skin . . . and inevitably losing. The disease and its treatment merged, combining inextricably to impact upon my personal experience and social identity; a sad fact that both were in effect demeaning. Skin disease can stigmatise. Stripped of my winter tan (derived from treatment) set me apart. Those who had insisted that psoriasis was not a handicap. I took my psoriasis and its treatment part of my life for the next 50 years and more.

Thus, I grew up with it. Years and life unfolded, inextricably tied to impact upon my personal experience and social identity—a fact I only grasped in my late 30s. In the 1950s.

Contributors: GE Gray was responsible for the conception, development, and overall writing of the article; she is also the guarantor. JAMcI provided the case report, gave obstetrical input, and helped to edit the manuscript.

Competing interests: None declared.

Provenance and peer review: Commissioned; externally peer reviewed.

Menstrual suppression has been recommended for medical conditions such as endometriosis, but it is also being proposed as a lifestyle choice for women who dislike menstruation or find it inconvenient. Articles in the professional and popular press have asserted that menstrual suppression is a reasonable lifestyle choice. Birth control options that reduce or eliminate periods are being developed. The oral contraceptive Seasonale, for example, combines 84 days of active pills (0.03 mg ethinyl oestradiol and 0.15 mg levonorgestrel) with seven days of placebo. Since menstrual flow occurs during the pill-free interval, a hormone-free interval every three months instead of the usual 21 days reduces the number of pill induced periods from 13 to four annually. Seasonale’s website (www.seasonale.com) states: “Fewer periods. More possibilities . . . you might want to consider asking about Seasonale if you . . . wish you had more time between periods, and less of them.”

The long term safety of menstrual suppression cannot currently be determined with experimental data. Seasonale, for example, has been approved by the Food and Drug Administration, but long term research was not required for approval. Overall, the existing data are limited, and whether or not long term risks exist remains uncertain: this would require lengthy study, of five years or more, and information about a broad range of users. Proponents have argued that menstrual suppression is safe, even beneficial, because monthly menstruation is unnecessary, even unhealthy. A seemingly scientific argument about the biological nature of women buttresses the idea that suppression can be considered safe even in the absence of experimental evidence. However, science involves logic and evidence, and the case against menstruation involves neither.

The case against menstruation was laid out in the book Is Menstruation Obsolete?—published by Oxford University Press in 1999; its authors argue that monthly menstruation throughout most of adult life is a modern development. In industrial societies the average woman has few children and therefore may have 450 menstrual cycles during a lifetime. Women in hunter-gatherer cultures and other societies without birth control average a total of 160 periods because they are either pregnant or breast feeding much of the time and, the authors assert, exemplify what was natural in the prehistoric past when human bodies evolved and throughout most of human history.

Monthly menstruation throughout adulthood is therefore at odds with what female bodies were designed to do; it is unnecessary and unnatural, and not surprisingly causes disease. To eliminate periods is a boon or at worst harmless.

But if it is more common today to have monthly menstrual cycles throughout adult life, this does not in itself mean that monthly menstruation is unnatural, much less that it is a medical problem. Human biology often permits variety and flexibility for different people in different situations. Nor is lifelong menstruation necessarily a modern invention. Women in cultures without birth control may average 160 menstrual cycles, but not every woman is the “average woman.” Today, some women in societies without birth control have few children. More likely than not, such women existed in prehistoric times as well. Throughout history women have been widowed, celibate for social or religious reasons, or angry with their spouses.

There probably have always been women who did not conceive quickly and men who were away from home for long stretches of time. Even ancient people may have used contraception. Malnourished women may stop ovulating without becoming amenorrhoeic. Further, why women menstruate is unknown. Menstruation is an anomaly in nature, and we have no idea why it evolved only among humans and non-human primates. We do know that menstruation is what naturally occurs when women don’t become pregnant, and that a menstruating woman is a healthy, probably fertile, woman—whereas unhealthy, malnourished, or massively stressed women are more likely to skip periods.

Even if prolonged monthly menstruation were unnatural and unhealthy, this would not prove that suppressing menstruation is better. Menstrual suppression itself is unnatural; a drug chronically overrides the physiological changes associated with the menstrual cycle, thereby creating an underlying hormonal environment that is not found in nature. Ovulation, the normal outcome of a menstrual cycle, is prevented because the hormones underlying ovulation have been suppressed. The menstrual flow is not a true period. Suppression may seem to mimic pregnancy and lactation, in the sense that there is no period, but the underlying hormonal milieu is far different.

The argument that menstruation is obsolete is illogical and unscientific. Reduced to its essentials, the argument amounts to this: too many periods can make women sick because women were meant to be constantly pregnant or breast feeding. The important questions are these: is there evidence that medications are safe and effective? What are the known benefits and risks, and what uncertainties exist with regard to future benefit and harm? Who should be using such medications? Are women provided with accurate information to make informed choices?

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Knowing what you don’t know

The light flashed on my buzzer. I paused for dramatic effect before saying, “Alexander Fleming.” The crowd went wild. I beamed—we had won, and I had captained our team in the primary school quarter finals of the local “Top of the Form” quiz. I had the sort of memory that retained facts easily. I am like most doctors.

A decade ago I was an evidence based medicine (EBM) “fact” groupie. I loved the wild swirling data, the mind expanding NNTs (numbers needed to treat), and the geeks who thumped out PowerPoint presentations and effectively smashed up the instruments of the old medical establishment. We got drunk on the power of EBM and how it would change the world. Occasional recreational use wasn’t enough—I was hooked. I pored over the classics of Cochrane and Bandolier and then sank further into Medline and PubMed. I wanted a David Sackett poster for my bedroom wall. With practice I got pretty good, and then the problems started.

I skipped discussion sections and went straight to the data tables. I started seeing confounding factors throughout papers. I lost sleep to intrusive concerns over study populations, study length, publication bias, surrogate endpoints, and a whole new concern, “commissioning bias,” which gives disproportionate weight to drug interventions: no research means no evidence.

But worst of all is the poor quality of the epidemiological foundation of all our facts. Simply put, the natural history of many conditions isn’t known.

Take the current demand for screening for chlamydial infection. What is the lifetime incidence of chlamydia if the point prevalence is 10%? Could the current observed increase merely reflect more and better testing? In the 1970s, when condoms and sexual health services were less available, surely chlamydia must have been more prevalent? What percentage of infections progress to pelvic inflammatory disease? Without this knowledge how can anyone suggest screening?

We doctors enjoy the comfort and power that facts bring, but unfortunately we apply them with an absolute certainty that they do not deserve. EBM runs the risk of becoming just as restrictive and conservative as the medical establishment that it replaced. The future challenge is to establish robust prospective epidemiological data for common medical conditions and to focus on what we don’t know rather than what we think we know.

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Grave expectations

A dearth of suitable bodies has long been a cause of sleepless nights for surgeons. Today, members of the Royal College of Surgeons may toss and turn in anxiety over a predicted 30% shortfall in the 1000 bodies medical schools need annually. In 1828, surgeons giving evidence to the select committee on anatomy were just as concerned at a 200 shortfall in the 700 cadavers needed by the London schools alone. Naturally enough the source of bodies for dissection has changed—as has the reason for the sleepless nights.

Before the 1832 Anatomy Act, surgeons were accustomed to being dragged out of bed in the early hours to pay exorbitant fees to lawless gangs of body snatchers for mouldering corpses filched from paupers’ graveyards. Indeed, if they did not make acceptable arrangements with the grave robbers, they might find body parts strewn at either end of their street—an easy signpost to the nightwatchmen—as anatomy teacher Joshua Brookes discovered to his cost.

But when bodies were in short supply, surgeons and students had to venture out at night to exhume suitable bodies—at the risk of being arrested, stoned, or even shot.

John Hunter almost certainly led students in night-time expeditions from his brother William’s Covent Garden school to plunder nearby churchyards in the mid-1700s. But long after most anatomy teachers had found it expedient to pay the Resurrection Men to dirty their hands for them, students in Scotland, Ireland, and America still had to shift for themselves.

One distinguished professor of anatomy, giving evidence to the 1828 committee, recalled student parties in Glasgow—to graveyard, not the students’ union bar—when he was often shot at by vigilante groups guarding their relatives’ graves. At least, if injured, there was always a surgeon on hand.

Later, discovered with a stolen skull while teaching in Edinburgh, he had been paraded through the town, pelted with stones, and tried “like a common criminal.”

In New York, surgeons had to seek refuge in the city jail when furious locals discovered their body-raising activities in 1788. And in Dublin medical students joined the university’s art students for nightly expeditions to lift bodies, even in the early 19th century.

If surgeons today are relieved that their nightly exploits are more mundane, they may still look back wistfully at the diminution of their persuasive powers in the committee rooms of Westminster since 1828. Sir Astley Cooper, then president of the Royal College of Surgeons, left MPs in no doubt of his useful connections when he informed them chillingly that, “there is no person, let his station in life be what it may, whom, if I were disposed to dissect, I could not obtain.” It certainly beat threatening to vote for the other side.

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FROM THE FRONTLINE
Des Spence

PAST CARING
Wendy Moore

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Green tea and monkey business

The name Le Fanu is not unknown to medicine in this country. There is, for example, the medical correspondent of one of our major newspapers, which it would be wrong to advertise, and W R LeFanu, who was the librarian of the Royal College of Surgeons between 1929 and 1968. A man of immense erudition, which puts one’s own ignorance to shame, he oversaw the removal of the library during the second world war to Shropshire, saving it from the destruction that the college itself suffered during the blitz. A bibliographer of distinction, especially in the field of Jennerian studies, he published a bibliography of Nehemiah Grew at the age of 86, in 1990.

Sheridan Le Fanu, the Irish writer of ghost stories, was an ancestor of his. Doctors featured very often in Le Fanu’s stories; one book, *In a Glass Darkly*, published in 1872, is a series of the cases of one Dr Hesselius, a German specialist in “metaphysical medicine.”

In the first and most famous of these stories, *Green Tea*, Dr Hesselius is consulted by the Reverend Mr Jennings, a clergyman in easy circumstances who, alas, is haunted. Already interested in the supernatural—books about which he stays up all night studying while drinking green tea—he one day sees two red eyes staring at him on an omnibus, which he then makes out to belong to a spectral monkey through which his umbrella can pass without meeting any resistance. The monkey stays with him for the rest of his days and grows ever more intrusive, jumping on to the Bible when he tries to read from it in church, then uttering terrible blasphemies whenever the Reverend Jennings tries to pray, and finally issuing him with commands, including that to commit suicide. Eventually, he does kill himself, by cutting his throat.

Dr Hesselius’s diagnosis of the Reverend Jennings’s distemper is cautious. It is one of Le Fanu’s themes that we can never fully or definitively interpret events, and Dr Hesselius is of like opinion. In this case, he goes in for what one might call agnostic multifactorialism. First was “the habitual use of such agents as green tea,” which disturb the equilibrium of the cerebral fluids. Interestingly, a National Institute of Health website informs us that when more than 8 to 10 cups of green tea per day are drunk, “symptoms of anxiety, delirium, agitation and psychosis may occur.” Nor is stopping the tea necessarily instantly beneficial in those with “affective disorder or schizoaffective disorder,” in whom caffeine withdrawal can cause “confusion, disorientation, excitement, restlessness, violent behaviour, or mania.”

In Dr Hesselius’s opinion, one of the effects of the tea is to influence the brain so that “disembodied spirits may operate in communication more effectively.” He thus makes it unclear as to whether he believes the black monkey with red eyes is a hallucination pure and simple, or an actually existing entity.

But Dr Hesselius doesn’t blame the tea alone. “[Jennings’] case was in the distinctive manner a complication, and the complaint under which he really succumbed, was hereditary suicidal mania.” So he was predisposed to kill himself, green tea and black monkey, or no green tea and black monkey.

As to therapy, Dr Hesselius says that iced eau de cologne applied to the forehead would have worked if applied long enough. What rubbish! Everyone knows that what the Reverend Jennings needed was an SSRI (selective serotonin reuptake inhibitor), because serotonin is the key to all human happiness and misery, and indeed to all behaviour.

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**MEDICAL CLASSICS**

The Final Diagnosis By Arthur Hailey

First published 1959

“As is your pathology, so is your practice,” said Sir William Osler, the philosopher-physician over 100 years ago. While today some may not entirely agree with the sweeping generalisation of the statement, it remains a fact that pathology forms the bedrock of medicine. Arthur Hailey, too, recognised this fact when he wrote *The Final Diagnosis* in 1959. While most novels and movies dealing with medicine revolve around clinicians, particularly surgeons, Hailey decided to make the department of pathology and the pathologist the core of the action. Surgeons and other physicians in the hospital are, of course, important players; they have to be, because, after all, pathology makes its existence felt after the surgeon has made the first move.

When I first read the book just over a quarter of a century ago, I fell in love with the idea of working in a big hospital. Small wonder then that I chose this book as a must read for all doctors (BMJ 2005; 331:1482).

In retrospect, having read it again recently, the plot is nothing spectacular: it’s just another month in the life of a busy general hospital, the Three Counties in Pennsylvania. But, as anyone who’s worked in a big hospital knows, every month is interesting and carries its own, different challenges. There is, just as in other Arthur Hailey novels, a multitude of characters, each with their own subplots. The story weaves around the working relationships between the many physicians and others who run the hospital.

Joe Pearson is the chief of pathology; once an excellent pathologist, he is now out of touch with the latest methods in laboratory medicine. Change is under way at the Three Counties Hospital, and Pearson faces the possibility of losing his job. That, however, could lead to loss of a substantial donation to the hospital, from a rich benefactor, who is a friend of Pearson’s. Just as the surgeon-administrator Kent O’Donnell weighs the pros and cons of his decisions, Hailey balances O’Donnell’s professional life with his love life. Tragedy surfaces in the book, as it does in real life in hospitals, when doctors make errors, or when terrifying diseases strike young, likeable people.

The story is readable nearly 50 years after it was first published. Some of the scenes are melodramatic, at least from a physician’s viewpoint. But the issues that Hailey deals with are as relevant now as in 1959. Equally striking—and a reflection of the meticulous research that the author was famous for—is the fact that there are no bloomers in Hailey’s descriptions of various medical procedures. Perhaps for the first time, non-medical readers were introduced to the concept of frozen sections, clinico-pathological conferences, and doubt and uncertainty in medicine.

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You may never eat a hamburger again after seeing *Fast Food Nation*. You may even become a vegetarian. This film, based on award winning journalist Eric Schlosser’s eponymous bestseller (*BMJ* 2002;324:1461), is far more than an expose of the fast food chains that have spread across the world, oozing like ketchup from their American birthplace and providing standardised hamburgers and fries (chips) to millions.

It describes the fast food industry’s influence on what we eat, on illegal immigration to the United States, on agriculture, on globalisation, on environmental impact, on dead-end and sometimes dangerous jobs, on real estate interests, and on how middle America thinks about work.

The film’s subtitle is “You want lies with that?”—a pun on McDonald’s “You want fries with that?”—whereas Schlosser’s book was subtitled “The Dark Side of the All-American Meal.” His opening chapter described a man who most days delivered pizza to the well guarded North American Aerospace Command inside Cheyenne Mountain in Colorado. Other chapters described the growth of the fast food industry.

The film is different and translates the complex history of the fast food industry into easily grasped fictional stories of the people involved. It begins with a group of young Mexicans illegally entering the United States with a dangerous journey through the Arizona desert. Some will die. Those who survive are transported to several cities for “off the books” work that nevertheless pays immensely more than they could earn at home. Some wind up in the imagined small city of Cody, Colorado.

In parallel, we see a marketing executive (played by Greg Kinnear), a nice family guy, who has been successful at his company by inventing and promoting “The Big One” hamburger for his fastfood chain, called Mickey’s, and who is involved in the chemical processes used to improve the burger’s smell and taste. However, like many middle Americans, he is worried about his job.

He hears from his boss that a watchdog group has found high levels of faecal coliform bacteria—*E coli*—in the frozen hamburger patties that Mickey’s ships from Colorado to its many fast food outlets, where the patties are quickly cooked and packed into “The Big One” hamburgers. “There’s shit in the meat,” barks his boss.

The marketing executive is sent to investigate the contamination problem at Cody, which supplies Mickey’s meat. Thousands of cattle fill mile after mile of huge feedlots, where their manure and urine contaminate the land and water all around. Then they are sent to a plant, where they are slaughtered, butchered, turned into round, pink hamburger patties, frozen, and shipped out nationwide. The executive is taken on a tour through an apparently spotless, sanitary plant. “You didn’t see the kill floor,” people tell him.

A man who sells cattle from ranchers to the meat-packing conglomerate—brilliantly played by Bruce Willis—discounts the problem of faecal contamination: “Meat is supposed to be cooked. Just cook it,” he says.

A rancher explains how real estate interests are trying to take over the land where he has raised cattle like his forefathers. They are building whole suburban communities on what was once ranchland.

The illegal Mexican immigrants find jobs at Cody’s meat processing plant. The work is gruelling and dangerous and the hours are long. Sexual exploitation of women is common.

Sometimes workers take drugs to take the edge off. Nevertheless, they are glad to have the jobs, which pay them more in an hour than they would make in a day in Mexico and enable them to send money home to their families. They are drawn into lower middle class life: buying a used car, taking a girlfriend out for a meal at a fast food restaurant.

Some scenes are scary, showing workers using sharp knives and electric blades with no apparent safety devices. One scene is devastating.

Beyond the obvious fast food story, the film cleverly entwines many aspects of US life: its corporate culture, which the film says is corrupt; companies’ need for illegal and poorly paid immigrant labour; workers who are only too happy to stay in terrible jobs for higher pay than they could get at home; and workers who are on drugs because their work is so demeaning, which puts them at risk of injury on the job.

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**Fast Food Nation**

**UK release date:** 4 May 2007.

**US release date:** 17 November 2006.

**Rating:** ★★★★☆

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**The film highlights fast food companies’ need for illegal and poorly paid immigrant labour**

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**REVIEW OF THE WEEK**

**Lies with everything**

Janice Hopkins Tanne is horrified by a film about America’s burger industry.
OBITUARIES

Geoffrey Battersby Barker

Former consultant psychiatrist Tooting Bec and St Thomas’ Hospitals (b 1919; q Cambridge/Westminster Hospital 1943; MA, DPM, FRCPsych), died from myeloma on 1 December 2006. Geoffrey Barker first worked in a neurological team dealing with head injuries from the D-Day landings. In 1948 he joined Tooting Bec Hospital, introducing an open-door policy in the day hospital and setting up the art therapy department. He specialised in women’s mental health and drug abuse, and during 1967-72 was medical administrator. Geoffrey was a tutor at the Tavistock Clinic and held a child guidance fellowship at Guy’s Hospital. He was adviser to the Arts Council, chairman of the Dyslexia Teaching Centre, and a founding member of the Alzheimer’s Society. In his career he was consultant to the Nuffield Provincial Hospitals Trust, and a founding member of the Royal College of Psychiatrists. In 1977 he was appointed consultant neurologist to Charing Cross, and Carers UK.

A Barker

Melville Robert (“Peter”) Fell

Former obstetrician and gynaecologist Salisbury (b 1920; q University College Hospital 1946; FRCOG), died from prostate cancer on 12 February 2007. After national service in the army as a general duties medical officer Peter Fell did junior obstetric posts at St George’s Hospital and the Samaritan and Middlesex before becoming resident obstetrician at Queen Charlotte’s Hospital. In 1957 he was appointed consultant in Salisbury, retiring in 1986. He served on many committees at the Royal College of Obstetricians and Gynaecologists, the Wessex Regional Health Authority, Southampton Medical School, and in Salisbury, being chairman on most, as well as of the Salisbury division of the BMA. Peter had a handicap of four in golf and played for his county. He leaves a wife and two children.

P M S Gillam

William George Grenville Loyn

Former consultant anaesthetist Bronglais Hospital, Aberystwyth (b 1924; q Middlesex Hospital 1947; ERD, TD, FFA), died from a chest infection on 1 March 2007. Gren Lown was called for service in the army after qualifying, and he later joined the Territorial Army, maintaining his membership until he developed poor health. Early in his career he was consultant anaesthetist at the Whittington Hospital for several years until he decided to return to his native Wales, where he was consultant anaesthetist at Bronglais Hospital until his retirement. He was the author of several publications— notably a section on anaesthetics and anaesthesia in Law and Friedman’s Midwifery. He leaves a wife and three children.

Hugh Herbert

Henry Gemmell Morgan

Emeritus professor of pathological biochemistry University of Glasgow (b 1922; q St Andrews 1946; BSc, FRCPath), d 31 October 2006. A pioneer of clinical biochemistry, Gemmell Morgan first developed the science at Dundee Royal Infirmary during 1952-65, implementing an undergraduate course in 1953. During his 23 years as professor in Glasgow his vision led to the opening of a new Institute of Biochemistry at the Royal Infirmary in 1977, which in his time trained 24 medical consultants. Gemmell held many influential positions, including chairmanship and presidency of the Association of Clinical Biochemists. He died from ultimate failure of a 30 year old graft of his left femoral artery, which had blocked from the long term effects of radiotherapy for a fist-sized malignant tumour when he was 18. He leaves a wife, Margaret; a daughter; and two grandchildren.

Jim Shepherd, Alan Shenkin

Robert Roaf

Former professor of orthopaedic surgery Liverpool University (b 1913; q Oxford 1938; MA, FRCS, MChOrth), d 16 February 2007. Robert Roaf was a world famous spinal surgeon and a Himalayan climber in the 1930s, as well as a thinker and philosopher. In 1947 he was appointed to the orthopaedic hospital in Oswestry, where he developed the now standard procedure of operating through the chest to correct scoliosis. In 1955 Robert was appointed director of clinical studies and research at Oswestry. In 1964 he was appointed professor at Liverpool University, retiring in 1976. He held many honorary fellowships and memberships of international medical associations. His main publications include Scoliosis (1966), Posture (1977), and Spinal Deformities (1980). Latterly he published his Himalayan experiences. Predeceased by his wife, Ceinwen, by a week, he leaves four children.

Roger Croston

Carl John Williams

Consultant orthopaedic surgeon Wythenshawe, Manchester (b 1967; q London 1992; BSc, MD, FRCS), d 4 December 2006. Carl was a good friend who managed to balance a tidy and organised life with a sense of fun and adventure. He had old fashioned values with a modern outlook, talent, and a positive personality. He removed a small skin lesion from himself five years ago, which turned out to be a melanoma. A lesser man might have given up, but Carl continued to work and play hard. Snowboarding, mountain biking, and windsurfing were his passions, together with the constant, continuous, and often radical home DIY projects. His ambition to be a consultant surgeon in a major teaching hospital was achieved about a year before his death. He leaves his father.

Simon Carley, Gary Boland
Recurrence of diarrhoea occurs in as many as 25% of patients after the successful resolution of Clostridium difficile infection. One strategy for breaking the cycle is described in Clinical Infectious Diseases (2007;44:846-8). Eight women who had each experienced 4-8 episodes of diarrhoea associated with C difficile were given a two week course of rifaximin when asymptomatic after completing their last course of vancomycin (the antibiotic used to treat C difficile). Seven out of the eight had no further recurrence of diarrhoea.

A UK breastfeeding manifesto is to be launched on 16 May 2007 (www.breastfeedingmanifesto.org.uk). Acting on this manifesto would, it is hoped, help reduce inequalities in health, improve the health of the nation, and save the NHS money while ensuring that the UK government fulfils its existing commitments to women. Campaigners say that if all babies were breastfed for at least three months, the reduction in the incidence of gastroenteritis alone would save the NHS in England and Wales more than £35m (€51m; $70m) a year.

Another way to save money is to treat epilepsy with surgery, according to a study in Neurology (2007;68:1290-9). For refractory epilepsy, surgery is effective but costly. But this cost should be offset by longer term savings because patients need fewer healthcare services. In this economic analysis, costs remained stable over two years for patients with temporal lobe epilepsy whose seizures persisted after surgery. But patients who became seizure-free used substantially less health care and far fewer drugs than before surgery.

A prospective 10 year comparison of reconstructions of the anterior cruciate ligament by autograft of either hamstring or patella tendon reports that both tendons make excellent materials to autograft (American Journal of Sports Medicine 2007;35:564-74). Reconstructions with hamstring tendon resulted in fewer symptoms at the site of the harvest, however, and also fewer changes of osteoarthritis on x rays.

Patients with Duchenne muscular dystrophy may eventually benefit from a drug that has recently been tested in mice (Nature 2007 Apr 22, doi:10.1038/nature05756). This condition and many other inherited diseases result when translation of messenger RNA into a protein stops prematurely. A small molecule called PTC124 has been shown to enable the translation machinery to bypass sites that cause the premature termination but still to stop normally at the end of the messenger RNA. And, in a well known mouse model, muscle function was restored.

An insight into traditional Chinese medicine and how it could be integrated into modern Western medicine is being offered by the Prince’s Foundation for Integrated Health by way of an eight day tour to Hong Kong and mainland China in September 2007. The trip is being organised with the school of public health, Chinese University of Hong Kong. Email iha@fhf.org.uk to find out more.

Raised circulating concentrations of homocysteine are associated with greater risk of cardiovascular disease, but the exact mechanism is unclear. To investigate whether the association is mediated through blood pressure, a team in New Zealand gave vitamins to reduce homocysteine to a group of healthy older people (Journal of Nutrition 2007;137:1183-7).

The team’s randomised placebo controlled trial showed that despite significantly lower homocysteine in the vitamin group, blood and pulse pressures were not significantly different than in the placebo group.

Barbershops owned by black people seem to be useful places for monitoring high blood pressure in black men in the United States. Barbers did well in two feasibility studies designed to test whether they could carry out useful and long term programmes to monitor blood pressure (Hypertension 2007;49:1040-53). An additional benefit was that customers seemed to take their drugs more regularly, and control of blood pressure improved more as the number of interventions increased.

There is often a conflict between what people need and the costs involved in meeting these needs. A study of the cost and value of building nursing homes with private or shared bedrooms has found that almost all outcomes are better with private rooms (Gerontologist 2007;47:169-83). To build homes with private rooms costs more than a third more, but the difference is recouped within two years if the rooms are fully occupied.