Editor's choice

Going to extremes
Tony Delamothe
BMJ 2007;335, doi:10.1136/bmj.39385.488796.47

Editorials

Paramedic practitioners and emergency admissions
Malcolm Woollard

Occupational therapy after stroke
Kathryn M McPherson, Caroline Ellis-Hill
BMJ 2007;335:894-895, doi:10.1136/bmj.39370.600729.BE

Device therapy in heart failure
Finlay A McAlister

Diet and the risk of cancer
Tim Key
BMJ 2007;335:897, doi:10.1136/bmj.39373.676204.BE

Mental Capacity Act 2005
Andrew Alonzi, Mike Pringle
BMJ 2007;335:898, doi:10.1136/bmj.39372.691076.80

Letters

This week’s letters

Allergy after breast feeding: Study was not designed to test the hypothesis
Karen M Silvers, Michael J Epton, Chris M Frampton
Abdominal aortic aneurysm: Screening reduces all cause mortality in men
Hisato Takagi, Norikazu Kawai, Takuya Umemoto
BMJ 2007;335:899, doi:10.1136/bmj.39381.395197.BE

Value of video clips: Useful in acute upper airway obstruction in children
Graham A M Wilson, Thomas Engelhardt, Bruno Marciniak

Honouring advance decisions: You don't in psychiatry
Thomas Szasz
BMJ 2007;335:900, doi:10.1136/bmj.39381.503287.BE

Observational studies: More than high standards needed
Guy Lloyd
BMJ 2007;335:900, doi:10.1136/bmj.39381.434919.BE

Talk of psychosocial factors: Tell the whole story
Charles T Vivian
BMJ 2007;335:900, doi:10.1136/bmj.39381.514780.BE

News

UK report calls for new services to improve out of hours acute care
Susan Mayor
BMJ 2007;335:901, doi:10.1136/bmj.39384.593634.DB

Cardiopulmonary resuscitation decisions should be extended to nurses
Caroline White
BMJ 2007;335:901, doi:10.1136/bmj.39384.681829.DB

In Brief: News
BMJ 2007;335:902, doi:10.1136/bmj.39384.555336.4E

Prison inspector's report slates mental health provision
Anne Gulland
BMJ 2007;335:902, doi:10.1136/bmj.39381.445150.DB

No evidence backs reduction in abortion time limit, minister says
Adrian O'Dowd
BMJ 2007;335:903, doi:10.1136/bmj.39381.521481.DB

US Congress asked to suspend funding for Planned Parenthood
Janice Hopkins Tanne
BMJ 2007;335:903, doi:10.1136/bmj.39384.487326.4E

GP who benefited from patient's will failed to disclose details when signing cremation form
London trusts overhaul primary care without consultation
Caroline White
BMJ 2007;335:904, doi:10.1136/bmj.39384.586262.DB

Striking medics in Gaza temporarily return to work after talks with Hamas
Merav Sarig
BMJ 2007;335:904-905, doi:10.1136/bmj.39384.458935.DB

Watchdog could close hospitals in a day to tackle infections
Helen Mooney
BMJ 2007;335:904-905, doi:10.1136/bmj.39381.464907.DB

German doctors may have to report patients who have piercings and beauty treatments
Annette Tuffs
BMJ 2007;335:905, doi:10.1136/bmj.39384.581377.DB

US passes bill granting mandatory access to data
Jeanne Lenzer
BMJ 2007;335:906, doi:10.1136/bmj.39384.638241.DB

Beauty is truth, truth beauty
Lynn Eaton
BMJ 2007;335:906, doi:10.1136/bmj.39381.738947.DB

Health authority forced to publish private contract for hospital build
Bryan Christie
BMJ 2007;335:906-907, doi:10.1136/bmj.39384.520486.4E

Agency urges researchers to make more use of yellow card data
Roger Dobson
BMJ 2007;335:907, doi:10.1136/bmj.39381.659688.DB

European Commission asked to investigate use of snus to reduce smoking
Rory Watson
BMJ 2007;335:907, doi:10.1136/bmj.39381.528507.DB

Government backs MRC chairman's appointment
Caroline White
BMJ 2007;335:907, doi:10.1136/bmj.39381.713218.DB

Practice based commissioning lacks adequate information and support
Andrew Cole
BMJ 2007;335:907, doi:10.1136/bmj.39381.490139.DB
UN official warns of deteriorating health situation in Gaza Strip
John Zarocostas
BMJ  2007;335:907, doi:10.1136/bmj.39384.526944.DB

Shortcuts from other journals:  Doctors and patients feel the same after medical errors
BMJ  2007;335:908, doi:10.1136/bmj.39380.679039.80

Shortcuts from other journals:  Still no consensus over link between hysterectomy and incontinence
BMJ  2007;335:908, doi:10.1136/bmj.335.7626.908-a

Shortcuts from other journals:  Provide for the world's poorest first
BMJ  2007;335:908, doi:10.1136/bmj.335.7626.908-b

Shortcuts from other journals:  Basal insulin safest in badly controlled type 2 diabetes
BMJ  2007;335:908-909, doi:10.1136/bmj.335.7626.908-c

Shortcuts from other journals:  Atrial natriuretic peptide helps limit infarct size after heart attack
BMJ  2007;335:909, doi:10.1136/bmj.335.7626.909

Shortcuts from other journals:  Hepatitis A vaccination is effective after exposure
BMJ  2007;335:909, doi:10.1136/bmj.335.7626.909-a

Shortcuts from other journals:  An unhealthier future for most Americans
BMJ  2007;335:909, doi:10.1136/bmj.335.7626.909-b

Shortcuts from other journals:  Inequality drives the HIV epidemic
BMJ  2007;335:909, doi:10.1136/bmj.335.7626.909-c

Feature
Lyme wars
Alison Tonks
BMJ  2007;335:910-912, doi:10.1136/bmj.39363.530961.AD

Observations
Body Politic: Observations
Nigel Hawkes
BMJ  2007;335:913, doi:10.1136/bmj.39381.648681.47

Analysis
Uncertainty in heterogeneity estimates in meta-analyses
John P A Ioannidis, Nikolaos A Patsopoulos, Evangelos Evangelou
BMJ  2007;335:914-916, doi:10.1136/bmj.39343.408449.80

Measuring quality through performance: Improving the quality of care with performance indicators
Azeem Majeed, Helen Lester, Andrew B Bindman
Research

Effectiveness of paramedic practitioners in attending 999 calls from elderly people in the community: cluster randomised controlled trial
Suzanne Mason, Emma Knowles, Brigitte Colwell, Simon Dixon, Jim Wardrope, Robert Gorringe, Helen Snooks, Julie Perrin, Jon Nicholl

Occupational therapy for patients with problems in personal activities of daily living after stroke: systematic review of randomised trials
Lynn Legg, Avril Drummond, Jo Leonardi-Bee, J R F Gladman, Susan Corr, Mireille Donkervoort, Judi Edmans, Louise Gilbertson, Lyn Jongbloed, Pip Logan, Catherine Sackley, Marion Walker, Peter Langhorne

Combined resynchronisation and implantable defibrillator therapy in left ventricular dysfunction: Bayesian network meta-analysis of randomised controlled trials
Simon K H Lam, Andrew Owen

Clinical review

Management of sepsis
Iain Mackenzie, Andrew Lever
BMJ 2007;335:929-932, doi:10.1136/bmj.39346.696620.AE

Practice

Pregnancy Plus: Systemic lupus erythematosus
Lucy H Mackillop, Sarah J Germain, Catherine Nelson-Piercy
BMJ 2007;335:933-936, doi:10.1136/bmj.39358.519491.AD

Lesson of the week: Anal ulceration induced by nicorandil
Fayyaz Akbar, Andrew Maw, Arnab Bhowmick
BMJ 2007;335:936-937, doi:10.1136/bmj.39246.714896.BE

Views & reviews

Personal view: The price of life
Brendan D Kelly, Sharon R Foley
BMJ 2007;335:938, doi:10.1136/bmj.39378.691296.3A

Review of the week: Life through a lens
Amy Davis
BMJ 2007;335:939, doi:10.1136/bmj.39384.456181.34

From the frontline: The baby shambles
Des Spence
BMJ 2007;335:940, doi:10.1136/bmj.39384.481308.59
The bigger picture: **Crown of thorns**
Mary E Black
BMJ 2007;335:940, doi:10.1136/bmj.39384.530833.59

Between the lines: **The therapy of obedience**
Theodore Dalrymple
BMJ 2007;335:941, doi:10.1136/bmj.39384.494769.59

Medical Classics: **The Doctor, his Patient and the Illness**
James Curran
BMJ 2007;335:941, doi:10.1136/bmj.39384.467928.94

**Obituaries**

**This week’s obituaries**

**John Douglas Andrew**
Alan Craft, Andrew Cottrell
BMJ 2007;335:942, doi:10.1136/bmj.39364.740671.BE

**Rex Penny Edward Barton**
Nicola Barton
BMJ 2007;335:942, doi:10.1136/bmj.39364.695463.BE

**Edwin Melville Mack Besterman**
E M M Besterman
BMJ 2007;335:942, doi:10.1136/bmj.39364.591887.BE

**Anne Gall (née Kirkby)**
Jean Mcmillan, Joanna Gall
BMJ 2007;335:942, doi:10.1136/bmj.39372.661238.BE

**Geoffrey Brooke Hirst**
J Hirst
BMJ 2007;335:942, doi:10.1136/bmj.39377.694387.BE

**Andrew Wilson Lees**
Andrew Dickie
BMJ 2007;335:942, doi:10.1136/bmj.39364.651944.BE

**William Mathews**
Hilary M L Mathews
BMJ 2007;335:943, doi:10.1136/bmj.39377.586840.BE

**Anthony John Membrey**
Helen Membrey
BMJ 2007;335:943, doi:10.1136/bmj.39379.539572.BE

**Kusum Mehta**
Moira Pinkney, Nick Edwards, Hanza Mehta
BMJ 2007;335:943, doi:10.1136/bmj.39364.727002.BE
**Thilliampalam Paramananthan**
B Thalayasingam, Ratna Paramananthan, A D Piyasena
BMJ 2007;335:943, doi:10.1136/bmj.39377.640185.BE

**Seyed Abdolmajid Rooholamini**
Bita Manzouri
BMJ 2007;335:943, doi:10.1136/bmj.39365.540718.BE

**James Picton Douglas Thomas**
John Peters, M F Scanlon
BMJ 2007;335:943, doi:10.1136/bmj.39365.499248.BE

**Maxwell Herman Turner**
Deborah C Turner
BMJ 2007;335:943, doi:10.1136/bmj.39377.710602.BE

---

**Minerva**

**Minerva**
BMJ 2007;335:944, doi:10.1136/bmj.39381.454387.471

**Minerva**
O Kulkarni, D Gosal, T Majeed
BMJ 2007;335:944, doi:10.1136/bmj.39381.454387.47

---

**Corrections**

**Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies**
BMJ 2007;335, doi:10.1136/bmj.39386.490150.94
Editorials represent the opinions of the authors and not necessarily those of the BMJ or BMA

For the full versions of these articles see bmj.com

**Paramedic practitioners and emergency admissions**

Evidence suggests a positive effect, but future programmes need rigorous assessment before being expanded

In this week’s BMJ, Mason and colleagues report a cluster randomised controlled trial examining the effects of a “paramedic practitioner” service in a UK urban setting. The trial focused on managing older patients without life threatening conditions who accessed the emergency ambulance service. It aimed to increase the proportion receiving care in the community and reduce admissions to the emergency department. It found that people in the intervention group were less likely to attend the emergency department (relative risk 0.72, 95% confidence interval 0.68 to 0.75) or need hospital admission within 28 days (0.87, 0.81 to 0.94). However, use of secondary care services after the initial episode increased (1.21, 1.06 to 1.38).

Paramedic practitioners undertook a three week theory course followed by 45 days of supervised clinical experience. Their scope of practice was restricted to common presentations considered unlikely to result in serious injury, including falls, lacerations, epistaxis, and minor burns. Skills acquired beyond those normally practised by UK paramedics included wound care and suturing; examination of the joints; examination of the neurological, cardiovascular, respiratory, and ear, nose, and throat systems; social needs assessment; administration of antibiotics, simple analgesics, and tetanus toxoid; and referral of patients for radiography or to a general practitioner, district nurse, or social services.

As long ago as 1994, it was reported that services that deputised for general practitioners often could not cope with the demand for out of hours consultations. In addition, calls for emergency ambulances have been rising persistently by as much as 8% each year, yet half of patients taken to emergency departments by ambulance are discharged without being treated or referred. The increased demand for emergency ambulances may have been exacerbated by the introduction of general practitioner contracts that do not require the provision of out of hours services, although this has not been proved. Ambulances often have to queue outside emergency departments because a lack of trolley bays means that patients cannot be admitted. This in turn results in a lack of ambulances to respond to further emergency calls. Similar problems have occurred in Australia, New Zealand, the United States, and Canada. This, along with the need to tackle the challenges of providing health care to remote populations, has led to the formation of the International Roundtable on Community Paramedicine (www.ircp.info).

Emergency care practitioners were introduced with the aim of reducing admissions to the emergency department for a broader range of patients than those discussed by Mason and colleagues. A pilot programme began in the Warwickshire Ambulance Service in 2002, with the support of Coventry University and the changing workforce programme. It was subsequently expanded to encompass 17 pilot sites. Although this was intended to promote a standardised 15 week university based course, with all practitioners having a similar scope of practice, several centres opted for alternative approaches, including that described by Mason and colleagues. Most emergency care practitioners are paramedics working in ambulance services, but some are nurses or physiotherapists, and most work in out of hours and primary care services or emergency departments. Similar paramedic based programmes in other countries include those of the Queensland and New South Wales Ambulance Services in Australia.

Few high quality evaluations of the emergency care practitioner scheme and other extended scope paramedic practitioner schemes have been published to date. A changing workforce programme review reported that emergency care practitioners could reduce admissions to emergency departments by 100 to 358 patients each year in rural and urban settings, respectively. For a training investment of £24 250 (€34 800; $50 000), this would save the National Health Service £62 000-£72 000 each year for each practitioner. In Wales, autonomous “advanced paramedic practitioners,” who are educated to masters degree level, responded to about 25% (n=635) of 999 calls received in one primary care trust area. Of these, 292 (46%) patients were treated and discharged at the scene; 75 (12%) were re-graded to non-emergency transport; and 34 (5%) were admitted to hospital destinations other than the emergency department. Although emergency care practitioners are typically targeted to calls triaged as “low priority” by ambulance dispatchers, the Welsh scheme found that the greatest proportion of patients with altered care pathways fell within high and medium priority categories (24% and 22%, respectively, v 17% in the lowest priority category).

In a scheme in the west of England, 48/170 (28%)
patients were treated “on scene” by emergency care practitioners with a BSc in emergency care, compared with 60/331 (18%) attended by paramedics. A more recent evaluation found that 62% of patients seen by emergency care practitioners were not admitted and 38% were referred; practitioners self reported that their intervention prevented an acute admission in 60% of cases.

The trial by Mason and colleagues is the first adequately powered randomised controlled trial to investigate the effect of an extended scope paramedic programme on admissions to the emergency department. Although their results are largely positive, they cannot be generalised beyond the scheme evaluated. Perhaps, most importantly, the trial shows that high quality study designs are feasible in this setting. Such trials should, therefore, be used to evaluate the more widespread emergency care practitioner scheme and other extended scope paramedic programmes before further costly expansions take place.

**Occupational therapy after stroke**

Improves personal activities of daily living, but evidence remains sparse on other potential effects

In this week’s *BMJ*, Legg and colleagues present a systematic review of randomised trials assessing the effect of occupational therapy on personal activities of daily life in people who have had a stroke.

Stroke is a leading cause of death and disability and sadly, despite medical advances and public health initiatives, its incidence is not declining. The sequelae are often devastating and can affect the full range of human life and functioning. The impact of stroke extends beyond the individual to the people closest to them—carers experience high rates of distress, depression, and social isolation; reduced health status; and even premature death. Prevention and acute medical management are a fundamental part of the response to the problem, but improving life after stroke is also important and, as increasing evidence indicates, possible.

Occupational therapists have for many years been identified as key contributors to the rehabilitation of people with stroke. The 2004 national clinical guidelines for stroke stated that “a specialist stroke team should include staff with specialist knowledge of stroke including an occupational therapist.” Despite the fact that their input has long been seen as important, the level of evidence for this recommendation was limited to expert committee reports, opinions, or experience of respected authorities, with an indication that directly applicable clinical studies of good quality were absent.

The review by Legg and colleagues synthesises data collected over the past decade and finds that occupational therapy targeted towards activities of daily living significantly increased performance on scores of personal activities of daily living (standardised mean difference 0.18, P=0.01) and reduced the risk of poor outcome (deterioration or dependency in personal activities of daily living: odds ratio 0.67, 95% confidence interval 0.51 to 0.87). The review, which includes a wide range of studies, provides strong evidence that occupational therapy after stroke improves outcome and prevents deterioration in functional performance. As many people struggle with the consequences of a stroke for years, policies should ensure a satisfactory level of service provision and appropriate staff capacity, and should optimise appropriate referral and management from health professionals.

Legg and colleagues focused on the effect of occupational therapy targeted at enhancing activities of daily living. Although this is a key intervention, it is just one aspect of occupational therapy after stroke. Other activities undertaken by therapists aim to enhance participation in domestic and leisure activities and facilitate engagement in activities that people find meaningful—occupation in the widest sense of the word. As a result, assessing occupational therapy along with other aspects of rehabilitation is complex, and the evidence from Legg and colleagues focuses on an aspect that is perhaps the easiest to capture. The challenge ahead is to build on and maintain this evidence base.

As Legg and colleagues note, key questions remain:

about which occupational therapy interventions are most beneficial and for whom. In the meantime, occupational therapists, medical practitioners, and others involved in the care of people with stroke should be heartened by these findings. For therapists, the evidence clearly shows that occupational therapy does make a difference. For general practitioners and community service providers, referral to occupational therapy may make a real difference for stroke survivors and their families. Not everyone will benefit from occupational therapy, however, and challenges include identifying those who will benefit and deciding exactly how to provide services.

So what needs to happen next? Undoubtedly, more people who have had a stroke should be referred to occupational therapy with activities of daily life. We still don’t know which people are most likely to benefit (age, type of stroke, location of insult, duration of time since stroke); whether occupational therapy makes a difference to outcomes such as participation in meaningful activities like work and other life roles; and which outcomes are most important to people who have had a stroke and whether they are accounted for in rehabilitation interventions.12

Rehabilitation has often been labelled as comprising “black box” interventions12 and being a “Cinderella” discipline.10 The promising results from Legg and colleagues’ trial should stimulate research into other areas of occupational therapy practice and encourage better provision of such services for people who have had a stroke.

primary prevention have been estimated to receive an appropriate shock and survive at least one year.\(^5\) Thus, we urgently need to develop and validate cheap and easily applied tools that can accurately identify those people most likely to benefit from either (or both) of these devices.

Secondly, although the benefits of both devices seemed to be relatively stable over time in the randomised trials (survival curves of patients with and without the devices did not converge as follow-up lengthened), these trials were of relatively short duration. Thus, long term follow-up data are essential to confirm that the benefits do not attenuate over time, particularly in light of the frequency with which Food and Drug Administration advisories and device recalls arise years after efficacy studies are completed.\(^6\) Everyone who has one of these devices implanted should therefore enter into a registry and followed for long term risks and benefits. This would have the added benefit of tracking changes in the success rates and complications of implantation procedures over time as the sophistication of devices and technical expertise of those implanting them evolves.

Thirdly, data are lacking on the safety and effectiveness of either device when applied outside the confines of a clinical trial. These trials could possibly have overestimated the potential benefit-safety ratio because half of the people randomised were drawn from trials in which they were randomised after successful implantation of the device (thus, the 7% implantation failure seen for cardiac resynchronisation devices and 0.5-1% peri-procedural mortality seen with both devices are not factored into the effect estimates presented by Lam and Owen). Moreover, while the trials proving the efficacy of both devices enrolled relatively young patients, these devices are now being implanted into older people with more comorbidities.\(^7\) They are also being implanted by less experienced providers working in hospitals with lower implant volumes.\(^8\) Moreover, people with heart failure with less severe symptoms (NYHA class I or II) or common comorbidities (such as bradyarrhythmias, atrial fibrillation, or chronic kidney disease) were largely excluded from the published trials. Again, this emphasises the potential value of a prospective registry in defining the benefits and safety of these devices in a wider spectrum of patients.

Finally, the finding by Lam and Owen of uncertain incremental benefits for the combined device over single devices is important. Is it plausible that a combined device would not be better than either device alone? The answer is yes. Increases in the use of angiotensin converting enzyme inhibitors and β blockers over the past decade mean that people with heart failure are now more likely to die of progressive heart failure than sudden death.\(^9\) Also, cardiac resynchronisation alone seems to reduce the frequency of ventricular arrhythmias\(^10\) and—at least in the trial with the longest follow-up—the incidence of sudden death.\(^11\)

While several trials are ongoing to define the incremental benefits of combined devices over implantable cardioverter defibrillators alone in patients with heart failure, I agree with Lam and Owen that further randomised trials are needed to define the incremental benefit of combined devices over cardiac resynchronisation alone. As both devices have been shown to prevent morbidity and mortality in similar patient populations (see table on bmj.com), some may argue that such trials are not needed and would advocate the use of combined devices in all patients except those with severe comorbidities. However, consideration of the costs of the two options (£5074 (£7249; £10253) for cardiac resynchronisation therapy versus £17266 for a combined device)\(^12\) brings the matter clearly into focus—in publicly funded healthcare systems with finite budgets, should we reallocate resources from other areas to pay for expensive technologies that offer uncertain incremental benefits over cheaper options?\(^13\) Until a trial definitively proves that a combined device is better than cardiac resynchronisation alone, such devices should be reserved for people with heart failure who are eligible for cardiac resynchronisation and have the highest risk of sudden cardiac death.

1 Lam SKH, Owen A. Combined resynchronisation and defibrillation therapy in left ventricular dysfunction: Bayesian network meta-analysis of randomised controlled trials. BMJ 2007 doi: 10.1136/bmj.39343.511389.BE.
5 Stevenson IW. Implantable cardioverter-defibrillators for primary prevention of sudden death in heart failure: are there enough bangs for the bucks? Circulation 2006;114:1013-5.
Diet and the risk of cancer

New report shows obesity and alcohol are the strongest risk factors

This week, the World Cancer Research Fund (WCRF) launches its second report on diet and cancer through simultaneous conferences in London and Washington. Entitled *Food, Nutrition, Physical Activity, and the Prevention of Cancer*, the report updates the previous publication from the charity. It is the culmination of five years’ work by scientists in nine universities from four countries who have assessed the original research according to a specially developed standardised review protocol.¹

The possible influence of diet on the risk of cancer is constantly topical. The subject is important because people can change their diets, and even a moderate effect on risk could prevent several thousand cancers each year in a country the size of the United Kingdom. However, apart from the confirmed adverse effects of alcohol and obesity on the risk for some types of cancer,²³ progress in understanding has been slow and the evidence remains confusing.

The conclusions in the WCRF report about the effects of obesity and alcohol are similar to those reached by other expert consultations.¹⁻³ Obesity increases the risk of cancer of the oesophagus, colorectum, pancreas, breast, endometrium, and kidney. The report’s public health goal for obesity is for the median body mass index of the population to be between 21 and 23. Mean body mass index in adults in the UK is now about 27.⁴ Enormous efforts by individuals, society, and government will be needed to reverse the current trend and approach the goal proposed—mean body mass index in the UK has not fallen into the target range since the 1940s. The mean body mass index is also in the overweight range in most other Western countries and is rising rapidly from previously low levels in many developing countries.⁷

Alcohol increases the risk for cancers of the mouth, pharynx, larynx, oesophagus, colorectum, and breast and also causes cirrhosis, which predisposes to liver cancer. Globally, alcohol consumption has increased in recent decades, with the highest consumption in Europe and North America.⁷ The WCRF panel made recommendations that men should not drink more than two units of alcohol a day and that women should not consume more than one unit a day. These recommendations are much lower than current government advice in Britain of up to three or four drinks a day for men and two or three for women.⁸ A substantial shift in drinking habits would be needed to achieve these goals.

The role of fruit and vegetables remains poorly understood. The panel concluded that the evidence that diets rich in vegetables and fruits protect against cancer is overall less compelling than it was in the mid-1990s. They judged that vegetables, fruits, and other foods containing dietary fibre probably protect against several cancers, but that the evidence was not convincing for any specific cancer. Despite the absence of convincing evidence for a protective effect, the panel reiterated the previous recommendation that people should eat at least five portions of vegetables and fruits each day, and pointed out that, to meet this individual recommendation, the average consumption in the population would need to be about 7.5 portions a day. Currently, only a minority of the world’s population consumes the recommended five portions of fruit and vegetables a day, and consumption is low in many regions of the developing world.⁹ The average consumption in Britain is currently about three portions a day,⁴ so the consumption of fruit and vegetables would need to be more than doubled.

The major new conclusion in the report is that red and processed meat convincingly cause colorectal cancer. The previous WCRF report concluded that the evidence for this link was “probable,” and the 1998 Department of Health report concluded that the evidence was “moderate.”⁻²⁻³ This new conclusion is based mainly on results from prospective observational studies, supported by results from case-control studies. On average, people who ate the most red or processed meat had about a 30% increased risk compared with those who ate the least. On the basis of their conclusion, the panel proposed a public health goal that the average intake of red and processed meat in the population should be no more than 300 g each week. Consumption of meat has been rising in most of the world, and total meat consumption is well above the 300 g per week goal in most regions except Africa and South Asia.⁵ The current mean intake of red and processed meat in Britain is about 970 g a week in men and about 550 g a week in women,² so reaching this goal would require a large reduction in meat consumption.

Many challenges remain. Obesity and excessive alcohol intake definitely increase the risk of cancer but are hard to control, while our understanding of whether and how particular foods affect risk is still rudimentary. The goal for intake of vegetables and fruits requires careful consideration—achieving the goal may not reduce rates of cancer, whereas the financial and environmental costs could be large. Vegetables and fruits provide only small amounts of energy and protein, so an increase in intake may be largely on top of the rest of the diet. This could be expensive for people, and it has implications for the optimal use of agricultural land, water, pesticides, transport, etc. It may be better to concentrate efforts on increasing the consumption of plant foods such as cereals and beans, which supply energy and protein and can therefore partially replace meat. The production of Staple plant foods is usually more efficient than the production of meat, so replacing some meat with plant foods should reduce the demands on the environment.¹⁰ These wider questions will be dealt with in the WCRF’s policy report, due to be published next year.

All references are on bmj.com
Mental Capacity Act 2005
Should guide doctors to help protect vulnerable people

The Mental Capacity Act 2005, which was fully implemented on 1 October 2007, is intended to protect people who lack capacity to make decisions and to encourage them to participate in the decisions that are intended to help them. It presents a new range of challenges for doctors, but it should help clarify actions in difficult situations.

A helpful code of practice that supports the act guides people treating or caring for adults who lack the capacity to make decisions about their treatment or care, and it is all most doctors will need. This code has statutory force, which means that practitioners now have a legal duty to take note of the code when working with or caring for adults who lack capacity to make decisions for themselves. However, there is no legal duty to comply with the code, although evidence of non-compliance may be used by a court or tribunal—for example, in a claim for damages for clinical negligence.

Several principles underpin the act. A person must be assumed to have capacity to make decisions unless evidence to the contrary is available. All practical steps must be taken to help someone make a decision before incapacity is assumed. Just because someone makes an unwise decision does not mean that they are incapacitated. If you make a decision on someone's behalf, it must be in their best interests, and there must be no better way of achieving the same outcome.

Who lacks mental capacity? The answer is any person who is unable to make a particular decision or take a particular action at the time the decision or action needs to be taken. A doctor has to judge whether the functioning of the mind or brain is sufficiently impaired or disturbed, permanently or temporarily, that the person lacks the capacity to make a particular decision.

How does a doctor act in the patient’s best interest? To determine what is in a person's best interests, the doctor should consider the views and factors that would have influenced them if they had capacity to make the decision (such as evidence of past and present wishes and feelings; religious, cultural, or moral beliefs and values); avoid assumptions about best interests based on age, appearance, condition, or behaviour; consider whether they are likely to regain capacity after medical treatment (which implies that the decision could be delayed until then); and not be motivated by a desire to bring about death or be influenced by assumptions about quality of life, if the decision is about life sustaining medical treatment.

The doctor should consult with others—while being careful not to breach confidentiality—for their views when trying to determine what is in the person's best interests, and to see if they have any information about the person's wishes, feelings, beliefs, and values. Whatever is decided must also be the least restrictive option available to the person, in terms of their rights and freedoms. The doctor must record how the decision on best interests was reached (for example, the reasons, who was consulted, and what special factors were considered).

Can a doctor be liable for his or her decision? If certain conditions are met, doctors are protected from civil or criminal liability when performing tasks in the best interests of a person who lacks capacity. In emergency situations, for example, it will almost always be in the person's best interests to give urgent treatment without delay, unless a valid and applicable advance decision to refuse medical treatment is in place.

This protection does not, however, provide defence against a claim of negligence. For example, if a person who lacks capacity is restrained, the act does not protect against liability unless it can reasonably be believed that restraint is needed to prevent harm to the person. The amount and type of restraint used and the time that it lasts must also be proportionate to the likelihood and seriousness of harm.

The act also covers advance decisions to refuse medical treatment. If a valid, applicable advance decision to refuse treatment exists a doctor must respect it. A doctor following an advance decision will be protected from liability. If the doctor knows such a decision exists and does not follow it, the doctor will not be covered. Even if an advance decision is not valid or applicable to the circumstances, it still should be considered by healthcare staff as an expression of previous wishes when working out the person's best interests.

Whenever treating a person who might have impaired capacity, the code needs to form a conscious part of a doctor's decision making process. Clear evidence of alignment with the code's guidance must exist, particularly if decisions or treatments are called into question. This will require education for staff at all levels. Health professionals should be encouraged to reflect on their practice in the context of the code's guidance and to discuss experiences openly and frankly.

We select the letters for these pages from the rapid responses posted on bmj.com favouring those received within five days of publication of the article to which they refer. Letters are thus an early selection of rapid responses on a particular topic. Readers should consult the website for the full list of responses and any authors’ replies, which usually arrive after our selection.

LETTERS

ALLERGY AFTER BREAST FEEDING

Study was not designed to test the hypothesis

The PROBIT study is a large randomised controlled study aimed at reducing childhood gastrointestinal infection by promoting breast feeding. Secondary outcomes included atopic eczema and asthma. However, the recent paper was written as if the study’s main aim was to test the association between prolonged and exclusive breast feeding and asthma and allergy. When no statistical difference was found, the authors erroneously concluded that breast feeding has no effect on these outcomes.

This conclusion cannot be drawn from this study design and cannot be extended to different populations. The post hoc analysis, with grouped breastfeeding classes, is more suited to the aim of the paper, but it has methodological and interpretative limitations, such as confounding.

The intervention promoted exclusive and prolonged breast feeding in women who wished to breast feed. This approach can test only whether the duration of breast feeding or exclusion of allergens in the first months of life reduces risk of asthma and allergy in the children of mothers who wish to breast feed. It cannot investigate differences in asthma and allergy rates resulting from a mother’s decision to breast feed, or the effect of colostrum or immediate skin to skin contact after birth.

The results cannot readily be extrapolated to populations with higher rates of asthma and allergy. The prevalence of allergy was low—family (parental and sibling) history of atopy was <5% compared with >80% (excluding siblings) in New Zealand. The wide confidence intervals suggest that all important confounding and predictor variables may not have been included in the multivariate model. Major concerns exist about the quality of the skin prick test—the only objective measure of atopy used.

Breast feeding may not protect against asthma and allergy, but this study cannot prove this hypothesis. Rather, it shows that in a Belarusian population, promotion of breast feeding in women who wish to breast feed does not alter the risk of asthma and allergy at 6.5 years.

Karen M Silvers
Senior research fellow, University of Otago, Christchurch PD Box 4356, Christchurch, New Zealand karen.silvers@otago.ac.nz

Michael J Epton
Senior lecturer in medicine, Chris M Frampton
Associate professor

Competing interests: None declared.


ABDOMINAL AORTIC ANEURYSM

Screening reduces all cause mortality in men

Greenhalgh and Powell1 cite a recent Cochrane review, which reported that screening asymptomatic people for abdominal aortic aneurysm (AAA) significantly reduced not all cause but AAA related mortality in men aged 65-79. The review, however, excluded some recent studies with long follow-up.2,4 Therefore, we performed a meta-analysis of randomised controlled studies with long follow-up of screening for AAA in men (both AAA related and all cause mortality).3

Our comprehensive search identified four reports—the Chichester study (over 15 year follow-up),2 the Viborg country study (median 9.6 year follow-up),3 the Western Australia study (median 3.6 year follow-up), and the multicentre aneurysm screening study (mean 7.1 year follow-up).4 Pooled analysis of the four reports showed a statistically significant reduction in AAA related mortality (risk difference −0.25%, 95% confidence interval −0.46% to −0.04%) and all cause mortality (−1.06%, −1.81% to −0.31%) with screening relative to control in a random effects model.5

Thus, our meta-analysis,3 an update of the Cochrane review, showed that screening for AAA significantly reduced not merely AAA related but also all cause mortality in men aged >65 years.

Hisato Takagi
Consultant cardiovascular surgeon, Shizuoka Medical Centre, Shizuoka 411-8611, Japan kfgth973@ybb.ne.jp
Nonikazu Kawai
Registrar, Takuya Umemoto
Consultant cardiovascular surgeon

Competing interests: None declared.


VALUE OF VIDEO CLIPS

Useful in acute upper airway obstruction in children

Ashworth argues that mobile phone video footage is useful when treating sick children.1 We know of two recent cases in which such video footage provided by parents was valuable in the diagnosis and treatment of upper airway obstruction. A previously healthy 2.5 year old boy was reported by his parents to have...

Still from video showing respiratory distress while asleep
severe respiratory distress at night, which completely resolved during the day. He was seen several times by a family doctor and ear, nose, and throat specialist. No diagnosis was made as he seemed well. Finally, his parents presented a video recording showing him in severe respiratory distress while asleep (figure). Direct laryngoscopy and bronchoscopy were then carried out under general anaesthesia. He needed urgent adenotonsillectomy and made an uneventful and complete recovery. The second patient was a 13 year old girl with cystic fibrosis who was due to have a scheduled bronchoscopy. She seemed well when she presented for an anaesthesia assessment, with no signs of respiratory distress, but her parents supplied a video recording from a mobile phone that showed her in respiratory distress in the morning or when anxious. She successfully underwent a diagnostic bronchoscopy and postoperative respiratory symptoms were consistent with the mobile phone recordings. These cases highlight the usefulness of modern technology in the diagnosis of problems of uncertain severity in children and may represent a useful alternative to inpatient admissions.

Graham A M Wilson consultant paediatric anaesthetist, Royal Aberdeen Children’s Hospital, Aberdeen AB25 2ZN graham.wilson@nhs.net

Thomas Engelhardt consultant paediatric anaesthetist, Bruno Marciniak staff anaesthetist, Clinique d’Anesthésie Reanimation de l’Hôpital Jeanne de Flandre, CHRU Lille, 59037 Lille Cedex, France

Competing interests: None declared.

1 Ashworth AJ. Mobile phone videos could help treat sick children. BMJ 2007;335:627. (29 September)

HONOURING ADVANCE DECISIONS

You don’t in psychiatry

Dyer reports, “A new statutory right for patients to say in advance what treatments they would want to refuse if they later lose the capacity to take decisions came into force this week. Doctors will have to abide by the capacity to take decisions came into force this week. Doctors will have to abide by the new statutory right for patients to say in advance what treatments they would want to refuse if they later lose the capacity to take decisions.”

Dyer adds that “Patients will not be able to . . . require a doctor to do anything unlawful.” There is the rub. In psychiatry, procedures that incarcerated mental patients view as protection of their civil rights, psychiatrists regard as interference with their duty to protect patients and the public from the ravages of mental illness, an interpretation the courts uphold.

In short, the perceived moral-psychiatric need to prevent harm to self and others precludes the use of advance directives in psychiatry. Doctors and their patients ought to be aware of this limitation of advance directives.

Thomas Szasz professor emeritus of psychiatry, SUNY Upstate Medical University, Syracuse, New York 13210
tszasz@aol.com

Competing interests: None declared.

1 Dyer C. Patients win right to have their advance decisions honoured by medical staff. BMJ 2007;335:688-9. (6 October)

OBSERVATIONAL STUDIES

More than high standards needed

Von Elm et al provide a welcome set of criteria to judge prospective observational studies. What they do not include is the health warning that should accompany such publications. The accompanying editorial highlights the usefulness of these studies to examine rare diseases, but such studies are often used for common illnesses like cardiovascular disease and cancer. End points are frequent and prevalence high enough to make randomised controlled trials more reliable for assessing these illnesses.

The quoted examples seem to prove the importance of cohorts, but a list from cardiology alone shows that results of observational studies are often seriously flawed. Observational studies of the cardioprotective effects of female sex hormones, the usefulness of antioxidants or homocysteine lowering strategies, and rhythm control for atrial fibrillation suggested a clear treatment effect and greatly influenced practice. But subsequent randomised trials refuted each hypothesis.

The main problem is interacting factors that cannot all be statistically accounted for. For example, in general, overweight people do less exercise, have a high saturated fat intake, smoke, and do not attend to their insulin therapy or take their blood pressure tablets. So, the results of cohort studies are often wrong if cohorts are considered in isolation. This would not be a problem if cohort studies were not acted upon until a randomised trial is conducted. Glasziou et al suggested that a combined rates ratio of at least 10 and a P value of <0.01 should be used to distinguish between a true effect and background population “noise.” Few of our current favourite targets—mild obesity, salt intake, or passive smoking—would pass this test. The findings of cohort studies should start rather than close the debate. Experts are too hasty to present a hypothesis as a proven fact, and the medical profession is too willing to accept such findings uncritically.

Guy Lloyd consultant cardiologist, Eastbourne District General Hospital, Eastbourne BN21 2UD
guy.lloyd@ctbopianworld.com

Competing interests: None declared.


2 Rothwell PM, Bhatia M. Reporting of observational studies. BMJ 2007;335:783-4. (20 October)


TALK OF PSYCHOSOCIAL FACTORS

Tell the whole story

Goldacre says he sounded like an ass when explaining the complex pathogenesis of back pain on radio, but he is unduly harsh on himself. His message is not wrong, but might have been better gift wrapped.

Western medicine is based on the biomedical model. This model is reductionist—all symptoms can be explained by underlying pathology—and dualist—if there is no pathology, it’s all in your head. This model was drilled into us at medical school and is the principal model for the National Health Service.

But it’s wrong. For up to 90% of people presenting to their general practitioner with genuine physical symptoms, the symptoms are not explained by pathology. It is also not appropriate to label most of these patients as anxious or depressed. I now explain this to patients, and tell them that the problem lies with the model, not with them. It is normal to have genuine physical symptoms that cannot be explained through radiographs or blood tests.

You can then help the patient understand that extensive research has proved what will help. The psychological yellow flags act as obstacles to recovery and return to work. These include catastrophising, low mood, avoidance behaviour, and having an external locus of control. These all inhibit recovery. Cognitive behaviour therapy is excellent for tackling these obstacles (www.livinglifetothefull.com). When coupled with graded exercise programmes, the outcomes are excellent.

Charles T Vivian consultant occupational physician, Gloucestershire Royal Hospital, Gloucester GL1 3NN charlie.vivian@glos.nhs.uk

Competing interests: None declared.

1 Goldacre B. Beware of mentioning psychosocial factors. BMJ 2007;335:801. (20 October)
Royal College of Physicians calls for new services to improve out of hours acute care

Susan Mayor LONDON
People who are acutely ill out of hours should have easy access to a wider range of innovative medical services in the community to improve their care and reduce unnecessary hospital visits, a report by the Royal College of Physicians recommends.

The report, Acute Medical Care: The Right Person, in the Right Setting, First Time, argues that current out of hours care is generally inadequate and inflexible, so patients with acute illness go to hospitals because there is no alternative. It recommends that provision of acute, unscheduled medical care in the community should expand with a range of different levels of emergency care, offering extended opening times and direct access to competent staff.

New options might include urgent care centres in the community; rapid access medical outpatient clinics; and specialist outreach services from hospitals for acute deterioration of long term illness. These services must be evidence based, and the professionals delivering them must have the same competencies in acute medical care as hospital providers, it says.

Competent decision making requires diagnostic support, says the report, which calls for improved availability of these services. The task force that developed the recommendations, based on a review of available evidence, wants to replace “see and greet”—in which services provide an initial assessment before referring on—with “see and treat”—providing accurate assessment and delivery of treatment at the first contact.

Bryan Williams, professor of medicine at the University of Leicester, and chairman of the task force, said, “Getting it right for acute medical care needs changes in the way care is organised to get the most and the best out of staff and local resources and to provide fast and efficient care for patients. It needs changes in the way we work as professionals across the board, to provide wider and more flexible access to clinical decision makers.”

Big acute hospitals that serve local regions should provide the most intensive level of emergency and complex acute medical care in each area. They should have emergency departments located close to acute medical and critical care units, ideally as part of an emergency floor.

To ensure that people are aware of the range of services, the report recommends developing local navigation hubs, each with a single, well publicised access telephone number distinct from 999, the emergency services number.

The report, Acute Medical Care: The Right Person, in the Right Setting, First Time, is available from the Royal College of Physicians, London NW1 4LE, priced £12.

Nurses should be allowed to make resuscitation decisions

Caroline White LONDON
Suitably qualified nurses should be allowed to decide whether to begin resuscitation after cardiac arrest, says new UK guidance on decisions relating to cardiopulmonary resuscitation.

To date, only consultants and family doctors have been able to make these decisions.

The guidance, which has been issued jointly by the BMA, the Royal College of Nursing, and the Resuscitation Council, updates previous guidelines issued in 2001.

It aims to clarify lingering uncertainties about when and for whom the procedure is suitable, and to pinpoint the key legal and ethical issues that should inform every decision.

These include when patients lack the mental capacity to make their own decisions or when they have made an advance decision to refuse the procedure.

Every decision should be taken based on an individual assessment of each patient’s case, and if the procedure is unlikely to resuscitate the patient it should not be attempted, the guidance recommends.

It also emphasises the importance of good record keeping and effectively communicating decisions with members of the healthcare team and with patients.

And healthcare professionals should tell patients and their families the truth about the effectiveness of resuscitation, says the guidance.

Despite its portrayal in television medical dramas as a successful life saving technique, only 15-20% of hospital patients who are resuscitated after cardiorespiratory arrest survive to discharge. This falls to 5-10% for people who undergo arrest outside hospital.

And the risks of accompanying internal fractures are high.

Prison inspector’s report slates mental health provision

Anne Gulland LONDON

Mental health care in prisons has improved but there are still too many gaps in provision and demand for mental health services will continue to outstrip the capacity of the NHS to meet the need, a report from the chief inspector of prisons has found.

The report, by Anne Owers, found that since the Department of Health took over responsibility for the provision of health care in prisons in 2003 “the quality and extent of treatment available to mentally ill prisoners” has improved. However, two findings “stand out starkly from this report.”

Ms Owers said, “The first is that there are still too many gaps in provision and too much unmet and sometimes unrecognised need in prisons. The second, equally important, is that the need will always remain greater than the capacity, unless mental health and community services outside prison are improved and people are appropriately directed to them: before . . . and after custody.”

Although she praises the efforts of NHS staff and the mental health in-reach teams that “rode to the rescue of embattled prison staff” she says “this infusion of skilled personnel” has established “beyond doubt not only the scale but also the complexity of the need.”

The report called for prison services to make more use of court diversion and liaison schemes, which divert prisoners to mental health units if necessary. Only two out of the 23 primary care trusts questioned were aware of such schemes, despite the fact that 23 primary care trusts questioned were aware of such schemes, despite the fact that

GPs working in prison were often doing so in isolation
No evidence backs reduction in abortion time limit, minister says

Adrian O'Dowd MARGATE

No medical evidence indicates that the limit of 24 weeks for abortions in the United Kingdom should be reduced, according to a government minister.

The health minister Dawn Primarolo defended the existing time limit in UK law when she gave evidence to the House of Commons science and technology committee last week, as part of its inquiry into whether abortion laws in England and Wales need to be updated.

“The Department of Health’s view and the advice to me is . . . that the act works as intended and doesn’t require further amendment at the present time,” Ms Primarolo told the committee’s MPs. She said this was why there were no proposals from the government to amend the act.

The minister said that most abortions (89%) took place in the first trimester and that 11% of babies born at 23 weeks survive, while the viability is 1% at 22 weeks and zero at 21 weeks.

“In this very complex area with regards to time and viability, we are following the medical consensus, and that consensus still indicates that while improvements have been made in care, at the moment that concept of viability cannot constantly be pushed back in weeks,” she said.

Nadine Dorries, committee member and Conservative MP for Mid-Bedfordshire, said, “You are on the record as saying you are committed to the liberalisation of the abortion law. Do you think that given your opinion that you are the right minister for the job and maybe somebody with a fairer viewpoint on this issue should be in your place?”

Ms Primarolo replied, “I am not here to discuss my personal views. I’m here as the minister to answer the questions the committee puts to me about the information the department has.”

GP who benefited from patient’s will failed to disclose details

Owen Dyer LONDON

A GP who signed a patient’s cremation documents without disclosing that he was a beneficiary in her will was last week suspended for 10 months by the UK General Medical Council.

Alan Howlett of the Fremington Medical Centre in Barnstaple, Devon, stated on form B of an Application for Cremation that he had no pecuniary interest in the death of his 91 year old patient, named only as Mrs A. In fact he already knew that she had bequeathed him a share of her estate.

He had become friendly with Mrs A when attending to her husband at the time of his death. He learnt that he had been included in Mrs A’s will, he told the panel, in March 2006, four months before she died. But he did not inform his colleagues until after her death.

Upon learning of the omission in the cremation documents, his practice colleagues informed the North Devon Primary Care Trust, and Dr Howlett was cautioned by police in November 2006 for willfully making a false statement with a view to the burning of human remains contrary to the Cremation Act of 1908.

Dr Howlett told the GMC’s fitness to practise panel, “I knew what I was doing was wrong, but I was doing it to fulfil the wish of my patient that she would not have to undergo a postmortem [examination].”

US Congress asked to suspend funding for Planned Parenthood

Janice Hopkins Tanne NEW YORK

Antiabortion activists have asked the US Congress to suspend the $300m (£150m; €210m) federal funding granted to Planned Parenthood until a case against the organisation in Kansas is settled.

Planned Parenthood, a non-profit making organisation, is the largest provider of family planning and reproductive health services, including abortions, in the United States.

But Phill Kline, an antiabortion Republican, has filed 107 charges against Planned Parenthood of Kansas and Mid-Missouri, which provides services to Kansas and parts of the neighbouring state of Missouri.

Mr Kline, who was voted out of office as Kansas state attorney general, is now district attorney for Johnson County, Kansas.

He claims that the Planned Parenthood Clinic in Overland Park, a suburb of Kansas City, performed late term abortions without determining whether the fetus could survive outside the womb. He also charges the clinic with supplying false information, unlawful failure to maintain records, and unlawful failure to determine viability for a late term abortion.

Planned Parenthood denies performing any abortions beyond 22 weeks of pregnancy.

Roger Evans, its senior director for public policy, litigation, and law, told the BMJ that the charges were unclear. It would take 30 or 40 days for the organisation to get all the details of the complaints, he added. The next hearing in the case is set for 16 November.

Mr Evans said that Mr Kline had used his previous office to try to eliminate or reduce access to abortion. While Kansas’s attorney general, he had requested clinic records from Planned Parenthood.
London trusts overhaul primary care without consultation

Caroline White LONDON
Primary care trusts have already started implementing radical proposals for overhauling London's health services, despite the fact that these have not been put out to formal consultation, family doctors have claimed.

The capital's strategic health authority, NHS London, recommended Ara Darzi's proposals to each of the city's 31 primary care trusts (PCTs) in August to give them time to work out the logistics of formal consultation (BMJ 2007;335:61).

That process starts this month and runs until February. There will be further consultation on local plans.

But at a meeting organised last week by the BMA’s London Regional Council to discuss the proposals, several GPs, and a Pensioners Forum representative, claimed that their trusts had already started the ball rolling.

These included earmarking buildings and land for polyclinics or supersurgeries, one of the most hotly debated of the six suggested models of healthcare delivery.

Concerns were also raised that trusts were continuing to press ahead with service cuts and reconfigurations before the outcome of discussions on the proposals was known.

“Every PCT is already looking at where their polyclinics are to be located,” said Chaand Nagpaul, a negotiator on the BMA's General Practitioners Committee, adding that this was distracting them from patient care.

Bill Gillespie of NHS London reassured delegates that trusts would have to consult widely.

“But that’s not the reality on the ground,” said Dr Nagpaul. “Perhaps there is some work to be done telling the PCTs who are implementing already.”

John Lister, information director for the pressure group London Health Emergency, said Professor Darzi’s calculations were based on very big assumptions and contained “dodgy numbers” and “few hard facts.”

“[They] aim to save £1.5bn (£2bn; $3bn) a year, but what about the costs of reorganisation?” added Dr Nagpaul.

Views on the proposals can be submitted to hfl@London.nhs.uk.

Watchdog could close hospitals in a day to tackle infections

Helen Mooney LONDON
A new health watchdog could have the power to close English hospitals in 24 hours to fight against infections acquired in healthcare settings, the Department of Health has announced.

The Care Quality Commission will be able to shut down wards and hospitals; carry out inspections; and fine underperforming healthcare providers. The government will also give the regulator new powers that cover private hospitals and healthcare providers.

The health secretary, Alan Johnson, said, “Despite progress, tackling infection remains a challenge for the NHS. I am determined that we will take action where necessary to safeguard patients and ensure staff feel able to report concerns.”

Mr Johnson said that the regulator would be given “tougher powers” to inspect and close wards if necessary.

“NHS staff, such as matrons, nurses, and porters, who spend every day on the wards, need to feel able to report concerns to the new regulator,” he added.

Many of the new regulator’s powers are already available to the existing regulators, but the government hopes tougher action will be taken by merging the responsibilities into one body.

The Care Quality Commission replaces the Commission for Social Care Inspection, the Healthcare Commission, and the Mental Health Act Commission.

The proposals are included in the Department of Health’s response to a consultation launched in November 2006.

The regulatory framework is to be outlined in a health and social care bill, which will be introduced to parliament later this year.

However, Hamish Meldrum, chairman of the BMA, criticised the hasty abolition of the Healthcare Commission: “While we recognise some of the arguments for rationalising the process of regulation, the BMA is concerned that, only a few years after the Healthcare Commission was set up, it is about to be abolished to make way for yet another, new regulatory body.

“The NHS has been suffering from too much reorganisation and it appears that as soon as doctors and managers start getting used to one system, it’s all change.”

Gill Morgan, chief executive of the NHS Confederation, warned that the new regulator must not signal a “year zero” approach that discards what has gone before.
German doctors may have to report patients who have piercings and beauty treatments

Annette Tuffs
HEIDELBERG

Plans to introduce a law in Germany that would force doctors to notify a patient’s health insurance company if medical treatment is for a complication of a beauty operation or piercing have been heavily criticised by doctors and welfare organisations.

Health insurance companies, the law says, would have to deny covering the entire costs for complications of such unnecessary treatments. This would save some €50m (£35m; $72m) in healthcare costs, the German health ministry says. However, its main intention is to strengthen the personal responsibility for health.

At the moment, patients have to pay the costs of medically unnecessary cosmetic treatments themselves (BMJ 2007;335:114). But complications are still covered by their health insurance company. Doctors usually report diagnoses to the patient’s health insurance company but not the causes unless they are because of occupational disease, trauma, unintentional injury, and injuries or complications from vaccinations or malpractice.

The president of the German Medical Association, Jörg-Dietrich Hoppe, criticised the government’s plan and called it an attack on doctor-patient confidentiality.

“Patients will not be able to trust their doctors any more if the doctors are trying to sound them out and blow the whistle on them to their health insurance companies,” he said.

The German health ministry was surprised by the public outcry. “We are just implementing health reform,” said a spokeswoman.

An artist at work at last year’s tattoo convention in Berlin

Merav Sarig
JERUSALEM

A month long strike by doctors in Gaza, as political factions struggle for control, came to an end last week. The move was billed as a gesture of goodwill at the end of the Muslim religious period Ramadan.

The strike began because those who were supporters of the ousted Fatah government lost their jobs under the Hamas government, which took over the Gaza Strip from Fatah in June. The new government appointed Bassem Naim as minister of health. He fired the directors of Gaza’s main hospitals, who were identified with Fatah, as well as many doctors and medical personnel. They were replaced with people who identified with Hamas.

Among those who lost their jobs was Jomaa Alsaqqa, deputy director of Shifa Hospital, who had worked as a surgeon at Shifa for 20 years. “I was fired only because I support Fatah,” Dr Alsaqqa says. In the past few months he has, he says, been arrested and beaten by Hamas three times.

“After I was dismissed they threatened to kill me, to shoot me, if I entered the hospital again.” According to Dr Alsaqqa, about 600 doctors were “fired or pushed out of their jobs.”

Mahmoud Daher, the World Health Organization representative in Gaza, said that the doctors went on strike in protest at these measures. “The doctors cut their work day in the public hospitals to just three hours a day,” he said.

Mr Daher denied that the strike began with a direct order from the chairman of the Palestinian Authority and Fatah leader, Mahmoud Abbas (Abu Mazen), who retains control in the West Bank, and who pays the doctors’ salaries from Ramallah.

“Perhaps an indirect order was given, but it was the doctors’ organisations that called the strike,” Mr Daher said. Nevertheless, many doctors claimed that they were “forced” to strike, on pain of losing their salaries. Mr Daher confirmed that “the salaries of over one thousand doctors were stopped during the strike, apparently because of opposition to the strike. On the other hand, many doctors who are identified with Hamas agreed to strike out of fear of losing their source of livelihood.”

In response to the strike, Hamas accused the government of Abu Mazen of attempting to bring down its regime in Gaza and of inciting Hamas supporters to civil revolt. According to the director of the crisis unit in the health ministry of the Hamas government, Dr Medhat Abas, “the hospital managers weren’t fired for political reasons: they were fired because of managerial, financial, and moral corruption in the hospitals.”

In an effort to bring the strike to an end, the doctors’ organisations asked Hamas to leave politics out of the health system, to stop using its armed forces against medical personnel and to reverse its dismissals and political appointments.

“Some of the demands were met,” Mr Daher said.

Gaza’s doctors decided to suspend their strike after 35 days, “temporarily, as a goodwill gesture for the holy month of Ramadan,” Dr Alsaqqa explained.
US Senate passes bill granting mandatory access to data

Jeanne Lenzer BOSTON
Free public access is to be made available to the results of research funded by the National Institutes of Health, the US Senate has decided.

Widespread non-compliance with an existing voluntary public access initiative has led to support for the mandatory programme. According to a government report issued in January 2006, less than 4% of articles were made publicly available in the eight month period initiation of the voluntary programme in May 2005 (http://publicaccess.nih.gov/Final_Report_20060201.pdf).

The Senate passed a bill on 23 October that requires researchers who are funded by the National Institutes of Health to submit their manuscripts to the agency’s National Library of Medicine for publication in PubMed within 12 months of publication in a peer reviewed journal.

Passage of the bill was urged by 26 Nobel prize winners who signed a letter to Congress stating that patients and researchers stand to benefit from free access to research supported by taxpayers, which they said “can maximise the return on our collective investment in science and . . . further the public good.”

The bill will become law after reconcile via with the ruling of the US Senate after reconcilia

Patients and researchers stand to benefit from free access to research

Heather Joseph, executive director of the Scholarly Publishing and Academic Resources Coalition (SPARC) lauded the passage of the bill. She told the BMJ that researchers stand to benefit because “no library can subscribe to everything,” making it difficult to perform in-depth literature searches at times.

“One of the biggest places it will make a difference,” she said, was for people who go to the internet and “if they can’t interpret [the studies] themselves, they take the information they find to their doctors—and that can only benefit everyone.”

The bill’s provisions do not affect researchers who fail to, or choose not to, have their study results published in a peer reviewed journal. Neither is there provision requiring authors to share underlying data.

Health authority forced to publish PFI contract for hospital

Bryan Christie EDINBURGH
A Scottish health authority has failed to prevent details being publicly released of a private contract to build one of the United Kingdom’s most expensive hospitals.

NHS Lothian has been ordered under Freedom of Information legislation to release the contract it signed with a private consortium to build and maintain the £184m (£263m; $378m) Edinburgh Royal Infirmary.

The hospital, which was opened in 2003, is one of the biggest to have been built under the private finance initiative, now known as public private partnerships. Under the initiative, the private sector builds and pays for new health facilities. In return, the NHS pays an annual charge to the private sector—often for 30 years or more.

NHS Lothian initially rejected a Freedom of Information request for a copy of the contract, claiming the information was exempt under the terms of the legislation.

It said the private consortium, Consort Healthcare, considered the information to be commercially sensitive and that its release would amount to an actionable breach of confidence.

An appeal was then made to the Scottish information commissioner, who asked NHS Lothian to supply a copy of the contract and explain why its component parts should be considered exempt.

The commissioner, Kevin Dunion, sharply criticised the health board on several counts. He said that it failed to provide the full range of information at the outset and only supplied the complete documentation late into his investigation. He also said that it tried to claim a blanket exemption of confidentiality while providing “virtually no arguments to justify withholding the contract.”

NHS Lothian has said it will comply with the ruling.

The full decision is at www.itstpublicknowledge.info.
Agency urges researchers to use yellow card data more

Roger Dobson ABERGAVENNY

Researchers are being urged to make more use of yellow card data on reported adverse reactions to drugs in the United Kingdom.

The call from the Medicines and Healthcare Products Regulatory Agency comes after the publication of the first annual report by its independent scientific advisory committee. The committee reviews the scientific merit of proposals for using data from the card scheme and the general practice research database in research.

“The potential of the data we hold for public health research is unparalleled, and I am delighted that the launch of this first report shows that this is increasingly recognised by researchers,” said Alasdair Breckenridge, chairman of the agency.

“Although general practice research database data have been available for some time, opening up access to the yellow card scheme database was a new venture.”

The advisory committee was set up in 2006 to give advice on research related requests to access data from the general practice research database and yellow card scheme. The research database can provide data from anonymised longitudinal medical records in primary care, and the yellow card scheme was set up in 1964 to collect reports on suspected adverse drug reactions.

The annual report says that with increasing amounts of data being stored on databases in the UK and Europe, the importance of rigorous scientific review to safeguard data held by the agency has never been greater.

The report shows that most of the general practice research database applications (62%) were from academia, with 17% from the drug industry and 13% from government.

It also highlights reasons why applications for data from the yellow card scheme may be rejected, including research hypotheses that are not specific enough and those about reactions to drugs that are already known. It also says that commercial use of data could not be approved where it has been freely and voluntarily supplied for the public good.

But there have been critics of the yellow card system. Andrew Herxheimer, a clinical pharmacologist and former editor of the Drug and Therapeutics Bulletin, who now works at the international Cochrane Collaboration, said, “There is a problem in the brevity and anonymity of the data. They are keen to protect the confidentiality of the patients and the doctors, which is right and proper, but the reports are so thin, just a few sentences, and you cannot understand what is happening without going back to patient or doctor.

“The problem is that there is nowhere on the yellow card forms for the patient or doctor to say they agree to being contacted if further information is needed. It means all the data in there are blocked because you cannot get beyond them.”

The report is available at www.mhra.gov.uk.

European Commission asked to investigate use of snus tobacco

Rory Watson BRUSSELS

Campaigners who want to relax the Europe-wide ban on snus, an oral tobacco, have succeeded in formally asking the European Commission to investigate whether its use could help people to stop smoking.

MEPs called on the commission on 24 October “to investigate the health risks associated with consumption of snus and its impact on the consumption of cigarettes” as part of a wide ranging strategy towards a smoke-free Europe.

The tobacco has been banned throughout the European Union since 1992 and is allowed only in Sweden, where it is so much a part of national culture that the government negotiated a specific exemption when the country joined the European Union.

Liz Lynn, the British Liberal Democrat MEP who led the call for the new investigation, explained, “Snus may be one of the possible ways of ensuring a smoke-free environment and help people to quit smoking. But there are still risks and it is important that the EU investigates these fully.”

A founding member of the “MEPs against cancer” group in the European parliament, Mrs Lynn recently hosted a meeting to take evidence from experts on the risks of certain types of smokeless tobacco. Afterwards she said, “No one is saying that snus is in any way good for you. It may cause a variety of cancers. But it is suspected that Sweden’s low cancer mortality may be connected to its use as people make the switch from cigarettes.”

Her Swedish Conservative colleague, Christofer Fjellner, a confirmed snus user, argues for a complete lifting of the ban. “If you take snus, you do not have normal cancer effects. Sweden consumes about the same amount of tobacco as elsewhere in Europe, but in a different way.”

The latest move comes just three weeks after British American Tobacco publicly pressed European regulators to reconsider the ban.
Doctors and patients feel the same after medical errors

When doctors make serious mistakes they feel guilty, afraid, and alone. Patients and families harmed by those mistakes feel the same guilt, the same fear, and the same isolation say two US doctors who interviewed victims of medical error while making a film.

Relatives feel guilty because they weren’t around to protect their loved one. Patients and families fear retribution or poor care if they speak out. Both emotions are exacerbated when doctors back away, too paralysed by their own feelings to speak openly, discuss their mistakes, and maybe even say sorry. Hospital managers, lawyers, and insurers don’t help by telling doctors to choose their words carefully and avoid accepting liability. The result is an impersonal dialogue that seems cold and uncaring.

About 30 US states already have “I’m sorry” laws under which doctors’ comments to patients after a medical error are admissible for the purposes of establishing fault. These laws should be universal, say the doctors. It is also time to build a formal structure for coping with the aftermath of medical error that removes stigma and supports direct and sympathetic communication. Whatever that structure finally looks like, patients and their families must help to build it.


Still no consensus over link between hysterectomy and incontinence

Hysterectomy is a common operation in developed countries, and experts have been arguing for years about possible late side effects including urinary incontinence. The latest evidence comes from a large observational study comparing 165 260 women who had a hysterectomy for benign disease with 479 506 age matched controls who didn’t. Women who had had a hysterectomy were more than twice as likely to need surgery for stress incontinence (hazard ratio 2.4, 95% CI 2.3 to 2.5), particularly in the first five years after surgery.

Having children multiplied the risk, which was more than 16 times greater for women having four or more vaginal births. The authors are now fairly certain that hysterectomy causes incontinence, and urge women and their doctors to try less invasive treatments before opting for surgery.

At least one commentator disagrees (p 1462). Despite its size, this observational study simply isn’t robust enough to resolve the debate either way, he says. Perhaps hysterectomy does predispose women to later incontinence, but it is just as likely that some other factor is behind both. These authors had no data on smoking or body mass index, for example.

Lancet 2007;370:1494-9

Provide for the world’s poorest first

In 2000, the United Nations set a target to reduce global child mortality by two thirds between 1990 and 2015 (Millennium Development Goal 4). Progress has been slow in many developing countries. To find out how to target resources better in the regions that are lagging behind, researchers looked at the likely effect on child mortality of better nutrition, clean water, and cleaner fuel in Latin America and the Caribbean, South Asia, and sub-Saharan Africa.

After a complex analysis of published research and national survey data they concluded that child mortality would fall 14-31% a year if interventions to clean up water, provide clean fuel for cooking, and improve children’s nutrition reached everyone who needed them. If coverage was a more realistic 50%, then the poorest families should be targeted first. The researchers estimate that such a strategy would reduce child mortality 30-75% more than targeting the wealthier (but still poor) end of the socioeconomic spectrum. It would also be more ethical.

JAMA 2007;298:1876-87

Basal insulin safest in badly controlled type 2 diabetes

![EFFECT OF DIFFERENT INSULIN TYPES ON GLYCAEMIA AND WEIGHT](image)

Many patients with type 2 diabetes eventually need insulin. But which regimen works best for people with poor control despite maximum doses of oral agents? In one trial, none of the options worked particularly well. Only a minority of patients in each group reached their target concentration of glycated haemoglobin during the first year of treatment (16% of all 708 participants). Participants who took their insulin before each meal or had biphasic insulin twice a day did significantly better than those who took basal insulin at bedtime. But both regimens were associated with worse...
hypoglycaemia and substantial weight gain. Patients on prandial insulin gained more than 5 kg on average.

The authors hesitate to make final recommendations as their study is continuing for another two years and the findings may look very different in the end. An editorial agrees that doctors shouldn’t change their practice in response to these interim results (p 1759). Basal insulin is still the best and safest first line option for those who need it. Aggressive management of blood pressure, lipids, platelets, and lifestyles is equally important. *N Engl J Med* 2007;357:1716-30

Atrial natriuretic peptide helps limit infarct size after heart attack

![EFFECT OF ANP ON INFARCT SIZE AND EJECTION FRACTION AFTER HEART ATTACK](image)

Early treatments for heart attack have come a long way in recent years, but researchers are still looking for a drug to help protect what’s left of the myocardium from ischaemic and reperfusion injuries. Atrial natriuretic peptide (ANP) is one candidate that looked promising in a recent clinical trial. Patients given the drug for three days after a percutaneous coronary intervention ended up with infarcts that were nearly 15% smaller than placebo (95% CI 3.0% to 24.9%). They also had slightly better ventricular function at six months and a lower risk of heart failure or death from cardiac disease (hazard ratio 0.27, 95% CI 0.12 to 0.54). Fewer than 5% of both groups developed symptomatic hepatitis A (25/568 (4.4%) receiving the vaccine v 17/522 (3.3%) receiving immunoglobulin). The small difference wasn’t significant and the authors declared the vaccine “non-inferior” to immunoglobulin.

Vaccination is more convenient and potentially less painful than an injection of immunoglobulin. It is also more readily available. In the US, for example, the public health authorities rely on a single supplier of immunoglobulin. Stocks are limited and prices are rising. These difficulties, coupled with worries about the safety of blood products, have prompted many developed countries to switch from immunoglobulin to vaccination for post exposure prophylaxis. This first head to head trial suggests their citizens will come to no harm. Authorities in the US have just reached the same conclusion and announced a change in policy. *N Engl J Med* 2007;357:1685-94

Hepatitis A vaccination is effective after exposure

A recent large trial from Kazakhstan suggests there is little to choose between vaccination and immune globulin for post exposure prophylaxis against hepatitis A. Contacts of people with hepatitis A were given an intramuscular injection of immune globulin or vaccinated against the virus at some time during the two weeks after exposure. Fewer than 5% of both groups developed symptomatic hepatitis A (25/568 (4.4%) receiving the vaccine v 17/522 (3.3%) receiving immunoglobulin). The small difference wasn’t significant and the authors declared the vaccine “non-inferior” to immunoglobulin.

Vaccination is more convenient and potentially less painful than an injection of immunoglobulin. It is also more readily available. In the US, for example, the public health authorities rely on a single supplier of immunoglobulin. Stocks are limited and prices are rising. These difficulties, coupled with worries about the safety of blood products, have prompted many developed countries to switch from immunoglobulin to vaccination for post exposure prophylaxis. This first head to head trial suggests their citizens will come to no harm. Authorities in the US have just reached the same conclusion and announced a change in policy. *N Engl J Med* 2007;357:1685-94

An unhealthier future for most Americans

Most Americans are getting poorer. Incomes are going down and the proportion of families below the poverty line is going up. Only the rich are getting richer, says one public health expert from Virginia. Chief executives of US corporations earn 245 times more than their employees. Apart from the obvious injustice of this situation, worsening poverty means worsening health. Future generations of all but the richest Americans will have more cardiovascular disease, diabetes, and cancer than the generations alive today. The current healthcare system is already under strain and is unlikely to cope with the extra burden, he writes.

Training more health professionals and building more hospitals and other facilities is one option. But it won’t be enough, even if it were possible. Policy makers must instead tackle economic hardship head on. Changing tax policy, increasing the minimum wage, promoting new job sectors, and setting up initiatives to get people into jobs with prospects could all help increase incomes across the board. Education may be even more important. If all US adults had college degrees, the prevalence of heart disease could fall by 40%, and the prevalence of diabetes and stroke by 50%, he writes. The economy would be healthier too. *JAMA* 2007;298:1931-3

Inequality drives the HIV epidemic

HIV and poverty go hand in hand. Poor countries have a higher prevalence of infection, and the poorest people in those countries are disproportionately affected. Poverty is part of the cause of HIV and is also its inevitable result. A closer look at the economic reality of HIV, however, suggests that inequality—not just poverty—is the dominant driving force behind the epidemic, say experts from the Joint United Nations Programme on HIV/AIDS.

In sub-Saharan Africa, countries with the most unequal distribution of wealth such as Botswana, Namibia, and South Africa have the highest prevalence of HIV. Inequality between the sexes is also important. Women who are financially dependent on men have little power to negotiate safe sex. The link goes beyond the purely economic to marginalised groups such as drug users and migrants who have unequal access to social benefits and human rights, say the experts.

Controlling the spread of HIV will be a lot more complicated than alleviating poverty, which is complicated enough. Economic development may even fuel the epidemic by exacerbating inequality. Projects to reduce poverty and encourage development must be aimed at the poorest, be aware of HIV, and be tailored to the conditions, particularly the inequalities, operating locally. PLoS Med 2007;4:e314 doi: 10.1371/journal.pmed.0040314

On bmj.com: for a weekly review of the general medical journals, visit Richard Lehman’s blog at http://blogs.bmj.com/bmj/category/comment/richard-lehmans-weekly-review-of-medical-journals/
Lyme wars

Patients with long term symptoms, lack of a scientific explanation, and insurance companies’ reluctance to pay for treatment have created a perfect breeding ground for dissent, Alison Tonks reports

Lyme disease is a simple bacterial infection spread by ticks. There is a fairly characteristic rash, a well documented pattern of symptoms, and a safe effective treatment. But in the US, Lyme disease is at the centre of a long running and bitter controversy. It is no longer a disease but a legal and political battleground. At the core of the disagreement is the possibility that the Lyme bacterium could survive initial treatment, evade detection, and cause disabling symptoms for months or even years. A growing and vociferous patient lobby thinks it can. Mainstream medical opinion thinks it can’t. Why does it matter? Because those who believe in chronic infection also believe in long term treatments, including repeated or prolonged courses of antibiotics that doctors are reluctant to prescribe and insurance companies are reluctant to pay for.

**The trigger**
The latest exchange of fire between the two sides was triggered by official treatment guidelines published by the Infectious Diseases Society of America. An update at the end of last year repeated that there was no evidence for existence of chronic infection, then listed 12 treatments that doctors ought not to give patients with Lyme disease. Long term antibiotics were on the list, alongside “hyperbaric oxygen, ozone, fever therapy, intravenous immunoglobulin, cholestyramine, intravenous hydrogen peroxide, and specific nutritional supplements.”

Lyme advocacy organisations such as the Lyme Disease Association and the International Lyme and Associated Diseases Society dismiss the wackier treatment options such as fever therapy (hyperthermia), bee venom, and antioxidants, but both strongly support the option of long term or repeated courses of antibiotics for some patients. They argue that the update effectively blocks access to treatments by giving insurance companies a good excuse to stop paying for them. An excuse they have been quick to exploit, according to Pat Smith, president of the Lyme Disease Association. “Even pharmacies are now refusing to fill prescriptions for antibiotics not recommended by the latest update,” she says.

**The challenge**
The Lyme lobby has recruited some powerful allies. Arguably the most powerful is Connecticut’s attorney general, Richard Blumenthal. He is an elected official and “the public’s lawyer” in a state crawling with infected ticks. Late last year his office launched an unprecedented investigation, alleging the Infectious Diseases Society’s updated guidelines breached anti-trust legislation.

Anti-trust laws are designed to “promote competition and level the playing field in our marketplace,” according to the attorney general’s website. His office is investigating whether the guidelines are anticompetitive and unfair, denying healthcare providers legitimate income by denying patients legitimate forms of treatment.

The attorney general takes a close interest in Connecticut’s Lyme disease problem. His state has the highest incidence of reported cases in the US. In 2004, he colourfully described the infection as “a disease that is pernicious, insidious, immensely destructive, costly to our state, and particularly to our children” and warned that no one should be complacent, even in the coldest weather. “The ticks that carry this disease may be resting under the snow.”

Ms Smith applauds the attorney general’s pioneering investigation. She says the action is “vitaly necessary to protect the welfare of chronic Lyme patients nationwide” and that the guidelines “are being
used to deny treatment reimbursement and will have a continued chilling effect on the small numbers of treating physicians, since clinical discretion is not recommended in the guidelines.3 She said, “Sick patients have a right to more treatment if they relapse, or if their symptoms don’t resolve. There may be gaps in the evidence, but it’s wrong to leave patients hanging in the wind while you try to fill those gaps.”

The Infectious Diseases Society naturally takes a different view. Clinical guidelines are not mandatory and cannot replace individual doctors’ judgment, says the president Henry Masur. “The debate on how best to treat Lyme disease is a scientific one, and we believe it is best resolved scientifically. This challenge threatens the role of all professional societies to educate their members and the public about best medical practices.6 In an unusual move, the guidelines include a clear statement that the recommendations are voluntary.

The society’s lawyers say an anti-trust claim probably wouldn’t succeed. But the society has already spent thousands of dollars cooperating with the investigation. And they may have to spend many thousands more.

The politics

The adversarial politics of Lyme disease are not confined to Connecticut. State governments in Pennsylvania and Massachusetts are already considering bills that would sanction long term antibiotic therapy for chronic Lyme disease. Pennsylvania’s bill would also require insurance companies to pay for it. Both bills are pending. The Lyme Disease Association openly and enthusiastically supports the use of state laws to increase treatment options for patients. Political activism is their core territory. “Legislation is one of the most powerful advocacy tools available to the Lyme community” according to an article on its website.7

Hard line political activism often puts them in direct conflict with the majority of infectious disease specialists. In August, Dr Masur wrote to the chairman of the National Governors Association, warning of the damaging effects of misguided legislation. Long term antibiotics can be dangerous for patients and indirectly for everyone else by increasing the likelihood of resistant super bugs.8

The disease

In the US, acute Lyme disease is caused by the spirochete Borrelia burgdorferi, which is carried and spread by infected ticks endemic to many states.9 Some, but not all, patients develop a characteristic spreading rash called erythema migrans. The rash is accompanied by muscle aches and pains, arthralgia, headache, fatigue, and sometimes a fever. Left untreated, the spirochete can spread to joints (causing arthritis), nerves (facial nerve palsy is the commonest manifestation), and the heart (causing heart block).9 10 Several antibiotics, including oral doxycycline, kill the spirochete. Most treated patients get better after a course of no more than one month.10

Controversy arises over treatment of people who don’t respond to short courses of antibiotics. Up to one in six patients with erythema migrans still has fatigue, myalgia, or arthralgia a year after the rash has gone. About one in ten still has non-specific symptoms five years after their original treatment.10 The Lyme lobby believe these and other non-specific symptoms, including paraesthesias and disturbances of mood and memory, could be caused by persisting infection with live organisms. The mainstream view is that chronic symptoms are caused by something else.11

Jonathan Eddow, an associate professor of medicine at Harvard Medical School, lists among the possibilities permanent tissue damage caused by the initial infection, persistent inflammation not driven by live infection, some kind of autoimmune process, or a second illness triggered by Lyme disease such as anxiety, depression, fibromyalgia, or chronic fatigue syndrome. None of these would respond to further antibiotics. Many believe chronic Lyme disease is simply the latest in a long line of convenient labels for people with enduring non-specific symptoms that are hard to explain and challenging to treat. “Chronic candida syndrome” and “chronic Epstein-Barr virus infection” both come and gone.11

The ammunition

The two sides of the controversy have never seen eye to eye, but over the past decade, the accusations and counter accusations have become increasingly belligerent and entrenched. Mainstream specialists characterise doctors sympathetic to the Lyme camp as self serving mavericks who prescribe prolonged courses of expensive antibiotics to make money from desperate patients, or from drug company backhanders. Patient advocates both inside and outside the profession accuse the mainstream of being Lyme deniers who control the research agenda, the conference circuit, and the editorial boards of the main medical journals and who in turn accept consulting fees from insurance companies unwilling to pay out for long term treatments.

Both sides accuse each other of cherry picking the evidence to match their point of view, although mainstream opinion takes a harder line on acceptable kinds of evidence. Much is made, for example, of a paper published by the New England Journal of Medicine in 2001 which reported that prolonged antibiotic treatment doesn’t work.12

The paper actually reported two small randomised controlled trials in a total of 129 patients with chronic symptoms after documented infection with the Lyme spirochete. Both trials were stopped early because an interim analysis showed that 90 days of treatment with intravenous followed by oral antibiotics
had no effect on their quality of life.

The two sides are still arguing over the interpretation of these trials, which were small and included carefully selected patients. They are also still arguing about much of the other largely anecdotal evidence published about Lyme disease.

Disagreements are perhaps not surprising. Infection causes common non-specific symptoms (fatigue, muscle aches and pains, joint pain, stiff neck). Diagnosis is subjective. The only physical sign (erythema migrans) occurs with at least one other tick borne disease, is highly variable in appearance, and may even be absent. Many people don’t remember being bitten by a tick because the nymphs that commonly spread Lyme disease are too small to be noticeable. Blood tests for antibodies are unreliable, particularly in the long term. Other tests such as skin biopsies and culture are too cumbersome for the bed side. So in practice the diagnosis is almost always clinical. To complicate things further, the tick and Prevention has already warned doctors not to use these tests and urged patients to demand that their blood tests are approved and scientifically validated. The trouble is, the official diagnostic line (see box) is already 10 years old and anyway cannot rule out persistent infection in patients with persisting symptoms. Nothing can.

Evidence based medicine has nothing to offer in the diagnosis and treatment of patients who think they may have chronic Lyme disease. A few doctors are willing to take them on, but these doctors are often harassed by their peers and the medical licensing authorities. These patients are hard work, says Ms Smith. “History taking alone can take hours, and there isn’t a convenient cook book to follow for treatment. They need months or years of follow-up.”

To many doctors this sounds like familiar heartslitk territory. But these are heartslitk patients with a difference. They have a voice, they have friends in high places, and they have money. Earlier this year, funds from the Lyme Disease Association opened a new research centre for Lyme and tick borne diseases at Columbia University.

Beginnings of a resolution

It’s hard to know how the current acrimonious stand off will end, but both sides are beginning to show signs of battle fatigue. Even the most entrenched observer can see that mud slinging, muck raking, intimidation, and professional isolation is no way to conduct a scientific inquiry—particularly when vulnerable people are caught in the cross fire.

Fortunately, common ground is not hard to find for those willing to pause and look up from the fighting. A careful examination of guidelines from the two camps shows that both sides are working towards the same goals—a better scientific understanding of this complex infection, standardised definitions, reliable tests, and more, bigger, and better trials of treatment for early and late disease.

Alison Tunks associate editor, BMJ, London WC1H 9JR atonks@bmj.com
Competing interests: None declared.

CENTERS FOR DISEASE CONTROL AND PREVENTION RECOMMENDATIONS FOR DIAGNOSIS OF LYME DISEASE

- No tests are recommended for patients with a typical pattern of symptoms that includes erythema migrans
- Atypical patients should have a blood sample tested by enzyme linked immunosorbent assay (ELISA)
- If the first ELISA result is negative, no further tests are done. The patient is seronegative
- If the ELISA result is positive or equivocal, the same sample is retested using Western immunoblot analysis. A patient is seropositive if both tests are positive

The immunoblot analysis must be interpreted by staff at a qualified laboratory that follows CDC guidelines. Immunoblot analysis is not recommended in isolation because of the risk of a false positive result.

Patients in the early stages of Lyme disease may still be seronegative and should be retested during the convalescent phase.

The NHS stifles the entrepreneur in us all

Managers in the NHS do not innovate because there is nothing in it for them

Here’s a puzzle. How did Britain lose its motoring industry at the same time as it came to dominate motor racing? This may seem a long way from the politics of health, but bear with me: there is a parallel.

Racing cars are the cutting edge of vehicle engineering, a testbed for new ideas. In the 1950s and 60s the designs of John Cooper and Colin Chapman transformed Grand Prix motor racing. From this emerged a small and dynamic industry—Lotus, McLaren, Lola, Williams, Cosworth, among others—that had no need of government advice or sponsorship. These companies quickly became a dominant force in racing car design and, 30 years or more later, remain extraordinarily influential. It was to a British designer, Ross Brawn, that Ferrari turned to transform its fortunes in the 1990s.

Yet this coincided with the long death of the motor industry in Britain. Foreign manufacturers have set up plants successfully, so vehicle production is still important to the UK economy. But of Morris, Austin, Hillman Humber, and even Rover—once names that rolled off the tongue like battle honours—we hear no more. They are dead, defunct, or in the case of Rolls-Royce, a subsidiary of Volkswagen.

What, exactly, has this to do with the politics of the NHS? While the British motor industry was dying, the racing car designers proved we did not lack for talented engineers, skilful artisans, or entrepreneurs able to create new businesses. They did so outside the established structures, which were dominated by trade union power, entrenched rules and customs, centralised management, and a practised disregard for what the customer wanted. See where I’m coming from?

The NHS is widely and accurately regarded as slow to take up new ideas. Hardly a week passes without some company ringing me with a bright idea that, for some reason, they cannot persuade the NHS to buy. They get a dry laugh, I’m afraid. Selling new technology to the NHS is like stuffing a goose with corn, except that it’s unlikely to produce foie gras.

There is a wider parallel. During the years of British industrial decline, dozens of bodies were set up to try to force innovation down British industry’s throat. The biggest of these was the National Economic Development Council (Neddy), which was constantly telling businessmen of the need to invest. There was also a chain of research associations, each devoted to an industry sector, that largely cast their advice to the winds. Top-down advice has never worked if the climate for innovation is chilly.

Today, while the NHS makes do with old ideas and yesterday’s cures, British medical research continues to compare well with anywhere save the US, and pharmaceutical laboratories based in Britain have produced 20 of the top 100 drugs in use today. Innovation is alive and well in health care, just as it was in car design and engineering as the motor industry imploded.

Enter Lord Darzi and his interim report which, among other things, recommends the creation of a Health Innovation Council, chaired by himself and funded by £100m provided equally by the Department of Health and the Wellcome Trust. This idea is as appealing as an embrace with a blancmange. Here is Neddy reinvented, a council of the great and the good wasting perfectly good money on a scheme that anybody with common sense can see is unlikely to work.

Managers in the NHS do not innovate, because there is nothing in it for them. In Japan, when CT and MRI scanners emerged, clinics sprang up everywhere providing them, paid for by personal medical insurance—Japan has 10 times as many of these machines as we do in the UK, and they can provide a scan for as little as £50, at a couple of days’ notice. In the UK, scanners were seen not as an opportunity but as a cost. Radiologists had to struggle to get them, and even now they are poorly used. (And don’t say this is because Japan spends more of its gross domestic product on health than we do. It doesn’t.)

I could multiply examples indefinitely. The NHS is not only unfriendly to innovation, it is actively inhospitable. Like the British economy before Thatcher, it is run by staff on centrally negotiated contracts, full of unacknowledged restrictive practices, and subject to periodic and ill considered changes of government policy. That means that more than half of the extra £40bn provided in the past five years has gone in salaries and wages, and we are still not providing the medicines that patients in other countries take for granted.

My point is a simple one. The UK is not slow to adopt new technology, but the NHS stifles the entrepreneur in us all. One reason is that we set equity as a higher ideal than innovation. If all patients are entitled to equal access to a service or a medicine, we have to wait until the price is low enough for it to be “rolled out”—as they say in NHS-speak—across the whole service.

True innovation does not occur this way. Imagine if we had all had to wait until mobile phones were cheap enough for a centralised bureaucracy to buy them for us, out of taxes. We’d still be waiting. In fact, don’t trouble to imagine it—just try to recall how impossible it was to get any sort of telephone installed when the Post Office ran a monopoly. So long as equity rules the roost, the NHS will always be five years late, regardless of Lord Darzi’s council. So the next time somebody extols the “fairness” of the NHS, bear in mind that it comes at a cost.

Nigel Hawkes is health editor, the Times
nigel.hawkes@thetimes.co.uk
Uncertainty in heterogeneity estimates in meta-analyses

John Ioannidis, Nikolaos Patsopoulos, and Evangelos Evangelou argue that, although meta-analyses often measure heterogeneity between studies, these estimates can have large uncertainty, which must be taken into account when interpreting evidence.

An important aim of systematic reviews and meta-analyses is to assess the extent to which different studies give similar or dissimilar results. Clinical, methodological, and biological heterogeneity are often topic specific, but statistical heterogeneity can be examined with the same methods in all meta-analyses. Therefore, the perception of statistical heterogeneity or homogeneity often influences meta-analysts and clinicians in important decisions. These decisions include whether the data are similar enough to combine different studies; whether a treatment is applicable to all or should be “individualised” because of variable benefits or harms in different types of patients; and whether a risk factor affects all people exposed or only select populations. How uncertain is the extent of statistical heterogeneity in meta-analyses? Moreover, is this uncertainty properly factored in when interpreting the results?

Evaluating heterogeneity between studies

Many statistical tests are available for evaluating heterogeneity between studies. Until recently, the most popular was Cochran’s Q, a statistic based on the χ² test. Cochran’s Q usually has only low power to detect heterogeneity, however. It also depends on the number of studies and cannot be compared across different meta-analyses. Higgins and colleagues, in two highly cited papers, proposed the routine use of the I² statistic. I² is calculated as (Q–df)/Q×100%, where df is degrees of freedom (number of studies minus 1). Values of I² range from 0% to 100%, and it tells us what proportion of the total variation across studies is beyond chance. This statistic can be used to compare the amount of inconsistency across different meta-analyses even with different numbers of studies. I² is routinely implemented in all Cochrane reviews (standard option in RevMan) and is increasingly used in meta-analyses published in medical journals.

Higgins and colleagues suggested that we could “tentatively assign adjectives of low, moderate, and high to I² values of 25%, 50%, and 75%, respectively.” Like any metric, however, I² has some uncertainty, and Higgins and Thompson provided methods to calculate this uncertainty. Recently, other investigators compared the performance of I² and Q in Monte-Carlo simulations across diverse simulated meta-analytic conditions. They found that I² also has low statistical power with small numbers of studies and its confidence intervals can be large.

Interpreting heterogeneity in selected meta-analyses

Inferences about the extent of heterogeneity must be especially cautious when the 95% confidence intervals around I² are wide, ranging from low to high heterogeneity. Such uncertainty is usually ignored in systematic reviews, however. This can result in misconceptions. For example, a systematic review of corticosteroids for Kawasaki disease found a point estimate I²=59%. The authors decided to exclude the two studies that were most different, saying that their removal eliminated all of the across study heterogeneity (Q=5.59, P=0.588, I²=0.00). In fact, the 95% confidence interval for this I²=0% estimate still extends from 0% to 56%. With two small randomised trials and six non-randomised comparisons remaining, the meta-analysis concluded that corticosteroids consistently halve the risk of coronary aneurysms. However, the two largest randomised trials on this topic were published after the meta-analysis. Heterogeneity resurfaced: the largest trial found no effect on coronary dimensions, while the other trial showed an 80% reduction in the risk of coronary artery abnormalities.

Eight systematic reviews published in the BMJ between 1 January 2005 and 1 January 2006 performed meta-analyses of randomised trials and seven of them performed some statistical analysis of heterogeneity between studies (table on bmj.com). Each review stated that they had tried to interpret heterogeneity, and seven meta-analyses provided enough information for us to calculate the 95% confidence interval of I². The lower 95% confidence interval was always as low as 0% (rounded to integer percentage), with one exception. The upper 95% confidence interval always exceeded the 50% threshold, and in four cases it also exceeded the 75% threshold. A conclusive statement was feasible in only one case, where I² was 69%, the 95% confidence interval was 40% to 80%, the Q statistic had P<0.001, and the authors justifiably concluded that there was significant heterogeneity among these trials. This meta-analysis had 15 studies, so the power of both Q and I² was good. In all other meta-analyses (two to 12 studies each), strong statements in interpreting heterogeneity would be difficult to make. Only one review presented 95% confidence intervals for an I² estimate. The authors concluded that “we could not observe significant heterogeneity.” Indeed the Q statistic had P=0.19. However, with only five studies, the power...
to detect heterogeneity was negligible. The $I^2$ statistic was 35% and the 95% confidence interval ranged from 0% (no heterogeneity) to 76% (high heterogeneity).

**Uncertainty in $I^2$: large scale survey of meta-analyses**

This limitation is not confined to the selected examples presented here—it is probably the rule rather than the exception. We used two large datasets of meta-analyses to evaluate empirically the extent of uncertainty in $I^2$ estimates. Firstly, we looked at meta-analyses of the Cochrane Database of Systematic Reviews (Issue 4, 2005) that had four or more synthesised studies and binary outcomes. Because each Cochrane review may include several meta-analyses, we looked only at the one with the highest number of studies; in the case of ties, we used the one with the largest sample size. We did not look at meta-analyses of two or three studies. Such studies form a sizeable proportion of the Cochrane Library, but their 95% confidence intervals of $I^2$ almost always span a wide range of heterogeneity, unless the studies are large and they give very different results. In total, we calculated the $I^2$ statistic and its 95% confidence intervals for 1011 meta-analyses. The second dataset was a previously described database of 50 meta-analyses of gene-disease associations that had found a nominally statistically significant effect ($P<0.05$) for the proposed genetic risk factors.

Figure 1 shows the upper and lower 95% confidence intervals of $I^2$ for the two sets of meta-analyses. The pattern is similar. Of the meta-analyses where $I^2$ is ≤25% (low heterogeneity), 83% of the Cochrane meta-analyses and 73% of the genetic risk factor meta-analyses have upper 95% confidence intervals that cross into the range of large heterogeneity ($I^2 ≥50$%). Of the meta-analyses where $I^2$ is ≥50% (large heterogeneity), 67% of the Cochrane meta-analyses and 52% of the genetic risk factor meta-analyses have lower 95% confidence intervals that cross into the range of low heterogeneity ($I^2 ≤25$%).

Meta-analyses where $I^2$ is estimated at 0% are affected by an especially important misconception. Many reviews interpret this as absence of heterogeneity, but the upper 95% confidence interval may be substantial (as in the Kawasaki example discussed above). Figure 2 shows the uncertainty for the upper 95% confidence interval of $I^2$ for the two sets of meta-analyses, limited to those with $I^2=0$% (n=373 for Cochrane reviews, n=12 genetic studies). The upper 95% confidence interval exceeds 33% in all these meta-analyses. For 81% of the meta-analyses with $I^2=0$, the 95% confidence intervals are 50% or higher. Because of the way that research is currently reported, considerable heterogeneity between studies cannot be excluded with confidence in most meta-analyses. Some heterogeneity between studies is probably present in most meta-analyses. Claims for homogeneity may sometimes be stronger than the evidence allows. Trusting a non-significant $P$ value for the $Q$ statistic and an $I^2$ estimate of 0% may sometimes lead to spurious certainty about the comparability and similarity of study results.

**Technical aspects**

The confidence interval of $I^2$ can be calculated by several methods. Two methods, a test based approach and a non-central $\chi^2$ based approach, have been implemented in Stata (hetopi module). The performance of these two methods is comparable, although the test based approach often gives lower values for lower and upper confidence intervals, so that the non-central $\chi^2$ based approach may be preferable.

**Concluding comments**

All statistical tests for heterogeneity are weak, including $I^2$. The clinical implications of this are considerable and
must be examined on a case by case basis. Putting too much trust in homogeneity of effects may give a false sense of reassurance that one size fits all. Lack of evidence of heterogeneity is not evidence of homogeneity. Conversely, putting too much trust in the presence of heterogeneity of effects may lead to spurious subgroup and exploratory analyses. Given that I² is not precise, 95% confidence intervals should always be given.

**Contributors and sources:** It has a longstanding interest in meta-analyses and heterogeneity and had the original idea for this article. NP and EE collected the data. NP performed statistical analyses with help from JI and EE. JI wrote the manuscript and NP and EE commented on it. JI is guarantor.

**Competing interests:** None declared.

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


**SUMMARY POINTS**

The extent of between-study heterogeneity should be measured when interpreting results of meta-analyses Met-analysis rarely document uncertainty in estimates of heterogeneity. Our evaluation of a large number of meta-analyses shows a wide range of uncertainty about the extent of heterogeneity in most confidence intervals of I² should be calculated and considered when interpreting meta-analyses.

---

**Improving the quality of care with performance indicators**

Effective improvements in health care require methods to evaluate professional practice. Azeem Majeed, Helen Lester, and Andrew Bindman examine the assessment of quality.

The quality of services provided by primary care doctors varies widely, and there is often a large gap between optimal primary care services and actual practice.¹ This quality gap can have serious health consequences, including deaths from medical errors, increased rates of complications in chronic disease, hospital admissions for adverse drug reactions and interactions, and outbreaks of potentially preventable infectious diseases such as measles. It also has large financial costs for the healthcare system, national governments, and society, as well as affecting patients’ quality of life.

The reasons for the quality gap are not always within the doctors’ control. Sometimes the cause can lie with the public—for example, parents who refuse to allow their child to receive the measles, mumps, and rubella vaccine because of concerns about side effects. Even when the doctor and patient agree to follow a healthcare plan that meets the highest standard for quality, structural barriers related to the design or financing of healthcare systems can prevent the timely receipt of that service—for example, screening mammography for an appropriately aged woman. Nevertheless, the focus of this article and others in the series is on measuring the performance of doctors. Causes of the quality gap that lie with the doctor include being unaware of best practice and the latest guidance on managing a condition or being wary about using certain interventions, such as warfarin to reduce the risk of cerebrovascular disease, because of the fear of adverse events.

**What is quality and how do we measure it?**

The Institute of Medicine defines quality as: “The degree to which health services for individuals and populations increase the likelihood of desired health
outcomes and are consistent with current professional knowledge.

To measure how well health services meet this goal, a range of performance indicators (sometimes described as quality indicators or quality measures) have been developed.

Indicators are measurable elements of practice for which there is evidence or consensus that they reflect quality and hence help change the quality of care provided. Indicators are often based on routinely collected data, data from electronic medical records, and sometimes data from surveys.

**Current initiatives**

In England in the 1990s, the use of performance indicators initially developed ad hoc, with different regions developing their own indicators. The introduction of performance indicators was accompanied by various other quality improvement initiatives including a series of national service frameworks, which set out objectives for the health service, and the establishment of the National Institute for Clinical Excellence (now the National Institute for Health and Clinical Excellence), which provides guidance on promoting good health and preventing and treating ill health.

During the past decade, the development and implementation of performance indicators has been largely driven by an increased interest in the quality of care and the arrival of computerised administrative and clinical databases that, for the first time, could provide routine information on quality. Performance indicators have become increasingly sophisticated—for example, moving in the UK from relatively simple indicators based on administrative or claims data to more sophisticated measures based on clinical information from electronic medical records. In the United States, the development of quality measurement was initially driven by the rapidly increasing costs of health care and purchasers’ need to know they were getting value for money. Other important factors were the desire to make performance data available publicly and developments in health informatics, which have reduced the cost of producing performance indicators while steadily increasing their sophistication.

In April 2004, the UK government took the bold step of introducing standardised performance indicators across the country and linking performance to general practitioners’ pay. The quality and outcomes framework in the resulting new contract for general practitioners includes a range of performance measures for clinical, organisational, and other areas (such as cervical screening and contraceptive services) and also patient experience. Early results suggest that most general practices achieved high scores across the different parts of the framework. However, as indicators within the framework change and thresholds for achievement alter, we may begin to see greater variation between practices in measured quality of care.

**Public disclosure of performance data**

Public disclosure of performance data is becoming increasingly common in both the UK and the US. In the UK, practice data from the quality and outcomes framework is published online, giving the public access to standardised information on general practices for the first time (www.qof.ic.nhs.uk/). At present, this does not seem to have a large role in how patients choose their general practice, although public disclosure of performance data has been shown to encourage provider organisations to improve quality. However, use may change as the range of information on general practices increases and patients become more skilled at using the internet to view performance data.
What can we learn from other countries?

Performance monitoring systems and performance indicators have largely been developed in a manner that makes them unique to each country. This means it can be difficult to compare quality of care and to transfer performance indicators directly between different health systems, clinical practices, and cultures. However, although some indicators will inevitably be country specific, others, such as glycated haemoglobin concentrations in diabetic people or percentage of patients with coronary heart disease prescribed statins, need not be, and could be designed in a way that makes international comparisons possible.

Quality indicators can also be used to benchmark performance across countries to gain insights into what is achievable and how to improve quality. However, this requires investment in information systems to support measurement of quality. For example, it would have been difficult to implement a system of performance indicators throughout the UK without widespread computerisation of medical records in primary care. Furthermore, although the practice of primary care has many similarities in different countries, differences in the way in which clinical data are collected and coded complicates comparisons. For example, the UK uses Read codes, the US uses international classification of disease (ICD-9) codes, and many other countries use international classification of primary care (ICPC) codes. An internationally accepted set of data standards for coding diagnoses and other clinical data is needed as a first step towards routine comparisons of quality of health care across countries.

Information systems that can produce comparable information on process and outcomes of care are also needed to enable international comparisons. The need for substantive baseline data to compare change in quality against pre-existing trends, and the development of supporting educational strategies for health professionals are also issues that other countries may wish to consider if introducing a national system of performance indicators.

SUMMARY POINTS

The performance of primary care doctors is being monitored more closely in the US and UK.

- Purchasers of health care are also starting to link performance to pay.
- Public access to performance data is allowing more informed decisions when choosing doctors and health care.
- Computerisation will enable the development of increasingly sophisticated performance indicators.
- Greater standardisation of clinical data and performance indicators is needed for more meaningful international comparisons.

Finally, using performance indicators also has some potential adverse consequences. These include doctors declining to accept patients who could be difficult to manage; overtreatment of patients who may not benefit greatly from an intervention; and neglect of areas not covered by performance monitoring. Doctors may have to spend more time on collecting the performance data and less on dealing with patients. However, despite the pitfalls, performance measures in primary care are here to stay and will be used increasingly for quality improvement and performance management in the UK, Europe, United States, and elsewhere. Other articles in this series will discuss how quality measures have been used in the United States; the patient perspective on measuring quality; whether quality of care is determined by more than what is measurable; and future directions in measuring quality in primary care.

Competing interests: AM’s department has received funding for work on developing methods of measuring quality of care from the Department of Health and Dr Foster Intelligence. HL provides academic advice to the BMA and employers’ negotiating teams on the development of the quality and outcomes framework.

Contributors and sources: AM has research interests in the measurement of healthcare quality using administrative and clinical databases. HL has written about pay for performance and has a long research interest in health quality and inequalities. AB performs research on the impact of policies on low-income persons’ access to and quality of care in the United States. This article was based on previous reviews of the measurement of healthcare quality completed by the authors.

Provenance and peer review: Commissioned; externally peer reviewed.

Web resources

- Quality and outcomes framework data for general practices (www.qof.ic.nhs.uk/)—Provides information on the performance of general practices in England
- Quest for Quality and Improved Performance (http://212.72.48.4/QQUIP/index.aspx?ChapterId=19691)—Independent data and commentary about the quality and performance of health care in England
- National Quality Forum (www.qualityforum.org)—A private, not for profit organisation created to develop and implement a national strategy for measuring and reporting healthcare quality in the US

Effectiveness of paramedic practitioners in attending 999 calls from elderly people in the community: cluster randomised controlled trial

Suzanne Mason, reader in emergency medicine,1 Emma Knowles, research fellow,1 Brigitte Colwell, research associate,1 Simon Dixon, senior lecturer,3 Jim Wardrope, consultant in emergency medicine,2 Robert Gorringle, lead emergency care practitioner,4 Helen Snooks, professor of health services research,5 Julie Perrin, nurse consultant in emergency medicine,2 Jon Nicholl, professor1

ABSTRACT

Objective To evaluate the benefits of paramedic practitioners assessing and, when possible, treating older people in the community after minor injury or illness. Paramedic practitioners have been trained with extended skills to assess, treat, and discharge older patients with minor acute conditions in the community.

Design Cluster randomised controlled trial involving 56 clusters. Weeks were randomised to the paramedic practitioner service being active (intervention) or inactive (control) when the standard 999 service was available.

Setting A large urban area in England.

Participants 3018 patients aged over 60 who called the emergency services (n=1549 intervention, n=1469 control).

Main outcome measures Emergency department attendance or hospital admission between 0 and 28 days; interval from time of call to time of discharge; patients’ satisfaction with the service received.

Results Overall, patients in the intervention group were less likely to attend an emergency department (relative risk 0.72, 95% confidence interval 0.68 to 0.75) or require hospital admission within 28 days (0.87, 0.81 to 0.94) and experienced a shorter total episode time (235 ± 278 minutes, 95% confidence interval for difference ~ 60 minutes to −25 minutes). Patients in the intervention group were more likely to report being highly satisfied with their healthcare episode (relative risk 1.16, 1.09 to 1.23). There was no significant difference in 28 day mortality (0.87, 0.63 to 1.21).

Conclusions Paramedics with extended skills can provide a clinically effective alternative to standard ambulance transfer and treatment in an emergency department for elderly patients with acute minor conditions.

Trial registration ISRCTN27796329.

INTRODUCTION

The UK Department of Health’s strategy has been to encourage the increased use of non-medical staff to carry out assessments and treatments traditionally carried out by doctors.1 The introduction of new models of care, including further assessment, triage, and treatment skills for paramedics, has been recommended to help manage ever increasing demands for health care.2 Current evidence concerning safety, effectiveness, and costs to support these changes in practice, however, is lacking.3

Paramedics can be trained to assess and treat or refer patients with a range of conditions such as wounds,4 hypoglycaemia,5 falls, and epistaxis.6 The merits of a pre-hospital practitioner working in certain geographical areas such as rural locations in fulfilling a broader public health and primary care outreach role in the local community have also been discussed.7 Other authors, however, have cast doubt on the safety, feasibility, and cost effectiveness of paramedics assessing and treating apparently minor problems in the community.89

Elderly people make 12-21% of visits to emergency departments. Many of them attend after an accident or fall.1011 Recently completed studies suggest that an alternative approach to an emergency ambulance response would have the greatest chance of improving patients’ experience, as well as potentially helping to reduce demand, if it was targeted at elderly patients with minor complaints.1213

The South Yorkshire Ambulance Service developed the paramedic practitioner in older people’s support (PPOPS) scheme to deliver patient centred care to elderly people who call the emergency services with conditions triaged as not immediately life threatening. Practitioners underwent a three week full time theory based course with lectures from specialists in emergency medicine or care of the elderly. They spent a period of 45 days in supervised practice.

Seven experienced paramedics were selected through open competition and completed the training course to enable them to provide community based clinical assessment for patients aged over 60 who contacted the emergency ambulance service with minor acute conditions. Initial assessment and, when appropriate, treatment was delivered within the patient’s residence by an individual paramedic practitioner who responded to emergency calls. When the
paramedic practitioner deemed it necessary, patients were transported to an emergency department for further assessment or treatment such as radiological investigation. The box outlines the scope of practice.

Operational between the hours of 8am and 8pm each day, the service was activated by a 999 call or an urgent call from a general practitioner to the ambulance control room or from an ambulance crew attending an eligible patient.

We conducted a cluster randomised controlled trial to evaluate the effectiveness and safety of this new service.

METHODS

Patients were recruited from 1 September 2003 to 26 September 2004. Patients aged 60 and above were eligible for inclusion when the call to the ambulance service originated from a Sheffield postcode between 8am and 8pm, with a presenting complaint that fell within the scope of practice of the paramedic practitioners.

We used cluster randomisation to reduce the risk of contamination (practice in the control group being influenced by the presence of the paramedic practitioner in the community) and to allow service level, rather than individual patient level, evaluation of the intervention. Weeks were randomised before the start of the study (to allow for rostering of the paramedic practitioners) to the paramedic practitioner service being active (intervention) or inactive (control), when the standard 999 service was available. The forward roster was concealed from other members of the emergency services. During inactive weeks, the paramedic practitioners were removed from operational duties within the ambulance service, and undertook research duties including obtaining patients’ consent and follow-up. Randomisation of weeks was undertaken by computer random number generation.

Before the trial we carried out a four week pilot study to establish the number of weeks needed to complete recruitment and to test data collection methods.

Principal outcomes in the study protocol were attendance at emergency department and hospital admission between 0 and 28 days, interval from time of call to time of discharge, and patients’ satisfaction with the service received. Secondary outcomes were investigations and treatments prescribed, subsequent use of health services within 28 days, and health status and mortality at 28 days.

Recruitment of patients

During each week, a paramedic practitioner based in the ambulance control room identified eligible calls by the presenting complaint and notified a paramedic practitioner in the community (during intervention weeks) or in the emergency department (during control weeks). All identified patients were approached face to face either in the community or in the emergency department for written consent to follow-up. To avoid unnecessary burden on participants, patients who had more than one eligible episode were recruited only for their first episode.

If patients were unable to complete questionnaires—for example, because of cognitive impairment or who were unable to read English—we obtained consent for follow-up by review of clinical records only.

The research team independently checked the ambulance service call database at the end of each month for any additional eligible calls not identified by the paramedic practitioners at the time of the incident. We noted patients identified retrospectively to check for selection bias but did not follow them up.

Data collection

Routine data

The research team used the emergency department or ambulance service records to collect clinical data, including investigations, treatment, diagnoses, and discharge from the service, relating to the initial patient episode. Total episode time was derived by calculating the interval between the time the initial call was received in the ambulance control room to the time that the patient left the emergency department, was admitted to hospital, or, if the patient was discharged in to the community, the time that the paramedic practitioner or ambulance crew left the scene. These times therefore included any time spent waiting for assessment in the emergency department.

We used hospital records to collect information about unplanned hospital attendances or admissions within Sheffield in the 28 days after the initial episode and mortality at 28 days. Information relating to subsequent ambulance requests was collected from the local ambulance service. Attendance at an emergency department or hospital admission on day 0 was

---

Scope of practice of paramedic practitioners

**Presenting complaint**
- Falls
- Lacerations
- Epistaxis
- Minor burns
- Foreign body in ear, nose, or throat

**Practical skills**
- Local anaesthetic techniques
- Wound care and suturing techniques
- Principles of dressings and splintage

**Special skills**
- Joint examination
- Examination of neurological, cardiovascular, and respiratory system
- Examination of ear, nose, and throat
- Protocol led dispensing: simple analgesia, antibiotics, tetanus toxoid
- Assessment of mobility and social needs

**Additional options for referral and requesting investigations**
- Requests for radiography
- Referral processes: emergency department, general practitioner, district nurse, community social services
combined with any unplanned attendances at an emergency department or admissions in the 28 days that followed to provide information on overall unplanned use of hospital services.

**Survey of patients**
Follow-up was by postal questionnaire at three and 28 days after the incident. The three day questionnaire asked patients about examinations, treatments, advice, and satisfaction with the service they had received. One of our primary outcome measures of patients’ satisfaction was based on one question asking about overall satisfaction with the care received during the initial episode and was measured on a five point scale.

The 28 day questionnaire contained items on subsequent use of health services relating to the incident and perceived change in physical health and included the general health status measure, the EQ-5D.15

**Sample size**
We calculated our sample size on the basis of four primary outcomes: satisfaction with care, attendance at emergency department, hospital admission, and total episode time. The number of primary outcomes reflects the importance of considering different aspects of the impact of service delivery on patients and services in a pragmatic multi-dimensional study. If, as we expected, there is no clustering of data in relation to these outcomes within weeks, we needed about 1100 patients in each group to have an 80% chance of detecting a difference of 7.5% versus 82%. If we ignore the clustering, this sample size also gives 80% power to detect a change of 4% in the proportion of patients attending the emergency department, a change of 6% in the proportion of patients admitted, and a difference of 20 minutes in the mean total episode time (assuming an SD of 180 minutes).

On the basis on the results of the four week pilot study, to recruit two sets of 1100 patients to follow-up we randomly allocated 52 weeks, later extended to

---

**Trial profile, presented according to CONSORT flow diagram guidelines19**
56 weeks, to achieve the sample size. The 56 weeks were randomly allocated in an unrestricted design into control (n=26) and intervention (n=30) weeks.

Statistical analysis
Analysis was by randomisation, on an intention to treat basis, irrespective of the actual service received. During the intervention weeks, identified patients should have received an assessment by a paramedic practitioner in the community. This was not always possible if a paramedic practitioner was busy assessing another case when an eligible call was received. Such patients were attended by a standard emergency ambulance response and, according to ambulance service protocols, should have been taken to the emergency department by ambulance unless they refused transport. During the control weeks, identified patients were attended and treated according to standard practice as described above.

SPSSv.12 was used for initial statistical analysis of baseline differences between groups. Data were then exported to STATAv.8.0 to enable analysis at a cluster level. Generalised estimating equations were used to correct the standard errors of control and intervention comparisons for the effect of any correlation within weeks. To allow for a proper estimation of a relative risk, we used a Poisson error distribution with a robust standard error.

RESULTS
Trial numbers
During the trial, the paramedic practitioners identified 96% (3996/4175) of all eligible calls at the time of the incident (figure). There were no significant differences in terms of sex and presenting complaint between those identified by the paramedic practitioner and those identified retrospectively by the research team. Those identified by the paramedic practitioner, however, were a little older than those who were not identified (table 1).

Of the 2087 patients identified during the intervention weeks and 1909 during the control weeks, 978 patients did not consent to participate, resulting in the inclusion of 3018 patients into the trial. The figure shows details of why patients did not take part. There was a small difference in recruitment rates between intervention (74%) and control (77%) weeks, but no significant differences between the baseline demographics of those who were recruited and those who were not (table 2).

During intervention weeks most patients (n=1090) received the intended service (assessment by a paramedic practitioner). The other patients received the standard ambulance response and were (n=390) or were not (n=69) transported to the emergency department. During control weeks all patients received a standard ambulance response (1234), although 235 were not transported to the emergency department.

There were no differences between groups in terms of demographics or presenting complaint (table 3). The presenting complaint was identified as the primary complaint allocated by the call taker to the call that initiated the ambulance response.

Primary outcomes
Patients in the intervention group were less likely to have attended an emergency department either during the initial episode (day 0) or in the next 28 days (62.6% v 87.5%, P<0.001). They were also less likely to have required a hospital admission during the same time period (40.4% v 46.5%, P<0.001) (table 4). Respondents in the intervention group were more likely to report being “very satisfied” than those in the control group (85.5% v 73.8%, P<0.001). On average, patients in the intervention group experienced a shorter total episode time by around 42 minutes (235 v 278 minutes, P<0.001).

Secondary outcomes
Investigations received by patients during the trial included radiography, blood and urine tests, and electrocardiography. Patients in intervention weeks were less likely to undergo some form of investigation (49.7% v 67.9%, P<0.001) but were more likely to receive some form of treatment, including advice (81.3% v 72.8%, P<0.001).

Patients in the intervention group, however, were more likely to have subsequent unplanned contact with secondary care services, such as the ambulance service, emergency department, or hospital admission, in the 28 days after their initial episode (excluding the initial contact on day 0) (21.3% v 17.6%, P<0.01). They also less likely to report that their physical health had worsened compared with those in the control group (21.7% v 25.6%, P=0.13). The EQ-5D revealed no significant differences in health outcomes between the two groups.

In the 28 days after their initial episode 142 (4.7%) patients died. There were no significant differences between the two groups in terms of mortality.

DISCUSSION
This randomised controlled trial evaluated the impact on processes and outcomes of paramedics with
Presenting complaint: Incident occurred at usual residence 1336 (86.2) 1234 (84.0) 2570 (85.5) Living in own home 1209 (78.1) 1139 (77.5) 2348 (77.8) Mean (SD) age (years) 82.6 (8.3) 82.5 (8.3) 82.6 (8.3) Women 1115 (72.0) 1077 (73.3) 2192 (72.6)

Table 3 | Baseline characteristics of recruited patients. Figures are numbers (percentages) of patients unless stated otherwise

<table>
<thead>
<tr>
<th>Presenting complaint</th>
<th>Intervention (n=1549)</th>
<th>Control (n=1469)</th>
<th>Total (n=3018)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall</td>
<td>1369 (88.4)</td>
<td>1313 (89.4)</td>
<td>2682 (88.9)</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>93 (6.0)</td>
<td>78 (5.3)</td>
<td>171 (5.7)</td>
</tr>
<tr>
<td>Acute medical condition</td>
<td>86 (5.6)</td>
<td>78 (5.3)</td>
<td>164 (5.4)</td>
</tr>
</tbody>
</table>

extended skills managing patients with acute minor conditions. The service conveyed considerable benefits for patients and the NHS in terms of reduced overall attendances at an emergency department and hospital, shorter episode times, and higher levels of satisfaction among patients. The new service also seems to be safe in that we identified no differences in mortality or health outcomes after 28 days.

More than a quarter (29.6%, n=459) of patients in the intervention group did not receive the paramedic practitioner service. These patients therefore received the “normal service” but were still included in the “intervention” group as the results were analysed on a pragmatic intention to treat basis, reflecting the outcomes that could be expected were the intervention to be introduced more widely, and standard for the reporting of the results of health services research. This had the effect of considerably weakening the impact of the intervention.

The patients in this trial were categorised as having “minor” conditions at their initial contact with the emergency services. The most common presenting complaint was a fall. Within 28 days of the initial call, however, over 40% had required a hospital admission and 5% had died. This highlights the high risk nature of this group of patients. None the less, the service seemed to manage the risk appropriately and identify a group of patients who benefited from management at home.

There is increasing strategic pressure within the NHS to extend this type of approach. In 2003, the changing workforce programme, part of the NHS modernisation agency and the Department of Health, set up 17 initial emergency care practitioner pilot sites. These practitioners are mainly paramedics who receive extended skills training, as did the paramedic practitioners in this study (although for a shorter time period). More work is required to enable identification of patients who can benefit from this level of care rather than a full assessment in an emergency department. Some emergency care practitioner schemes are targeted at different populations and operate in different ways and thus the results of this study may not be fully transferable.

Limitations
This large open pragmatic trial has some limitations because of differences in recruitment of patients and response rates to follow-up questionnaires between the groups. In particular, the measurement of patients’ satisfaction depended on receipt of a three day follow-up questionnaire. Of the 3996 patients randomised to the trial, only 2293 agreed to receive a questionnaire. This was mainly because of the proportion of patients with cognitive impairment, who we excluded from this part of the study. Of the 2293 patients, 1482 (64.6%) responded, which is less than the number we calculated we needed (n=2200). The effects on the primary outcomes (hospital attendance and admission, episode times, and satisfaction), however, were all significant and sufficiently large for us to be confident that the effects are real.

The study was conducted in one large urban area of the UK. Therefore the generalisability of these results...
Patients find this approach more satisfactory than attending the emergency department and reduce the need for emergency department attendance by almost 25%.

WHAT THIS STUDY ADDS

Paramedics can be trained to see and treat elderly people with acute minor conditions and should be treated with some caution. We think that there is nothing unique about the patients or presenting complaints. Other health communities could replicate this model, and we are aware of similar services being set up in the UK and abroad. This does require major cooperation between organisations and considerable training and operational costs.

We acknowledge that there may have been some clustering at a practitioner level. Though our study was designed specifically to assess clustering by week, statistical software does not allow for cluster analysis of two variables simultaneously so we could not analyse clustering at a practitioner level.

Summary

Paramedics with extended skills working in the community can provide a clinically effective alternative to standard ambulance transfer and treatment in an emergency department for elderly patients with acute minor conditions.

Contributors: SM and JW initiated and designed the study. EK oversaw the data collected by BC. JN provided advice on design and statistical advice. SM and EK analysed the data. All authors contributed to the advancement of the study, with input from BC at practitioner level. SM drafted the first manuscript and provided specialist knowledge at study meetings and provided input in re-drafting the manuscript. SM drafted the first manuscript and wrote the final version, which was seen and approved by all of the authors. SM is guarantor.

Funding: Health Foundation.

Competing interests: None declared.

Ethical approval: North Sheffield research ethics committee.

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


4 Hale D, Sipprell K. Ability of EMT-Bs to determine which wounds can be prepared in the field. Prehosp Emerg Care 2000;4:245-9.


16 StaCorP. Statistical software: release 8.0. College Station, TX: Stata Corporation, 2003.


Accepted: 8 August 2007
Occupational therapy for patients with problems in personal activities of daily living after stroke: systematic review of randomised trials

Lynn Legg, CSO research training fellow,1 Avril Drummond, principal research fellow in rehabilitation,3 Jo Leonardi-Bee, lecturer in medical statistics,2 J R F Gladman, professor of medicine of older people,3 Susan Corr, reader in occupational science,4 Mireille Donkervoort, senior researcher department of rehabilitation medicine,5 Judi Edmans, research occupational therapist,6 Louise Gilbertson, clinical specialist occupational therapist in stroke,6 Lyn Jongbloed, associate professor,7 Pip Logan, principal research fellow,3 Catherine Sackley, professor of physiotherapy research,6 Marion Walker, associate professor and reader in stroke rehabilitation and associate director UK stroke research network,3 Peter Langhorne, professor of stroke care

ABSTRACT

Objective To determine whether occupational therapy focused specifically on personal activities of daily living improves recovery for patients after stroke.

Design Systematic review and meta-analysis.

Data sources The Cochrane stroke group trials register, the Cochrane central register of controlled trials, Medline, Embase, CINAHL, PsycLIT, AMED, Wilson Social Sciences Abstracts, Science Citation Index, Social Science Citation, Arts and Humanities Citation Index, Dissertations Abstracts register, Occupational Therapy Research Index, scanning reference lists, personal communication with authors, and hand searching.

Review methods Trials were included if they evaluated the effect of occupational therapy focused on practice of personal activities of daily living or where performance in such activities was the target of the occupational therapy intervention in a stroke population. Original data were sought from trialists. Two reviewers independently reviewed each trial for methodological quality. Disagreements were resolved by consensus.

Results Nine randomised controlled trials including 1258 participants met the inclusion criteria. Occupational therapy delivered to patients after stroke and targeted towards personal activities of daily living increased performance scores (standardised mean difference 0.18, 95% confidence interval 0.04 to 0.32, P=0.01) and reduced the risk of poor outcome (death, deterioration or dependency in personal activities of daily living) (odds ratio 0.67, 95% confidence interval 0.51 to 0.87, P=0.003). For every 100 people who received occupational therapy focused on personal activities of daily living, 11 (95% confidence interval 7 to 30) would be spared a poor outcome.

Conclusions Occupational therapy focused on improving personal activities of daily living after stroke can improve performance and reduce the risk of deterioration in these abilities. Focused occupational therapy should be available to everyone who has had a stroke.

INTRODUCTION

Stroke is the second leading cause of death in the world and the leading cause of serious, long term disability in adults; about half of those who survive are dependent on others for assistance with personal activities of daily living six months after the stroke.1,2 Personal activities of daily living are necessary for survival and include “those tasks which all of us undertake every day of our lives in order to maintain our level of care”3 such as feeding, dressing, toileting, grooming, transferring, and mobilising.4

Occupational therapy is an essential element in the rehabilitation of patients after stroke. It entails “use of purposeful activity or interventions designed to achieve functional outcomes which promote health, prevent injury or disability, and which develop, improve, sustain or restore the highest possible level of independence.”5 Personal activities of daily living is major component of treatment for people who have had a stroke.7 Level of dependence in such activities is an important measure of the success of stroke rehabilitation8 and a commonly used outcome in stroke trials.4

A systematic review of therapy based rehabilitation services delivered to stroke patients living at home within one year of stroke onset9 found that those who received rehabilitation based on therapy were more independent in personal activities of daily living and more likely to maintain that ability during the study period. This review, however, covered a heterogeneous group of interventions (physiotherapy, occupational therapy, or multidisciplinary staff working with patients primarily to improve task orientated behaviour) and concluded that the “different groups of interventions might differ in their effects.”
A subsequent analysis of data from individual patients from eight stroke trials focused on the effect of community occupational therapy on instrumental activities of daily living (including making a meal, using public transport, or using the telephone) and found benefits in personal activities of daily living (a secondary outcome) at the end of treatment but not at the end of scheduled follow-up. We are aware of more trials than were included in this review and in addition, occupational therapy is often given in settings other than the community, and its prime target is often to improve personal activities of daily living.

We conducted a systematic review to test the hypothesis that occupational therapy aimed at encouraging people to participate in personal activities of daily living after stroke will improve the recovery of ability to perform such activities.

METHODS

Eligibility criteria

We sought any randomised controlled trials that compared an occupational therapy intervention focused on activities of daily living with no routine input as the control intervention. The interventions had to be delivered by, or under the supervision of, a qualified occupational therapist. Our primary outcome of interest was independence in personal activities of daily living at the end of scheduled follow-up. The second primary outcome of interest was the extent to which participants had poor outcome, defined as death or deterioration of ability or dependency in personal activities of daily living. Secondary outcomes were death, institutionalisation, extended personal activities of daily living necessary for maintaining a dwelling in a given sociocultural setting (for example, preparing own meals, doing light housework, managing own money, shopping for personal items), patients’ mood and quality of life, carers’ mood and quality of life, and patients’ and carers’ satisfaction with services.

Search strategy for the identification of studies

We followed the search strategy developed for the stroke group of the Cochrane collaboration. This comprised a search of the Cochrane stroke group trials register (last searched by the review group coordinator on 7 November 2006), the Cochrane central register of controlled trials (Cochrane Library, issue 4, 2007), electronic bibliographic databases including Medline, Embase, CINAHL, PsycLIT, AMED, Wilson Social Sciences Abstracts, and the following Web of Science databases: Science Citation Index (1945 to March 2007), Social Science Citation Index (1956 to March 2007), Arts and Humanities Citation Index, dissertation abstracts register, and the occupational therapy research index. Other strategies to ensure identification of all potentially relevant trials included scanning reference lists of relevant articles and original papers, personal communication with authors, and hand searching journals. For full details of all journals searched, with dates, please see the full review in the Cochrane Library.

One reviewer read the titles of all the references identified and eliminated any obviously irrelevant studies—for example, pharmacological or surgical interventions and study designs other than randomised controlled trials. The abstracts of the remaining studies were obtained and selected according to the assessment of two reviewers. Differences in opinion regarding trial eligibility were resolved by consensus.

Data extraction

Two reviewers independently rated the methodological quality of studies using recognised criteria: method of randomisation, allocation concealment, blinding of outcome assessment, and use of an intention to treat analysis. We aimed to obtain standardised data through collaboration with the original trialists. Two independent reviewers extracted data using a standard data recording form.

Data analysis

We performed an intention to treat analysis to reduce potential biases (follow-up, publication, and reporting) associated with extracting data from published reports. We obtained original trial data for eight of the nine studies. This enabled a uniform approach to re-analysis of the data and standardisation of outcomes.

Eight studies used individuals as the unit of randomisation and analysis; one study used a randomised cluster trial design where the unit of randomisation was the nursing home. The data from the cluster randomised trial were analysed for the number of events (participants worse or dead) at the individual level using data for each participant in each cluster. We used an intraclass correlation coefficient of 0.02 to calculate the design effect and effective sample size.

Review Manager 4.27 was used for the statistical analysis. Binary outcomes were analysed with a fixed effect model, as Peto odds ratios with 95% confidence intervals. For continuous outcomes, we used the standardised mean difference with a random effects model to take account of statistical heterogeneity.
## Table 1: Description of trials included in review*

<table>
<thead>
<tr>
<th>Study (setting)</th>
<th>Sample size, characteristics, and theoretical framework (if specified)</th>
<th>Intervention and time scale</th>
<th>Outcomes</th>
<th>Baseline differences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Corr 1995</strong>¹⁷ (UK hospital outreach)</td>
<td>110 patients: 55 intervention, 55 control. Mean age 75.3, 37% men. Median Barthel index score at baseline: intervention 15 (IQR 2-20), control 14 (0-20). Clinical definition of stroke. Patients recruited before discharge from inpatient facility. Inclusion criteria: discharged alive from one of two stroke units regardless of discharge destination. Model of human occupation</td>
<td>Rehabilitation at home by occupational therapists versus usual care. Interventions included: teaching new skills; facilitating more independence in activities of daily living; facilitating return of function; enabling patients to use equipment supplied by other agencies; information provision to patient and carer; referring to or liaison with other agencies. Service provided by a qualified occupational therapist. Input at 2, 8, 16, and 24 weeks over 12 months, 95.5% followed up</td>
<td>Death, Barthel index, Nottingham extended ADL index, Geriatric depression scale (short form), Pearlin’s 6 point quality of life scale. Carer: Pearlin’s 6 point quality of life scale</td>
<td>More women in intervention group (P=0.03)</td>
</tr>
<tr>
<td><strong>Gilbertson 2000</strong>¹⁸ (UK hospital outreach)</td>
<td>138 patients: 67 intervention, 71 control. Median age 69, 45% men. Median Barthel index at baseline: intervention 17 (15-18), control 18 (16-19). Clinical definition of stroke. Patients recruited when discharged from hospital/day set. Inclusion criteria: discharged to private address; willing to cooperate; consent. Exclusion: made full recovery; discharged to institutional care; terminally ill; lived outside catchment area; severe cognitive or communication difficulties preventing consent, goal setting or completing outcome measures. Model of occupational performance</td>
<td>Domiciliary occupational therapy versus routine service. Domiciliary occupational therapy for a period of six weeks. Client-centred occupational therapy programme. Liaison with other agencies. Occupational therapy provided by a qualified occupational therapist. About 1.7 visits/week for 30-45 min over 6 months; 96.4% followed</td>
<td>Outcomes recorded at 7 weeks and 6 months. Primary outcomes: Nottingham extended ADL index; Barthel index; “Global” (death or deterioration) in Barthel index score. Secondary outcomes: Barthel index; Canadian occupational performance measure; EuroQol; satisfaction with outpatient services; resource use (staff time, hospital readmission, provision of equipment and services). Carer: general health questionnaire at 6 weeks</td>
<td>Favour control group</td>
</tr>
<tr>
<td><strong>Chiu 2004</strong>¹⁹ (Hong Kong hospital outreach)</td>
<td>53 patients: 30 intervention, 23 control. Mean age 72.1, 66% men. Barthel index at baseline: NA. Definition of stroke: unclear. Recruitment: inpatients and outpatients discharged from hospital for ≥2 weeks. Inclusion criteria: aged ≥55, diagnosis of stroke, able to follow instructions, able to communicate using speech, family support at home, required bathing device</td>
<td>Additional home based training intervention on the use of bathing devices versus no intervention. 2-3 visits intervention group over 3 months; 100% followed</td>
<td>Outcomes recorded 3 months after discharge. Primary outcome: NS. Outcome measures: functional independence measure (FIM); users evaluation of satisfaction with assistive technology</td>
<td>None</td>
</tr>
<tr>
<td><strong>Drummond 1995</strong>²⁰ (UK community)</td>
<td>65 patients: 42 intervention (21 in leisure intervention group, 21 in ADL intervention group), 23 control. Mean age 66, 57% men. Barthel index at baseline: not collected. Definition of stroke: unclear. Patients recruited at discharge from inpatient facility. Exclusion criteria: aged ≥65, diagnosis of stroke, unable to understand or speak English before stroke</td>
<td>Leisure versus conventional occupational therapy versus no occupational therapy. Leisure intervention: patients hobbies and interests were discussed in detail and the importance of maintaining a leisure programme stressed. Treatment reflected personal preferences and abilities. Help and advice included: treatment (eg practice of transfers and dressing practice needed for leisure pursuits); positioning; provision of equipment; adaptations; advice on obtaining financial assistance and transport; liaison with specialist organisations; and providing physical assistance. Conventional OT: OT activities such as transfers, washing and dressing practice, and when appropriate, perceptual treatments. Patients seen by OT for minimum of 30 min/week for 3 months, then 30 min/every 2 weeks up to 6 months; 98.5% followed</td>
<td>Outcomes recorded at 3 and 6 months. Nottingham extended ADL index. Nottingham health profile. Nottingham leisure questionnaire. Wakefield depression inventory</td>
<td>Favour leisure group</td>
</tr>
<tr>
<td><strong>Walker 1996</strong>²¹ (UK community)</td>
<td>30 patients: 15 intervention, 15 control. Mean age 68, 53% men. Barthel index at baseline: not collected. Definition of stroke: unclear. Patients recruited at discharge from inpatient facility. Exclusion criteria: blind, deaf, unable to understand or speak English before stroke</td>
<td>Domiciliary occupational therapy versus no occupational therapy intervention. Domiciliary occupational therapy over a three month period provided by a senior occupational therapist. Components of intervention: dressing practice on a regular basis; teaching patients and carers specific dressing techniques, energy conservation techniques, advice on clothing adaptation. Relative/carer involvement in therapy programme and “homework” between therapy sessions. Occupational therapy provided by a qualified occupational therapist. Amount of therapy provided at therapist’s discretion. Mean 6 visits over 6 months; 100% followed</td>
<td>Outcomes recorded at 3 and 6 months. Nottingham stroke dressing assessment. Rivermead ADL scale. Nottingham health profile</td>
<td>None</td>
</tr>
<tr>
<td><strong>Logan 1997</strong>²² (UK community)</td>
<td>111 patients: 53 intervention, 58 control. Mean age 55, 43% men. Barthel index at baseline: NA. Clinical definition of stroke. Inclusion criteria: first stroke and discharged from hospital and referred to social services occupational therapy department</td>
<td>Enhanced occupational therapy service versus usual care. Enhanced (dedicated, prompt, and intensive) occupational therapy service provided by social services, includes provision of equipment and appliances. Occupational therapy provided by a qualified occupational therapist. Single therapist. Duration 6 months; 85.6% followed</td>
<td>Outcomes recorded at 3 and 6 months. Nottingham extended ADL index. Barthel index. General health questionnaire. Carer: general health questionnaire</td>
<td>None</td>
</tr>
<tr>
<td><strong>Walker 1999</strong>²³ (UK community)</td>
<td>185 patients: 94 intervention, 91 control. Mean age 74; 51% men. Median Barthel index at baseline: intervention 18 (15-20); control 18 (15-20). Clinical definition of stroke. Patients recruited 1 month after stroke onset from home. Exclusion criteria: 11 month after stroke onset, history of dementia, living in nursing or residential home, unable to speak or understand English before stroke</td>
<td>Occupational therapy versus no occupational therapy. Occupational therapy intervention for a period of five months. Aim of therapy was to achieve independence in personal (bathing, dressing, feeding, stair mobility) and instrumental activities of daily living (outdoor mobility, driving a car, using public transport, household chores). Homework tasks were set in between therapy sessions. Occupational therapy provided by a single therapist. Frequency of visits arranged between therapist, patient, and carer (if appropriate). Mean of 5.8 visits/patient over 6 months; 95.1% followed</td>
<td>Outcomes recorded at 6 months. Primary outcomes: Nottingham extended ADL index; Barthel index</td>
<td>Favour intervention group</td>
</tr>
<tr>
<td><strong>Sackley 2006</strong>²⁴ (UK community nursing home)</td>
<td>12 nursing homes. 118 residents: 63 intervention, 55 control. Mean age 87.5, 19% men. Mean Barthel index at baseline: intervention 10.1 (SD 5.60); control 9.49 (5.2). Definition of stroke: unclear. Inclusion criteria: Barthel &lt;15. No specific approach</td>
<td>Occupational therapy versus standard care. Occupational therapy included activities of daily living practice, mobility practice, assessment and goal setting, communication with residents, staff, relatives, and other agencies, adaptive equipment and treatment of impairments. Mean visits 8.5, mean total time 4.7 hours/patient over 6 months; 100% followed</td>
<td>Outcomes recorded at 3 and 6 months. Primary outcome: Barthel index</td>
<td>None</td>
</tr>
</tbody>
</table>
Outreach

hospital

IQR=interquartile range, NS

2001w25 (UK

Parker

*Unit of randomisation and analysis was individual except in w24, which was nursing home with individual adjusted for clustering.

Statistical heterogeneity between studies was examined with $\chi^2$ and $P.$ An $P$ value over 50% was considered to indicate substantial inconsistency. Publication bias was assessed with a rank correlation test and a funnel plot.17

We planned sensitivity analyses to explore the influence of the method of randomisation, allocation concealment, blinding of final outcome assessment, and the presence of an intention to treat analysis.

RESULTS

Figure 1 outlines the results of the trial selection process. We identified 14 593 references from the searches, of which 14 528 were excluded from title or abstract, leaving 65 potentially eligible studies for inclusion. After we obtained full texts for these studies, we then excluded 54 as they did not fulfil the inclusion criteria. Reasons for exclusion were as follows: intervention provided by a healthcare professional other than occupational therapist (17 studies), multidisciplinary intervention including occupational therapy (eight), intervention not focused on personal activities of daily living (15), one type of occupational therapy versus another type of occupational therapy (six), not a randomised controlled trial (five), insufficient numbers of stroke participants (three), (detailed exclusions are given in the Cochrane Library version of the review). Two trials are not yet completed.15 w16 The remaining nine studies were included in the review and contained information on 1258 participants.17 w25 Table 1 gives details of the included studies. Table 2 provides information on the methodological quality of the included studies, and table 3 describes the six trials that we excluded from the review because they did not have a suitable control group.

The mean age of participants in studies ranged from 55 to 87.5 years and the proportion of men ranged from 19% to 66%. Baseline scores on the Barthel index were available for five trials.17 w18 w20-w22. Four trials included people with mild to moderate disability (range of Barthel index 14-18/20)17 w18 w20-w22 but one trial recruited more severely dependent participants (mean Barthel index 9-10/20).w24 Exclusion criteria were communication difficulties and cognitive or other co-existing conditions that would interfere with compliance or outcome assessment,w18 w20-w22 w25 inability to speak English,w20 w21 w23 w25 terminal illness,w18 w19 residence in, or about to be discharged to, a residential or nursing home,w18 w21 not living at home and without carer or family support,w15 and a Barthel score over 15.w24 One trial recruited participants who had not been admitted to hospital after stroke onset,w24 and another trial recruited only from nursing homes.w24 Six trials recruited from inpatient facilities.w17 w18 w20-w22 w25 One trial recruited participants two weeks after discharge from inpatient facilities.w10

Most studies had parallel groups with occupational therapy focused on personal activities of daily living compared with usual care or no routine intervention. Two trials compared two alternative interventions (occupational therapy based on leisure activities or personal activities of daily living) against usual care or no routine intervention in three parallel groups. One trial used a crossover design in which participants were given dressing practice followed by the personal activities of daily living intervention of interest, in sequence.1 w21 For further details of the interventions provided, see the Cochrane review.12

Eight trials clearly described concealed allocation, randomisation procedures, an objective, and explicit blinded outcome assessment for all participants.17 w18 w20-w25 Four studies explicitly reported the use of an intention to treat analysis.18 w22 w24-w25 Median time to follow-up was six months (range 3-12 months). Rates of loss to follow-up varied considerably across the reported outcomes. Sixty one (8.5%) participants from the intervention groups and 34 (6.3%) from the control groups died during follow-up.

Personal activities of daily living

Six studies used the Barthel index18 to measure personal activities of daily living.17 w18 w22-w25 one study used the self care section of the Rivermead personal activities of daily living scale,10 w25 and one study used the functional independence measure.20 w19 A score for personal activities of daily living was available for
961 (80.6%) participants from eight trials. The pooled result for all trials, combined as a standardised mean difference, was 0.18 (95% confidence interval 0.04 to 0.32; P=0.01) with no significant heterogeneity (P=0.33) (fig 2). Therefore, participants who received occupational therapy after stroke were significantly more independent in personal activities of daily living than those who received no intervention or usual care. The estimated standardised mean difference of 0.18 is equivalent to a one point (5%) difference on the 20 point Barthel index, assuming a population SD of six points.

There was no substantial change in results when we limited sensitivity analyses to the seven trials with clear allocation, randomisation procedures, or blinding (standardised mean difference 0.17, 0.02 to 0.33; P=0.03). When we restricted analysis to the four trials that performed an intention to treat analysis, the effect was reduced and became non-significant (0.12, 0.10 to 0.33; P=0.28).

In our post hoc analysis excluding the leisure based occupational therapy arms from the two trials that compared alternative forms of intervention (occupational therapy based on leisure activities or personal activities of daily living), we found similar results (0.20, 0.06 to 0.33; P=0.004) with no significant heterogeneity (P=0.56).

Deterioration in personal activities of daily living

The second outcome concerned the extent to which occupational therapy could influence the risk of deterioration in personal activities of daily living. We defined this as the combined “poor outcome” of death or experiencing a deterioration in ability to perform personal activities of daily living (experiencing a drop of one or more points in a given score for personal activities of daily living) or dependent (below a predefined threshold on a given personal activities of daily living scale; for the Barthel index this was 15), or requiring institutional care at the end of scheduled follow-up. Data on poor outcome were available for 1065 (90.6%) participants from seven trials and showed that the odds of a poor outcome were significantly lower in the participants who received occupational therapy (odds ratio 0.67, 0.51 to 0.87; P=0.003) with no significant heterogeneity between studies (P=0.28) (fig 3). The overall rate of a poor outcome for controls was 42%, which combined with an odds ratio of 0.67 gives an estimated number needed to treat of 11 (7 to 30).

Re-analysis for the outcome death and deterioration in the score for personal activities of daily living included information on 407 (98.5%) participants from four trials and produced similar results (odds ratio 0.60, 0.39 to 0.91; P=0.02) with no significant heterogeneity. Further analysis with exclusion of the leisure based occupational therapy arms from the two trials that compared alternative forms of interventions (occupational therapy based on leisure or personal activities of daily living) provided similar results (odds ratio 0.65, 0.49 to 0.86; P=0.002) with no significant heterogeneity between studies (P=0.37).

There was no substantial change in results when we conducted sensitivity analyses excluding trials with clear intention to treat analysis. If we assume that the participants who were missing (66/673 (9.8%) in intervention groups and 44/502 (8.8%) in control groups) had a poor outcome, then the odds of a poor outcome remained significantly reduced for those participants who received occupational therapy (odds ratio 0.67, 0.52 to 0.86; P=0.002) with no significant heterogeneity (P=0.27). Furthermore, if we assume that the participants who were missing from the treatment groups were alive and well and living at home, then the odds of a poor outcome were still significantly reduced for those who received occupational therapy (odds ratio 0.71, 0.55 to 0.92; P=0.009) with no significant heterogeneity (P=0.20).

We found no evidence of publication bias from the rank correlation test for the outcome death or “poor outcome” (P=0.108, seven studies) or in the funnel plot.

Secondary outcomes

We had scores on the Nottingham extended activities of daily living scale for 847 (78.8%) participants from six trials. Those who received occupational therapy were significantly more independent in instrumental activities of daily living (standardised mean difference 0.21, 0.03 to 0.39; P=0.02). There was a non-significant benefit in mood or distress scores.
Table 3 | Description of six trials of occupational therapy for stroke excluded from review

<table>
<thead>
<tr>
<th>Study (setting)</th>
<th>Participants</th>
<th>Intervention and outcomes</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donkervoort 2001 (inpatients)</td>
<td>113 participants, 56 strategy training, 57 usual occupational therapy. Mean age 65.4; 52% men. Inclusion criteria: left hemisphere stroke, apraxia, staying in inpatient care unit. Exclusion criteria: history of apraxia before current stroke, stroke onset &gt;4 weeks, aged &lt;25 or &gt;95, history of post-traumatic brain damage, history of brain tumour, unable to speak Dutch, premorbid or current psychiatric, psychogeriatric, addiction to alcohol or other drugs, premorbid personality, intellectual or learning disorder, history of severe consciousness impairments. Assessed not to require treatment</td>
<td>Strategy training integrated into occupational therapy v occupational therapy. Activities of daily living observations, apraxia test, Motricity index</td>
<td>Compared two types of occupational therapy</td>
</tr>
<tr>
<td>Edmans 2000 (inpatients)</td>
<td>80 participants, 40 in transfer of training group and 40 in functional training group. Inclusion criteria: sufficient cognitive, language, and functional ability to complete the Rivermead perceptual assessment battery, sufficient functional use of one hand to complete perceptual treatment activities, consent</td>
<td>Transfer of training approach v functional approach to treatment of perceptual problems. Perceptual treatment given for 2.5 hours/week for 6 weeks. Rivermead perceptual assessment battery, Barthel activities of daily living index, and Edmans activities of daily living index</td>
<td>Compared two types of occupational therapy</td>
</tr>
<tr>
<td>Jongbloed 1989 (inpatients)</td>
<td>90 participants, 43 in sensorimotor integrative treatment group and 47 in functional treatment group. Mean age 71.32; 45% men. Inclusion criteria: admitted to hospital &lt;12 weeks after first CVA, presented with unilateral upper and lower extremity weakness on admission to hospital, no experience of nursing, residential, or extended care before admission to hospital, no severe aphasia, able to consent</td>
<td>Sensorimotor integrative treatment techniques v functional treatment 40 min/day, 5 days/week for 8 weeks. Barthel index, meal preparation, sensorimotor integration tests</td>
<td>Compared two types of occupational therapy</td>
</tr>
<tr>
<td>Lui 2001 (inpatients)</td>
<td>22 participants, 12 intervention and 10 control. Mean age 71.3; 54% men. Inclusion criteria: unilateral stroke, independent in activities of daily living before stroke, able to communicate, medically stable</td>
<td>Connectionist model (task generalisation programme) v traditional learntask strategy on daily tasks. Evaluated on performance of tasks</td>
<td>Compared two types of occupational therapy</td>
</tr>
<tr>
<td>Morgan 2002 (hospital outreach)</td>
<td>Inclusion criteria: men &gt;40 and &lt;50 years, first stroke, middle cerebral artery syndrome of thromboembolic origin confirmed by CT, middle band in Garraway and coworkers neurological screening process. Exclusion criteria: considerable complications or comorbidities after stroke, any impairment that would prevent use of Canadian occupational performance measure such as aphasia</td>
<td>Client centred occupational therapy intervention programme v therapist led functional occupational therapy programme. Modified motor assessment scale, modified Barthel index, Canadian occupational performance measure</td>
<td>Compared two types of occupational therapy</td>
</tr>
<tr>
<td>Young 1983 (unclear)</td>
<td>27 participants (9 per group). Mean age 64.15. Inclusion criteria: right CVA, age 45-80, assessed to have left neglect or visual scanning deficits, or both. Exclusion: history of alcoholism, psychiatric treatment, or previous neurological impairment</td>
<td>Hour of routine occupational therapy/day v 20 min routine occupational therapy + 20 min cancellation training + 20 min visual scanning training v 20 min block design training + 20 min cancellation training + 20 min of visual scanning training. Letter cancellation task, wide range achievement test, copying and address, counting faces, activities of daily living (outcome measure not stated)</td>
<td>Compared different intensities of occupational therapy</td>
</tr>
</tbody>
</table>

CVA=cerebrovascular event, CT=computed tomography.

for participants and carers. Data on use of institutional care, participants’ and carers’ quality of life, and satisfaction with services were incomplete and available for only a few studies and therefore the results from pooled analysis were inconclusive.

**DISCUSSION**

Stroke patients who receive occupational therapy focused on personal activities of daily living, as opposed to no routine occupational therapy, are more likely to be independent in those activities.

**Limitations of the study**

It is difficult to design and conduct high quality clinical trials of rehabilitation. Firstly, the masking of therapies from patient and therapist is difficult, thus permitting the introduction of bias, particularly when the person providing the intervention is also the person doing the research, as is the case with many of the studies in this review. Secondly, while usual or standard care is recognised as an appropriate control, this may include interventions that promote activities, which potentially reduces the estimate of the intervention effect.21
Thirdly, it is more difficult to obtain acceptance of randomisation in an inpatient setting, particularly where an occupational therapy service is already established. We excluded four trials that compared one occupational therapy intervention within an active concurrent control arm provided in inpatient settings as they did not provide an unconfounded estimate of effect.\textsuperscript{14,24} Finally, trials of rehabilitation interventions typically have lengthy follow-up periods with a risk of study dropout. This makes performing a true intention to treat analysis with complex scores such as the Barthel index problematic as it is difficult to score for missing participants. Despite these potential concerns, however, the quality of the included trials was generally good and the results were consistent between trials.

Occupational therapy is a complex intervention. Practice includes skilled observation; the use of standardised and non-standardised assessments of the biological, psychiatric, social, and environmental determinants of health; clarification of the problem; formulation of individualised treatment goals; and the delivery of a set of individualised problem solving interventions. While we are confident that all the interventions in this review were consistent with this broad concept of occupational therapy, we recognise that the exact nature of the interventions in each study differed according to the type of patient, the expertise of the therapist, and the resources available. The interventions tested were probably provided by experts and not particularly constrained by day to day service factors. Our review did not compare occupational therapy with alternative rehabilitation interventions, nor did it examine the effect of occupational therapy combined with other interventions.

Comparison with previous studies
Previous reviews that have assessed the role of occupational therapy either have not specifically focused on stroke,\textsuperscript{22} have concentrated on instrumental activities of daily living in the subgroup of stroke patients living in the community,\textsuperscript{25} or have included a wide range of studies of varying methodological quality.\textsuperscript{23} Our review adds substantially to the literature by examining the effects of occupational therapy focused personal activities of daily living in stroke patients regardless of treatment setting.

Implications for research
Occupational therapy after stroke “works” in that it improves outcome in terms of ability in personal activities of daily living. The estimate that 11 (7 to 30) patients need to be treated to avoid one patient deteriorating in personal activities of daily living should be regarded as an approximate indicator. This is a relatively crude measure of outcome, which does not capture potential benefits in other domains of health. This figure also suggests, however, that not all patients treated by an occupational therapist will benefit. Further work is required to define those individuals who are most likely to benefit from occupational therapy, and economic studies are required to examine the cost effectiveness of occupational therapy. We believe that our findings should move the research agenda away from the questions surrounding whether occupational therapy (as a package of interventions) is effective to the identification of which specific interventions are effective for particular patients.
WHAT IS ALREADY KNOWN ON THIS TOPIC

Reviews of rehabilitation therapies show that they improve personal abilities in activities of daily living in people who have had a stroke, but the individual contribution from occupational therapy is not certain

Previous reviews of trials of occupational therapy in stroke have not specifically studied such personal ability

WHAT THIS STUDY ADDS

Occupational therapy is an effective intervention to improve personal ability in activities of daily living in patients who have had a stroke.

Around 11 (95% confidence interval 7 to 30) people with stroke would need to be treated to avoid a poor outcome in one person.

This study was done as a Cochrane systematic review under the auspices of the Cochrane Stroke Group, whose invaluable assistance is gratefully acknowledged.

Contributors: LL and AD planned the review. LL was lead reviewer and produced the first draft of the paper. AD, PLa, JL-B, and JRFG all collaborated on the final version before initial submission and took responsibility for the submitted version of the paper. SC, MD, JE, LG, LJ, PLc, CS, and MW were members of the occupational therapy trialists and obtained primary data and assisted in the editing of the paper. LL is guarantor.

Funding: The Big Lottery Fund and Chest Heart and Stroke Scotland funded staff time.

Competing interests: None declared.

Ethical approval: Not required.

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

1 Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. Lancet 1997;349:1269-76.

Accepted: 30 July 2007
Combined resynchronisation and implantable defibrillator therapy in left ventricular dysfunction: Bayesian network meta-analysis of randomised controlled trials

Simon K H Lam, MSc student,1 Andrew Owen, consultant2

ABSTRACT

Objective To review the evidence base from randomised controlled trials of combined cardiac resynchronisation therapy and implantable cardioverter defibrillator therapy in left ventricular impairment and symptomatic heart failure.

Design Bayesian network meta-analysis.

Data sources Medline, Embase, and Cochrane databases up to June 2006.

Review methods Two reviewers independently assessed trial eligibility and quality. Included trials compared cardiac resynchronisation therapy, implantable cardioverter defibrillator therapy, combined resynchronisation and implantable defibrillator therapy, and medical therapy alone, in patients with impaired left ventricular systolic function. Bayesian random effects network models were used to examine overall number of deaths.

Results 12 studies including 1636 events in 8307 patients were identified. Combined cardiac resynchronisation and implantable cardioverter defibrillator therapy reduced the number of deaths by one third compared with medical therapy alone (odds ratio 0.57, 95% credible interval 0.40 to 0.80) but did not further improve survival when compared with implantable defibrillator therapy (0.82, 0.57 to 1.18) or resynchronisation (0.85, 0.60 to 1.22) therapy alone.

Conclusion Evidence from randomised controlled trials is insufficient to show the superiority of combined cardiac resynchronisation and implantable cardioverter defibrillator therapy over cardiac resynchronisation therapy alone in patients with left ventricular impairment.

INTRODUCTION

Advances in medical therapy have improved the symptoms, quality of life, and survival of patients with symptomatic heart failure, but the prognosis remains unfavorable.1 Progressive pump failure and ventricular tachyarrhythmias are common causes of death in these patients despite optimal medical therapy. New pacing technologies have emerged to treat selected patients with heart failure.2 Cardiac resynchronisation therapy, or biventricular pacing, improves cardiac function by reducing or even abolishing the abnormal pattern of ventricular activation and contraction observed in some patients with left ventricular systolic dysfunction. Implantable cardioverter defibrillator therapy reduces sudden cardiac deaths by providing antitachycardia pacing and defibrillation to stop ventricular tachycardia and fibrillation in patients with heart failure who are at risk of developing malignant ventricular tachyarhythmias.

Current evidence based guidelines3-5 recommend an implantable cardioverter defibrillator for the primary prevention of sudden cardiac death in selected patients with impaired left ventricular function, and cardiac resynchronisation therapy for improvement of symptoms and survival in selected patients with abnormal ventricular conduction. Many patients may be eligible for both treatments but it does not necessarily follow that such patients would obtain additional benefit from the combined treatment over one treatment alone. There are, however, theoretical justifications for the combined treatment. Sudden cardiac deaths still account for about one third of all deaths in patients treated with resynchronisation therapy,6-9 and adding implantable cardioverter defibrillator backup to resynchronisation therapy might further reduce mortality. Conversely, resynchronisation therapy alone reduces the risk of worsening deaths owing to heart failure as well as sudden cardiac deaths10 suggesting that the addition of such therapy to implantable cardioverter defibrillation might further reduce the risk of death. It is therefore important to ascertain the efficacy of the combined treatment, which is more expensive than either treatment alone.

Several pairwise meta-analyses have compared the independent efficacies of resynchronisation therapy6-10 and of implantable cardioverter defibrillator therapy11-14 with medical therapy, whereas the effect of cardiac resynchronisation with an implantable defibrillator device was examined in exploratory meta-regression analyses.7,9 The overall evidence from randomised controlled trials for device therapy consists of pairwise comparisons between combined resynchronisation and implantable cardioverter defibrillator therapy, resynchronisation therapy, implantable cardioverter defibrillator therapy, and...
METHODS

The search strategy was based on a highly sensitive one for identifying randomised controlled trials.21 We used MeSH terms and keywords to search for intervention, with combined cardiac resynchronization and implantable cardioverter defibrillator therapy/cardiac resynchronization therapy/implantable cardioverter defibrillator devices (“Cardiac Resynchronization Therapy,” “Cardiac Pacing, Artificial,” “Heart Pacing,” “resynchroni?ation,” “(biventricular or dual?chamber or multi?site) adj (pacing or stimulat$),” “Defibrillators, Implantable,” “Electric Counter?shock,” “Automatic Cardioversion,” “Cardioversion; Defibrillation,” “(implant$ adj (defibrillator$ or cardioverter$)$)”) and for target condition of impaired left ventricular function [“Heart Failure, Congestive,” “Ventricular Dysfunction,” “Cardiac Output, Low,” “(cardiac or heart or ventricular or biventricular or systolic or diastolic) adj (failure or dysfunction or impair$)”).

We searched Medline (1966 to June 2006), Embase (1988 to 2006, week 26), and the Cochrane central register of controlled trials (2nd quarter 2006). In addition, we searched for studies in reports from the US Food and Drugs Administration and reference lists of identified studies and published meta-analyses. We applied no restrictions on types of cardiac resynchronization therapy or implantable cardioverter defibrillator devices or on language.

Selection criteria

Studies were eligible if they were randomised parallel controlled trials or randomised crossover trials; included patients with impaired left ventricular systolic function (ejection fraction <35%); compared cardiac resynchronization or combined resynchronization and implantable cardioverter defibrillator therapy with medical therapy or with medical therapy plus implantable cardioverter defibrillator therapy (studies including patients with pacing leads inserted through medical therapy. Most studies compared devices with medical therapy, with few directly comparing combined resynchronisation and implantable defibrillator therapy with either therapy alone. This network of evidence can be examined within a mixed treatment comparison framework without breaking randomisation, using either traditional or Bayesian models, to inform medical decision making by facilitating simultaneous comparison of all treatment options.17 18

The presence of three treatment groups (combined resynchronisation and implantable defibrillator therapy, resynchronisation alone, and control) in the medical therapy, pacing, and defibrillator in chronic heart failure trial97 creates an additional level of complexity in evidence synthesis because multiple pairwise comparisons (compared with a common control) are correlated.15 19 Previous studies either excluded data (because of lack of a separate implantable cardioverter defibrillator treatment arm) from the combined resynchronisation and implantable defibrillator therapy group, or divided data from the control group to incorporate comparisons with combined resynchronisation and implantable defibrillator therapy and resynchronisation therapy in the same analysis. These approaches are not ideally suited to investigate the potential incremental benefits of combined therapy, particularly as this is the largest trial examining the efficacy of this type of therapy. It is important to include data from all three treatment groups of the medical therapy, pacing, and defibrillator in chronic heart failure trial to provide evidence of a higher methodological quality, and appropriate modelling of random effects in multigroup trials can be implemented using a fully Bayesian model.19 20

We systematically reviewed overall evidence from randomised controlled trials for combined cardiac resynchronization and implantable cardioverter defibrillator therapy on survival compared with medical therapy, an implantable cardioverter defibrillator, and cardiac resynchronisation therapy in patients with left ventricular impairment, using Bayesian network meta-analysis.
the transthoracic route were eligible, whereas we excluded trials comparing different pacing strategies in themselves, or were primary prevention trials comparing implantable cardioverter defibrillator with usual medical therapy or with oral antiarrhythmics (we excluded studies with a mandatory requirement for inducible arrhythmias and secondary prevention trials); and reported all cause mortality. We excluded trials recruiting patients who had had a myocardial infarction or undergone coronary revascularisation within the past month. Consistent with previous systematic reviews, we excluded trials of less than two weeks’ duration.

Methodological assessment

We assessed concealment of treatment allocation, blinding (patient and investigator), and analysis using intention to treat for internal validity and graded these as yes, no, or unclear. We also noted studies where randomisation occurred after implantation of the device.

Data abstraction and outcomes

Both authors independently recorded trial design, recruitment criteria, baseline characteristics, efficacy outcomes, and quality assessment; any discrepancies were resolved by consensus. Primary outcomes were all cause mortality for combined resynchronisation and implantable cardioverter defibrillator therapy compared with medical therapy, with resynchronisation alone, and with implantable cardioverter defibrillator alone. For crossover trials we considered results from the first period only. We abstracted the total number of events and patients randomised to each treatment arm (intention to treat principle). Subgroup analyses were planned for patients with New York Heart Association class III or IV symptoms of heart failure at baseline.

Statistical analysis

For direct pairwise comparison meta-analysis we decided a priori to analyse trials using medical therapy as the control group separately from those using implantable cardioverter defibrillator therapy as the control because of prima facie evidence of clinical heterogeneity in the control groups (irrespective of estimated heterogeneity). To facilitate comparison with Bayesian network meta-analysis we expressed mortality outcomes from individual studies as odds ratios. We used random effects models to estimate the mean and 95% confidence interval for the overall treatment effect (if there were at least three studies). If all simulations.

We analysed the network of randomised controlled trials within a mixed treatment comparison framework using full Bayesian random effects models as described by Higgins and Whitehead and implemented by Caldwell et al. Specifically, we used binomial likelihood to model the probability of death within each treatment arm. In each trial we defined a study specific baseline effect using log odds of the control group mortality, and we modelled the effect of intervention (log odds ratio) for each treatment arm. For each treatment (device) we estimated the treatment specific effect (basic variable) from the mean intervention effect for each treatment compared with the medical therapy control. We derived comparisons between treatments (functional variables) from differences between basic variables. Mean and Bayesian 95% credible intervals for treatment effects were estimated and expressed as odds ratios for presentation.

The absolute benefit for each treatment (odds of death) was estimated by adding the treatment specific effect compared with medical therapy (basic variables) to the average effect of medical therapy (baseline odds). We used standard formulas to convert the absolute odds of death to overall mortality (for the purpose of reporting). In each simulation we ranked best the treatment option with the highest absolute odds. The probability that each treatment was best was derived from the percentage of best ranking across all simulations.

To ensure that overall effects were dominated by data from the trials and not influenced by choice of initial distribution we used low information (non-informative) prior distributions—that is, we used vague normal (mean 0, variance 10 000) and uniform (0-2) prior distributions for means and standard deviations, respectively. We examined the impact of different choices of prior distribution in sensitivity analyses.

The Bayesian models were implemented using WinBUGS version 1.4.1 (Imperial College and Medical Research Council, 2004). After convergence was achieved from an initial 5000 (burn-in)
Table 1: Study characteristics of included randomised controlled trials of combined cardiac resynchronisation therapy and implantable cardioverter defibrillator therapy in left ventricular impairment and symptomatic heart failure

<table>
<thead>
<tr>
<th>Study</th>
<th>No randomised (ratio)</th>
<th>Interventions</th>
<th>Follow-up* (months)</th>
<th>Mean (SD) Men (%)</th>
<th>IHD (%) NYHA class III (%)</th>
<th>LVEF (SD) %</th>
<th>ACEI or ARB (%)</th>
<th>β blockers (%)</th>
<th>Concealed allocation</th>
<th>Analysis by intention to treat</th>
<th>Blinding†</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARE-HF-ext†‡</td>
<td>813 (1:1)</td>
<td>MT + CRT</td>
<td>4.7</td>
<td>66 (11)</td>
<td>84</td>
<td>69</td>
<td>59</td>
<td>22 (7)</td>
<td>Yes</td>
<td>Yes</td>
<td>No, no, yes</td>
</tr>
<tr>
<td>COMPANION‡§</td>
<td>110 (1:2)</td>
<td>MT + CRT + ICD</td>
<td>6</td>
<td>67 (10)</td>
<td>77</td>
<td>70</td>
<td>89</td>
<td>24 (6)</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes, yes</td>
</tr>
<tr>
<td>MIRACLE-II†</td>
<td>453 (1:1)</td>
<td>CRT-off CRT</td>
<td>3</td>
<td>63 (12)</td>
<td>38</td>
<td>57</td>
<td>0</td>
<td>25 (7)</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes, yes</td>
</tr>
<tr>
<td>MIRACLE-ICD†</td>
<td>490 (1:1)</td>
<td>ICD + CRT</td>
<td>4.7</td>
<td>66 (11)</td>
<td>84</td>
<td>69</td>
<td>59</td>
<td>22 (7)</td>
<td>Unclear</td>
<td>Yes</td>
<td>No, yes</td>
</tr>
<tr>
<td>DEFINITE-II†‡</td>
<td>104 (1:1)</td>
<td>MT + ICD</td>
<td>4.7</td>
<td>66 (11)</td>
<td>84</td>
<td>69</td>
<td>59</td>
<td>22 (7)</td>
<td>Yes</td>
<td>Yes</td>
<td>No, no, yes</td>
</tr>
<tr>
<td>MADIT-II†</td>
<td>67 023 (2:3)</td>
<td>MT + CRT</td>
<td>20</td>
<td>64 (8)</td>
<td>85</td>
<td>100</td>
<td>24</td>
<td>23 (5)</td>
<td>Yes</td>
<td>Yes</td>
<td>No, no, yes</td>
</tr>
<tr>
<td>SCD-HeFT‡</td>
<td>2521 (1:1:1)</td>
<td>MT + placebo + CRT + MT + ICD</td>
<td>4.7</td>
<td>66 (11)</td>
<td>80</td>
<td>35</td>
<td>100</td>
<td>24 (7)</td>
<td>Yes</td>
<td>Yes</td>
<td>No, no, yes</td>
</tr>
</tbody>
</table>

AMIOVIRT=amiodarone versus implantable cardioverter-defibrillator randomised trial; CARE-HF-ext=cardiac resynchronisation-heart failure extension phase; COMPANION=comparison of medical therapy, pacing, and defibrillation in chronic heart failure; CONTAK-CDF=guidant CONTAK CD CRT-D system trial; DEFINITE=defibrillators non-ischemic cardiomyopathy treatment evaluation trial; MADIT-II=multicenter automatic defibrillator implantation trial II; MIRACLE=multicenter InSync randomised clinical evaluation ICD I; MIRACLE-II=multicenter InSync randomised clinical evaluation ICD II; MUSTIC-SR=multisite stimulation in cardiomyopathies sinus rhythm; SCD-HeFT=studies cardiac death in heart failure trial; ICH=Ischemic heart disease. NYHA=New York Heart Association. LVEF=Left ventricular ejection fraction; ACEI=Angiotensin converting enzyme inhibitors; ARB=Angiotensin receptor antagonist; CRT-off=active cardiac resynchronisation therapy; CRT-on=inactive cardiac resynchronisation therapy; ICD=CRT-on-active implantable cardioverter defibrillator therapy and active cardiac resynchronisation therapy; ICD=CRT-off-active implantable cardioverter defibrillator therapy but inactive cardiac resynchronisation therapy; MT=Medical therapy.

*Duration of follow-up for mortality outcome.
†Blinding for patient, investigator, and endpoint assessment.
‡Mean follow-up for main study was 29.4 months.
§Follow-up was 3 months for 222 patients and 6 months for 279 patients implanted with investigational device.

RESULTS

Figure 1 summarises the number of potential citations retrieved and the selection process. Both authors agreed on the selection and methodological assessment. Twelve independent studies met the selection criteria, including one multigroup trial that compared combined cardiac resynchronisation and implantable cardioverter defibrillator therapy, resynchronisation, and medical therapy. Several studies that used univentricular pacing as the comparator for cardiac resynchronisation or as the main experimental group did not meet the selection criteria. As per protocol two trials that exclusively recruited patients who had had a recent myocardial infarction or underwent recent coronary revascularisation were excluded. One unpublished study (not identified in the database search) was not included because of potential attrition bias (more than 50% of randomised patients in the control group were not available for follow-up). The potential impact of this study was examined in a post hoc sensitivity analysis.
therapies in 8307 patients with left ventricular dysfunction

Cardiac resynchronisation therapy

Implantable cardioverter defibrillator therapy

Device

Odds ratio (95% credible interval of all cause mortality)

0.57 (0.40 to 0.80)

0.66 (0.50 to 0.89)

0.69 (0.55 to 0.87)

Fig 3 | Results of Bayesian network meta-analysis of 12 randomised controlled studies of device therapies in 8307 patients with left ventricular dysfunction

Figure 2 shows the relation between the network of randomised controlled trials. In total, 1636 events occurred in 8307 patients randomised to cardiac resynchronisation therapy (245/1283), implantable cardioverter defibrillator therapy (367/2429), combined resynchronisation and implantable cardioverter defibrillator therapy (132/1112), amiodarone (247/897), and control (645/2586). Seven studies reported 1013 events in 4319 patients for subgroup analysis of New York Heart Association class III or IV heart failure, including five studies that recruited only patients with class III or IV heart failure and two studies that reported subgroup outcomes.

Table 1 summarises the design, baseline characteristics, and quality assessment of the included studies. All used the transvenous approach to implantation, whereas one included 11% of patients with leads implanted transthoracically. Most studies were analysed using the intention to treat principle, but concealment of treatment allocation was unclear in most trials. In several studies, blinding of investigators or patients, or both, was possible as only patients with successful device implantations were considered for randomisation.

One study was presented in two publications reporting independent results from patients with New York Heart Association class II or IV heart failure at baseline. The number of deaths reported was identical to a FDA report but different from an earlier version cited in previous reviews. In this review published outcomes were abstracted as per two independent studies. Mortality data were used from the extension phase of the cardiac resynchronisation heart failure trial.

Four studies accounted for 73% of patients and 88% of observed events. Baseline mortality was comparable in most studies except for five. In these five studies duration of follow-up was shorter and patients only with successfully implanted devices were randomised. No major asymmetry was seen in the funnel plots to suggest publication bias.

Quantitative analysis

Figures 3 and 4 summarise the all cause mortality data for Bayesian network and pairwise comparisons of device therapies compared with medical therapy. Combined resynchronisation and implantable defibrillator therapy significantly reduced mortality compared with medical therapy in one direct comparison study (odds ratio 0.64, 95% confidence interval 0.46 to 0.90), and in Bayesian network meta-analysis of 12 studies (0.57, 95% credible interval 0.40 to 0.80). Both resynchronisation (0.66, 95% credible interval 0.50 to 0.80) and implantable defibrillator therapy (0.69, 0.55 to 0.87) reduced mortality compared with medical therapy. Amiodarone did not have any apparent effect on mortality compared with medical therapy.

The overall mortality for combined resynchronisation and implantable defibrillator therapy was 9.1% compared with 14.0% for medical therapy, corresponding to a 35% relative risk reduction. The probability determined from the Bayesian analysis that combined resynchronisation and implantable defibrillator therapy was the best option (compared with other devices and optimal medical therapy) was 0.75 in all patients with impaired left ventricular function and 0.62 in the subgroup of patients with New York Heart Association class III or IV heart failure. The corresponding probabilities for resynchronisation therapy were 0.14 and 0.27 and for implantable defibrillator therapy were 0.10 and 0.08.

Figure 5 shows the results of head to head comparisons of combined resynchronisation and implantable defibrillator therapy with either therapy alone. When combined therapy was compared with implantable defibrillator therapy no evidence was found from pairwise meta-analysis (three studies, odds ratio 0.81, 95% confidence interval 0.48 to 1.37) and Bayesian network meta-analysis (12 studies, odds ratio 0.82, 95% credible interval 0.57 to 1.18; seven studies, New York Heart Association class III or IV subgroup, odds ratio 0.74, credible interval 0.39 to 1.57) to suggest that combined therapy further improved survival (fig 4). Similarly, when combined therapy was compared with resynchronisation therapy no evidence was found from one direct comparison study (odds ratio 0.79, 95% confidence interval 0.60 to 1.06) and Bayesian network meta-analysis (odds ratio 0.85, 95% credible interval 0.60 to 1.22; New York Heart Association class III or IV subgroup, odds ratio 0.89, 95% credible interval 0.45 to 1.76) for an incremental value of combined therapy.

Estimates of treatment effects were robust for study selection criteria (including a priori and post hoc sensitivity analyses) and for statistical assumption of prior distributions.

DISCUSSION

The present meta-analysis, based on a Bayesian network of 12 studies including 1636 events in 8307 patients, suggests that combined cardiac resynchronisation therapy and implantable cardioverter defibrillator therapy reduces all cause mortality by one third when compared with medical therapy. Assuming an annual mortality of 15% in patients with heart failure receiving optimal medical therapy, the number needed to treat to prevent one death is 20. Although it is probable that combined therapy is the best option for reducing

...
mortality (probability of 0.75 in present analysis) it has not been shown to be associated with a mortality different from that with either resynchronisation therapy or implantable defibrillator therapy. These findings also apply to the subgroup of patients with New York Heart Association class III or IV heart failure, a sicker group of patients who might be expected to gain greater benefit than that of patients with class II symptoms. Thus there is no direct evidence from clinical trials or systematic evidence from the present meta-analysis to support combined resynchronisation and implantable defibrillator therapy improving survival more than resynchronisation therapy or implantable defibrillator therapy alone in patients with left ventricular impairment.

**Limitations**

Limitations of the primary trials and potential confounders may affect the validity of the findings. Five studies, two of resynchronisation therapy and three of combined therapy compared with implantable cardioverter defibrillator therapy only randomised patients after successful implantation of the device. Although results of these studies were analysed using intention to treat (from randomisation), complications related to implantations were excluded. Event rates in these studies were lower than in other studies included in the review, but treatment effects were comparable. In addition, similar to previous meta-analyses, the present study was subject to potential publication bias, although funnel plots did not suggest the presence of such bias and an extensive search strategy was used to identify relevant trials.

Criteria for patient selection were different but overlapping in the primary trials examining implantable cardioverter defibrillator and cardiac resynchronisation therapy. Although both sets of trials recruited patients with impaired left ventricular function, prolonged QRS interval is a prerequisite only for patients undergoing resynchronisation. Thus interpretation of the results of the present meta-analysis is subject to this potential confounder. This situation is, however, no different from everyday clinical scenarios where the doctor needs to use clinical judgment informed by the same evidence base. The point of the present meta-analysis is to use all the available evidence to tackle the clinically relevant question of whether patients independently eligible for resynchronisation and for implantable defibrillator therapy would benefit from a combined device. The current evidence base is not ideal but it is the best available pending a definitive randomised controlled trial on this subject.

We excluded studies that compared resynchronisation therapy with univentricular pacing. This reduces the total number of cases available for analysis and potentially the overall statistical power. However, this strategy avoided the ambiguity in previous reviews, where patients treated with univentricular pacing were analysed in the same group (and hence assumed to have the same prognosis) as those receiving optimal medical therapy alone. It is possible to include patients from studies using right (or left) univentricular pacing as a sixth (or seventh) treatment group in the network analysis. This approach was not adopted in the present protocol because the a priori clinical question of interest was the value of resynchronisation therapy, and not univentricular pacing, in heart failure.

Trials included in this review were carried out over a period of evolving medical management of heart

---

<table>
<thead>
<tr>
<th>Study</th>
<th>Device</th>
<th>Medical therapy</th>
<th>All cause mortality device</th>
<th>Weight</th>
<th>Odds ratio (95% interval*)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac resynchronisation therapy v medical therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pairwise</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CARE-HF-ext</td>
<td>101/409</td>
<td>154/404</td>
<td>44.6</td>
<td>0.53 (0.39 to 0.72)</td>
<td></td>
</tr>
<tr>
<td>COMPANION</td>
<td>131/617</td>
<td>77/308</td>
<td>41.9</td>
<td>0.81 (0.59 to 1.12)</td>
<td></td>
</tr>
<tr>
<td>MIRACLE</td>
<td>12/228</td>
<td>16/225</td>
<td>12.7</td>
<td>0.73 (0.34 to 1.57)</td>
<td></td>
</tr>
<tr>
<td>MUSTIC-SR</td>
<td>1/29</td>
<td>0/29</td>
<td>0.8</td>
<td>3.11 (0.12 to 79.54)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>245/1283</td>
<td>247/966</td>
<td>100.0</td>
<td>0.67 (0.50 to 0.90)</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: χ²=4.42, P=0.22, I²=32%

Test for overall effect: z=3.90, P<0.001

**Bayesian network**

All studies (n=12) | 0.66 (0.50 to 0.89)

---

<table>
<thead>
<tr>
<th>Study</th>
<th>Device</th>
<th>Medical therapy</th>
<th>All cause mortality device</th>
<th>Weight</th>
<th>Odds ratio (95% interval*)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Implantable cardioverter defibrillator therapy v medical therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pairwise</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>182/829</td>
<td>244/847</td>
<td>56.1</td>
<td>0.70 (0.56 to 0.87)</td>
<td></td>
</tr>
<tr>
<td>MADIT-II</td>
<td>105/742</td>
<td>97/490</td>
<td>30.0</td>
<td>0.67 (0.49 to 0.90)</td>
<td></td>
</tr>
<tr>
<td>DEFINITE</td>
<td>26/229</td>
<td>40/229</td>
<td>10.1</td>
<td>0.66 (0.39 to 1.11)</td>
<td></td>
</tr>
<tr>
<td>CAT</td>
<td>13/50</td>
<td>17/54</td>
<td>3.8</td>
<td>0.76 (0.33 to 1.80)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>328/1850</td>
<td>398/1620</td>
<td>100.0</td>
<td>0.69 (0.58 to 0.81)</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: χ²=0.13, P=0.99, I²=0%

Test for overall effect: z=4.46, P<0.001

**Bayesian network**

All studies (n=12) | 0.69 (0.55 to 0.87)

---

<table>
<thead>
<tr>
<th>Study</th>
<th>Device</th>
<th>Medical therapy</th>
<th>All cause mortality device</th>
<th>Weight</th>
<th>Odds ratio (95% interval*)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combined cardiac resynchronisation and implantable cardioverter defibrillator therapy v medical therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pairwise</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMPANION</td>
<td>105/595</td>
<td>77/308</td>
<td>0.64</td>
<td>0.46 (0.46 to 0.90)</td>
<td></td>
</tr>
</tbody>
</table>

Test for overall effect: z=2.60, P=0.009

**Bayesian network**

All studies (n=12) | 0.57 (0.40 to 0.80)

---

**Fig 4** | Results of pairwise meta-analysis and Bayesian network analysis of device therapies compared with medical therapy for patients with left ventricular dysfunction. *95% confidence interval for pairwise comparison, 95% credible interval for Bayesian network comparison. See table 1 for full titles of studies.
failure; β blocker usage at baseline was less than 50% in several trials and the underlying risk of death in these studies might have been different had their usage been higher. In addition, the follow-up period was no more than six months for most trials of resynchronisation therapy (except the studies of cardiac resynchronisation heart failure and comparison of medical therapy, pacing, and defibrillator in chronic heart failure), potentially before the full benefits of resynchronisation therapy were realised. Several trials were underpowered to detect mortality benefits because recruitment was discontinued (owing to futility) before achieving the intended number of participants, and some studies were primarily designed to identify functional changes. Furthermore, one trial required a history of myocardial infarction for inclusion, and patients with a more recent history may respond less favorably to implantable cardioverter defibrillators. However, multiple sensitivity analyses suggested that these potential confounders did not affect the findings of this study.

The main efficacy outcome of interest in this study was mortality, but many primary trials did not report outcome in sufficient detail to permit abstraction of data on subgroups. Previous reviews provided good evidence that resynchronisation therapy improved functional outcomes and quality of life, but these outcomes were not reported in any primary trials of implantable cardioverter defibrillators included in the present review, and Bayesian network meta-analyses were not planned for these outcomes. Finally, data were limited for subgroup analysis of patients with New York Heart Association class III or IV heart failure (fewer patients in implantable cardioverter defibrillator trials had class III symptoms) leading to wide credibility intervals.

Relation to previous studies
In previous meta-analyses that compared resynchronisation therapy with no such therapy, trials with different comparison groups (resynchronisation versus medical therapy, resynchronisation versus univentricular pacing, and combined resynchronisation and implantable defibrillator versus implantable defibrillator) were combined making it impossible to determine the efficacy of combined therapy itself. The efficacy of combined therapy was inferred from exploratory metaregression analyses implemented using likelihood estimation or full Bayesian techniques, which found no significant variability between trials comparing resynchronisation therapy with medical therapy (or univentricular pacing) and trials comparing combined therapy with implantable defibrillator therapy. Only two trials compared combined therapy with implantable defibrillator therapy, and data from 395 patients from the comparison of medical therapy, pacing, and defibrillator in chronic heart failure trial treated with combined therapy were not incorporated. Thus results of these regression analyses may not be robust and the efficacy of combined resynchronisation and implantable defibrillator therapy itself cannot be quantified in these studies.

One previous meta-analysis reported that adding implantable cardioverter defibrillator to cardiac resynchronisation therapy resulted in an apparent reduction in mortality. This claim was, however, based on the pooled estimates of data from the comparison of medical therapy, pacing, and defibrillator in chronic heart failure trial and a non-randomised controlled trial. Although it is possible to include non-randomised studies within a general evidence synthesis framework it is not generally advised in systematic reviews of device therapy because of the possibility of introducing significant bias, especially when studies are few.

The present Bayesian network meta-analysis permits simultaneous comparison of all treatment options, and conclusions on the efficacies of resynchronisation therapy and of implantable defibrillator therapy are similar to the results of previous meta-analyses. No evidence was found from the present network analysis, however, that combined cardiac resynchronisation and implantable defibrillator therapy is better than either resynchronisation or implantable defibrillator alone.

The full Bayesian network approach provided evidence of a higher methodological quality by taking into account the multivariate relation between intervention effects of multigroup trials. All available evidence, including data from all three treatment groups of the comparison of medical therapy, pacing, and defibrillator in chronic heart failure trial, was incorporated without splitting or discarding groups, in contrast to previous exploratory metaregression analyses where this was not possible. Thus conclusions of the present study are based on all available current evidence from randomised controlled trials, and multiple sensitivity analyses suggest that these findings are robust for statistical assumptions and trial inclusion criteria.

Implications
Current guidelines from the American College of Cardiology, American Heart Association, and European Society of Cardiology for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death give a IIa (weight

<table>
<thead>
<tr>
<th>Therapy</th>
<th>All studies</th>
<th>NYHA class III or IV heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall mortality (%)</td>
<td>Probability of best treatment</td>
</tr>
<tr>
<td>Medical</td>
<td>14.0</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac resynchronisation</td>
<td>10.3</td>
<td>0.14</td>
</tr>
<tr>
<td>Implantable cardioverter defibrillator</td>
<td>10.6</td>
<td>0.10</td>
</tr>
<tr>
<td>Combined resynchronisation and implantable defibrillator</td>
<td>9.1</td>
<td>0.75</td>
</tr>
</tbody>
</table>

NYHA = New York Heart Association.
of evidence in favour of efficacy), level of evidence B (data derived from a single randomised trial or non-randomised studies) recommendation for combined resynchronisation and implantable defibrillator therapy in patients with New York Heart Association class III or IV heart failure and a broad QRS complex. A case exists for using combined therapy in patients who simultaneously satisfy the criteria for both therapies, and the present Bayesian analysis suggests that it is probable that combined therapy is the best option. However, this practice is based on extrapolated evidence from trials that showed efficacy of resynchronisation therapy or implantable defibrillator therapy compared with medical therapy. No direct evidence was found from primary trials or from the present Bayesian network meta-analysis to suggest that combined therapy is better than either therapies alone in patients with left ventricular impairment. As clinical practice guidelines are becoming prescriptive rather than offering guidance, many clinicians may feel compelled (despite this lack of direct evidence of superior efficacy) to implant a combined resynchronisation and cardioverter defibrillator device if patients fulfill criteria for both therapies.

It could be argued that cardiac resynchronisation should be added to an implantable cardioverter defibrillator in clinical practice to improve symptoms rather than survival itself, but resynchronisation therapy alone improves symptoms (as well as survival). The potential advantage of combined therapy over resynchronisation therapy alone is the theoretical incremental survival benefit (not proved in the present meta-analysis). The routine use of combined therapy in all patients eligible for both treatments, on the basis that it may prolong survival over cardiac resynchronisation therapy or implantable cardioverter defibrillator alone, would not seem to be appropriate. Trial evidence is usually required before a new treatment is used routinely.

The lack of definitive clinical evidence means that public funding bodies are unable to assess properly the comparative cost effectiveness of combined resynchronisation and implantable defibrillator therapy even if it does offer some advantage over either therapy alone. A simple pragmatic approach would be to use resynchronisation therapy, which may be more cost effective than combined therapy, to reduce symptoms and extend life in patients with New York Heart Association class III or IV heart failure, with the addition of an implantable cardioverter defibrillator left to clinical judgment on an individual basis when additional indications exist. When such an addition is contemplated the hypothesised incremental benefits in survival would need to be balanced by the possible increase in morbidity due to, for example, inappropriate shocks.

Ongoing clinical trials are examining the potential value of combined therapy for patients suitable for implantable cardioverter defibrillators who are not currently eligible for cardiac resynchronisation. These studies will provide important data on the value of adding resynchronisation therapy to treat patients who currently only satisfy criteria for implantable cardioverter defibrillators, but do not inform whether combined therapy offers any survival benefits over resynchronisation therapy in patients who have heart failure with a prolonged QRS interval. In view of the additional cost of combined therapy and potential morbidity associated with inappropriate defibrillation shocks, the burden of proof (requiring a major new clinical trial of thousands of patients) should ideally be on combined therapy to show superiority over resynchronisation therapy, and further studies are needed to identify the population most likely to benefit.

**Contributors:** SKHL carried out the literature search, data abstraction, and statistical analysis. SKHL and AO formulated the meta-analysis protocol and wrote and revised the report. AO independently abstracted the data. SKHL and AO are guarantors.

**Funding:** None.

**Competing interests:** None declared.

**Ethical approval:** Not required.
provides evidence of a higher methodological quality than previous meta-analyses. 

Evidence from a network of 12 studies (8307 patients) is insufficient to suggest that mortality of patients with heart failure by one third compared with medical therapy combined therapy remain unclear.

WHAT IS ALREADY KNOWN ON THIS TOPIC

WHAT THIS STUDY ADDS

Combined cardiac resynchronisation and implantable defibrillator therapy reduced all cause mortality of patients with heart failure by one third compared with medical therapy Evidence from a network of 12 studies (8307 patients) is insufficient to suggest that combined therapy is superior to resynchronisation therapy.

The Bayesian approach models the (multivariate) intervention effects of multimargroup trials and provides evidence of a higher methodological quality than previous meta-analyses.

Accepted: 6 August 2007
Management of sepsis

Iain Mackenzie,1 Andrew Lever2

This is the second of two reviews—the first discussed the definition, epidemiology, and diagnosis of sepsis, whereas this one focuses on management and outcome. Management of sepsis can conveniently be divided into general supportive measures and specific treatment.

What are the general supportive measures?

Circulatory compromise arises from the combination of vasodilatation, capillary leak, and reduced myocardial contractility, and needs early correction. Whether crystalloids or colloids are better for volume resuscitation remains unresolved. Few people now use human albumin after a controversial meta-analysis concluded that albumin was associated with a 6% excess mortality.1 A subsequent randomised controlled trial found no difference in any of the outcome measures examined, including mortality.2

Another question is how to gauge the adequacy of fluid resuscitation. The pulmonary artery catheter has not been shown to be associated with either harm or benefit,3,4 and its use is declining. Clinical end points (box 1) remain useful, although some centres are also using oesophageal Doppler or pulse contour analysis. These methods provide information on the effect of fluid loading on cardiac output and stroke volume. In ventilated patients, variation in stroke volume can be used as an index of preload.

Catecholamines are needed when fluids are insufficient to restore adequate tissue perfusion. The quality of evidence on which to base the choice of agents is poor. Currently, either noradrenaline (norepinephrine) or dopamine is recommended as first line agent. Noradrenaline increases the blood pressure more rapidly and reliably than dopamine and improves renal function, but it produces only a modest rise in cardiac output. Its effects on the liver and gastrointestinal mucosa are unpredictable. Dopamine, on the other hand, despite increasing splanchic blood flow at low doses, does not increase oxygen consumption in the gut or improve hepatic function. Moreover, unease is growing about its negative effects. These include reduction of gut motility, hypoprolactinaemia mediated immunosuppression, reduced anabolism, and impaired thyroid function. In a recent observational study, dopamine was associated with an increased risk of death in hospital.5 At high doses, dopamine may precipitate supraventricular arrhythmias. Adrenaline (epinephrine) is now rarely used as a single agent, if at all. It causes a fall in splanchic perfusion and, in some cases, a lactic acidosis. In the future, an increased understanding of the effects of adrenoreceptor up regulation and down regulation, adrenoreceptor gene polymorphism, and free radical alterations to adrenoreceptor activation may lead to better use of catecholamines.

The role of non-catecholamine drugs, such as vasopressin, levosimendan, methylene blue, and the phosphodiesterase inhibitors, to support the circulation in sepsis remains to be clarified. Timeliness of the intervention and attention to subtle signs of persisting tissue hypoperfusion are important. Survival is increased when volume loading to standard end points (box 2) is supplemented, where necessary, by blood, catecholamines, and even mechanical ventilation.6

Many patients with severe sepsis, even without pulmonary sepsis, need respiratory support because of the combined effects of increased ventilatory demand, hypoxaemia, and respiratory muscle dysfunction.7 Some patients develop the acute respiratory distress syndrome. The duration of mechanical ventilation can be reduced by daily interruptions of sedation,8 and a 9% increase in survival has been achieved in patients with acute lung injury or acute respiratory distress syndrome by using low tidal volumes (6 ml/kg ideal body weight).9

Renal failure occurs in 20-50% of patients, depending on severity. Some evidence shows that high volume haemofiltration temporarily reduces the need for vasopressors,10 but whether this translates into any long term advantages, in terms of either renal function or survival, has not been proved.

Nutrition is another area in which high quality data are scarce, particularly among non-surgical patients. In general, early enteral nutrition is recommended,11 but this was associated with increased morbidity in the only study in non-surgical patients.12 Furthermore, supplements designed to boost the immune system,
such as L-arginine and omega-3 fatty acids, actually increase mortality in patients with severe sepsis. Interpretation of these studies is confounded by the effect of hyperglycaemia. The combination of glycogenolysis and insulin resistance means that hyperglycaemia is common in patients with sepsis and is associated with a poorer outcome. Tight glycaemic control has been shown to reduce morbidity and mortality in a prospective randomised controlled trial in surgical patients. A similar study in non-surgical patients resulted in a reduction only in morbidity. We clearly need a more definitive understanding of the impact of hyperglycaemia and insulin treatment in patients with severe sepsis, which will hopefully be provided by an ongoing randomised controlled trial.

**What specific treatments are available?**

**Antimicrobials**

First and foremost among specific treatments are prompt appropriate empirical antimicrobials. Treatment within four hours of admission reduces mortality and length of stay. Delay in hypotensive patients increases mortality by 7.6% an hour. Since the late 1980s, Gram positive organisms have replaced Gram negative ones as the most common bacteria causing sepsis. Retrospectively, around 20% of infections originate from each of respiratory, intra-abdominal, and urinary tract sources. However, at presentation, the source of infection is often unknown. Antibiotic treatment must be guided by the patient’s susceptibility group (table) and local knowledge of bacterial resistance. Broad spectrum β lactam antibiotics would be the usual first line agent. If methicillin resistant *Staphylococcus aureus* is a risk, empirical vancomycin should be added. In the presence of risk factors for fungal infection, an antifungal agent may be prescribed initially or within 48 hours if no improvement occurs; decisions are guided by clinical judgment and the severity of the condition, ideally in consultation with infectious disease or microbiology colleagues. The importance of wide cover is illustrated by the much poorer prognosis in patients in whom the first line drugs are ineffective. If strong clues to the source of infection exist, targeted narrower spectrum treatment is probably justified.

**Corticosteroids**

Deficiency of adrenal steroid production in severe sepsis was originally described as acute haemorrhagic necrosis of the adrenal glands precipitating Addisonian crisis and death—the Waterhouse-Friderichsen syndrome. High dose corticosteroid treatment in severe sepsis was initially investigated as an anti-inflammatory treatment and found to be of no benefit. Attention has now returned to the problem of adrenal insufficiency in severe sepsis. Complete adrenal failure is rare, but relative adrenal insufficiency is much more common, although the incidence depends on the definition used. In one study, for example, which defined adrenal insufficiency as a cortisol increment of ≤248 nmol/l (9 µg/dl) 30-60 minutes after 0.25 mg of tetracosactrin, 54% of the patients with septic shock met the criteria. Two recent meta-analyses suggest that low dose hydrocortisone for five to 11 days in unselected patients with severe sepsis or septic shock significantly reduces both the duration of shock and in-hospital mortality, without incurring additional complications. The positive effect of low dose steroid replacement treatment may be even greater if it is restricted to patients selected on the basis of proved adrenal insufficiency.

**Immunoglobulins and statins**

Other therapeutic approaches deserve further investigation. Of these, intravenous immunoglobulin and statins are nearest to clinical evaluation. Intravenous immunoglobulin is not without adverse effects, which vary from hypotensive reactions to aseptic meningitis. Most of the infused antibody will not be specific for the organism

---

**Box 2 | Resuscitation end points in the study by Rivers and colleagues**

- Central venous pressure of 8-12 mm Hg
- Mean arterial pressure ≥65 mm Hg
- Urine output ≥0.5 ml/kg/hr
- Central venous oxygen saturation ≥70%

---

**Patients’ susceptibilities and implications for treatment**

<table>
<thead>
<tr>
<th>Susceptibility</th>
<th>Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>In hospital or other institution</td>
<td>Resistant organisms, especially methicillin resistant <em>Staphylococcus aureus</em> (MRSA) and extended spectrum β lactamase producing Gram negative enteric organisms</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>Capsulated bacteria, especially <em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td>School, university, or military</td>
<td><em>Neisseria meningitidis</em></td>
</tr>
<tr>
<td>Intravascular catheter</td>
<td><em>Staphylococci</em></td>
</tr>
<tr>
<td>Intubation and ventilation</td>
<td>Gram negative enteric organisms, pseudomonads, MRSA, Candida</td>
</tr>
<tr>
<td>Pharmacologically immunosuppressed</td>
<td>Pneumocystis jirovecii, cytomegalovirus, Candida spp, Aspergillus spp, Nocardia spp</td>
</tr>
<tr>
<td>Foreign travel</td>
<td>Malaria, legionella</td>
</tr>
<tr>
<td>Potential exposure to rat urine</td>
<td>Leptospirosis</td>
</tr>
<tr>
<td>Very young or very old</td>
<td><em>Listeria monocytogenes</em></td>
</tr>
</tbody>
</table>
We searched Medline with the search phrase "((sepsis[title] OR septic*[title]) NOT (infant* OR neonat* OR child*))" and restricted the search to articles published in English in the previous three years. We individually reviewed the titles of the 2620 articles retrieved to identify major themes. Where necessary, we made additional searches based on key words or concepts that had been identified in the initial search. We also searched the Cochrane Library and Clinical Evidence. We then each used this information supplemented by knowledge and experience from our own field to prepare a brief review of the sections with which we were most familiar.

TIPS FOR NON-SPECIALISTS

- A favourable outcome is very dependent on early diagnosis and prompt treatment
- Appropriate samples for microbiological examination should precede antibiotic treatment, providing that this does not delay treatment
- Early, broad spectrum, empirical intravenous antimicrobial treatment and aggressive circulatory support are the mainstays of management

HMG1-B

Among the inflammatory response mediators being targeted, high mobility group box 1 (HMGB-1) protein is of particular interest. HMGB-1 is an essential nuclear DNA binding protein that acts as an “architectural” transcriptional cofactor. Secreted HMGB-1 is a potent inflammatory mediator that appears late in the septic cascade. It has several actions, including increased expression of a distinct gene set including those for inflammatory cytokines. Injection of recombinant HMGB-1 replicates the clinical features of sepsis in mice, including multiple organ failure and death. Conversely, antagonism of HMGB-1 in a rodent model of sepsis reduces organ damage and improves survival, even when treatment is started after the septic insult. Circulating concentrations of HMGB-1 are significantly increased in patients with severe infection and are lower in survivors than in non-survivors. Two very different interventions seem to usefully reduce release of HMGB-1. Firstly, ethyl pyruvate, a stable aliphatic ester of pyruvate, effects a dose dependent reduction in HMGB-1 concentration and reduces mortality in a murine model of indolent sepsis, even when given 24 hours after its onset. Ethyl pyruvate has already been investigated in phase 1 studies in man. Secondly, release is inhibited by agonists of the a7-nicotinic acetylcholine receptor expressed on the surface of human macrophages, whose natural ligand is acetylcholine released from nerve endings of the common coeliac branch of the vagus nerve within the spleen. This represents the effector arm of the “cholinergic anti-inflammatory pathway” and suggests intriguing therapeutic possibilities not only for pharmacological intervention using synthetic agonists but perhaps even for psychological and biofeedback manipulation of the inflammatory response.

Multiple system organ failure and outcome

Until the progression of the septic process has been brought under control with effective antimicrobials and, where necessary, surgery, patients are at risk of sequential organ failure (box 3). Mortality is strongly associated with the number of failed organs (figure). In the medium term and long term, the only organs that show obvious residual dysfunction are the kidneys. Of patients who develop acute renal failure, less than 20% need dialysis on discharge from hospital and more than 50% of these eventually become independent of dialysis. The literature describing the medium term and long term quality of life of survivors is sparse, includes few patients, and is generally of poor quality. In one study, almost 30% of survivors had failed to return to their usual activities six months after discharge from intensive care; even after 16 months, survivors were significantly less well than age matched controls.
CLINICAL REVIEW

ADDITIONAL EDUCATIONAL RESOURCES
European Society of Intensive Care Medicine (www.esicm.org)—Access to a range of guidelines, including the surviving sepsis campaign guidelines for the management of severe sepsis and septic shock
Society of Critical Care Medicine (www.sccm.org/SCCM/LeamCU/Quick-Links)—Access to a range of guidelines
American Thoracic Society (www.thoracic.org/sections/clinical-information/critical-care/evidence-based-critical-care)—Useful information and access to guidelines
Information resources for patients
Meningitis Research Foundation (www.meningitis.org)—A UK based charity aimed at supporting research into meningitis and septicaemia, as well as providing education and awareness to reduce death and disability and give support to people affected
Intensive Care Society (www.iscs.ac.uk/patrel/patrel.asp)—For information about many aspects of intensive care that might be of interest to the friends and family of a patient with septicaemia
Society of Critical Care Medicine (www.myicucare.org/sccm/MyICUCare)—For information that is relevant to patients in the United States

SUMMARY POINTS
A favourable outcome depends on early, aggressive, treatment
Antimicrobial treatment must take into account both patient susceptibilities and local resistance patterns; advice from infectious disease or microbiology colleagues is often helpful
Volume resuscitation and cardiovascular support should be titrated to simple clinical end points
Subtle signs of organ hypoperfusion should be sought in physically robust patients
The role of activated protein C and low dose steroids remains to be clarified

Conclusion
The severity of sepsis, its heterogeneous causation, the urgency of treatment, and the high mortality make it a problem area for randomised placebo controlled clinical trials, although the area is in striking need of these, particularly with newer biological therapeutic agents appearing. Meta-analysis and clinical experience are left to guide us through current therapeutic controversies. All of these, however, are of little use without a high index of clinical suspicion and the ability to act without delay when sepsis threatens.

Contributors: Each author researched and drafted the sections with which they were most familiar. IM combined the separate contributions. Both authors contributed to and approved the submitted and final versions of the manuscript. IM is the guarantor.
Competing interests: None declared.
Provenance and peer review: Commissioned; externally peer reviewed.

Systemic lupus erythematosus (SLE) is a multisystem relapsing and remitting autoimmune disease. The management of this condition in pregnancy provides the obstetrician, physician, and general practitioner with particular challenges and concerns related to the mother and her baby (see scenario box).

**How common is SLE?**

The condition is much more common in women than men (9:1), with peak onset during childbearing years. A recent extensive review of published epidemiology studies showed that the prevalence ranges from 0.07 per 1000 in white Americans to 1.59 per 1000 in British Afro-Caribbeans.\(^4\)

**How does pregnancy affect SLE?**

Several case studies suggest that pregnancy exacerbates SLE and increases the likelihood of a flare antenatally or in the puerperium.\(^2\)\(^5\) In one prospective case-control study 65% of patients with SLE who were pregnant had a flare compared with 42% of those who were not pregnant during the same time period.\(^3\) The type of flare usually follows previous patterns. The postpartum period is also a time of susceptibility to developing autoimmune disorders.\(^6\)\(^7\)

Renal involvement is one of the more serious complications of SLE, and, as with all types of renal disease, there is a risk of deterioration of renal function in pregnancy, particularly in patients with hypertension, heavy proteinuria, and high baseline serum creatinine concentration.\(^8\)\(^9\) A recent meta-analysis reported that renal impairment occurred in 3-27% of cases of lupus nephritis flare; in 0-10% of these cases it was irreversible.\(^10\) Nephritis in SLE may also present for the first time during pregnancy but can be difficult to diagnose.

With the physiological changes in clotting factors in pregnancy (see a previous article in the BMJ Pregnancy Plus series), women with SLE are at particular risk of maternal thrombosis (venous and arterial), especially in the puerperium, and thrombosis is usually associated with the presence of antiphospholipid antibodies.\(^7\)

**How does SLE affect pregnancy?**

SLE may affect the health of the mother or her baby. SLE does not usually affect fertility (although its treatment may), but it is associated with increased risks of early miscarriage, intrauterine fetal death, pre-eclampsia, intrauterine growth restriction, and preterm delivery.\(^2\)\(^8\)

Thirty to forty per cent of women with SLE have antiphospholipid antibodies (including anticardiolipin antibodies or lupus anticoagulant).\(^11\) The combination of antiphospholipid antibodies and one or more of the characteristic clinical features (box 1) is known as the antiphospholipid syndrome. In a prospective study of
267 pregnancies in 203 patients with SLE, live birth rate was 86% (incidence of prematurity 31%, small for gestational age 23%). Most of the fetal losses were in women with associated antiphospholipid antibodies.\(^9\)

Pregnancy outcome is particularly affected by renal disease. Even quiescent renal lupus is associated with increased risk of fetal loss, pre-eclampsia, intrauterine growth restriction, and premature delivery, particularly if there is hypertension or proteinuria.\(^3\) Pulmonary hypertension, reported in up to 14% of patients with lupus, is associated with a high risk of maternal death.\(^8-9\) Conversely, for women with SLE in remission and without hypertension, renal involvement, or the antiphospholipid syndrome, the risk of problems in pregnancy is no higher than in the general population.\(^8\)

Antibodies to extractable nuclear antigens, particularly anti-Ro and anti-La antibodies, may be present in women with SLE. However, these antibodies may also be present in asymptomatic women or in those with Sjögren’s syndrome, where they are associated with a characteristic photosensitive rash. The neonate may be affected by transplacental passage of these antibodies. Cutaneous neonatal lupus is the most common manifestation of neonatal lupus, occurring in the newborns of up to 16% of women with these antibodies in one prospective study.\(^\text{w10}\) It presents with a characteristic rash (figure) at about 2 weeks of life. Congenital heart block is the most serious manifestation and may present as early as 16 weeks’ gestation. It affects about 2% of mothers with anti-Ro or anti-La antibodies and may lead to fetal demise.\(^\text{w11-w12}\) The risk of congenital heart block increases to 15-20% if one child has been affected and to 50% if two children are affected.

Box 2 summarises the disease factors that increase the likelihood of adverse outcome in pregnancy.

**How do you manage SLE in pregnancy?**

Pregnancy care is best given in multidisciplinary clinics where physicians and obstetricians can regularly monitor disease activity and markers of fetal wellbeing.

**Preconception counselling**

Knowledge of renal function, blood pressure, and the presence and titres of anti-Ro or anti-La antibodies and antiphospholipid antibodies allows prediction of the risks to the woman and her baby. An extensive meta-analysis has shown that the outlook is better if conception occurs during remission.\(^\text{w13}\) Case-control studies in women with lupus nephritis suggest that avoidance of pregnancy for at least six months after a flare improves outcome,\(^4\) and expert opinion suggests a similar time period for stabilisation of any preconception drug changes.

**Maternal surveillance**

Several baseline investigations should be done in early pregnancy (box 3). Medication should be optimised, and in women with the antiphospholipid syndrome the decision to start aspirin and/or heparin can be made\(^3\); evidence exists that these anticoagulants improve fetal outcome,\(^\text{w14}\) and thromboprophylaxis is essential in women who have the antiphospholipid syndrome and have had previous thromboembolism. Both aspirin and heparin are safe in pregnancy. Heparin does not cross the placenta, and maternal heparin induced thrombocytopenia and osteopenia are extremely rare in pregnancy when low molecular weight heparin is used.\(^\text{w15}\)

Regular follow-up to monitor serological disease markers (full blood count, double stranded DNA, complement 3 and 4), maternal symptoms, blood pressure, and urine analysis will be needed, with frequency dependent on disease activity. Delivery method can be based on obstetric indications. Decision on timing of delivery depends on disease activity and maternal and fetal health and is made on a case by case basis.

**Fetal surveillance**

In addition to a detailed morphology scan at 20 weeks, regular growth scans (typically at 28, 32, and 36 weeks) should be done—especially in women with hypertension, renal disease, or the antiphospholipid syndrome—to look at fetal growth and markers of fetal wellbeing. In women with anti-Ro or anti-La antibodies, fetal echocardiography may be offered at 18 weeks and again in the third trimester to identify any cardiac conduction abnormalities.

**What if the disease flares up in pregnancy?**

SLE flares may be difficult to diagnose during pregnancy as many clinical features of flares are common to pregnancy too (box 4). Differentiation of active renal lupus from pre-eclampsia is notoriously difficult, and the two conditions may occur together (table 1). In addition, an increasing degree of proteinuria may be the result of normal physiological changes during pregnancy or the withdrawal of angiotensin converting enzyme inhibitors.

It is important to diagnose a flare as it must be appropriately and aggressively managed to minimise maternal and fetal morbidity. Management includes analgesics for joint pain, immunosuppression for more severe disease, and intensive surveillance of the mother and the fetus.

Evidence conflicts as to whether corticosteroids prevent flares.\(^4\) Current expert opinion suggests that prescribing prophylactic steroids is not indicated.\(^2\)
Table 2 | Evidence for adverse effects of immunosuppressants used in pregnancy and breast feeding (adapted from review by Ostensen 12)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Evidence</th>
<th>Whether drug can be used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine and chloroquine</td>
<td>No increased risk of miscarriage, congenital malformation, or stillbirth at doses used in rheumatic diseases (for example, hydroxychloroquine 200-400 mg/day). Cessation increases risk of flare, and a long half life means that stopping does not prevent fetal exposure.</td>
<td>Yes</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Fetus lacks enzyme to convert to active form. Fetal and neonatal immunosuppression is minimal if dose is &lt;2 mg/kg and maternal white cell count is normal.</td>
<td>Yes</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>No increase in congenital malformations. Trend towards prematurity and intrauterine growth restriction is not significant and probably related to more severe maternal disease. Small amounts in breast milk, but no adverse effects reported.</td>
<td>Yes</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>No increase in congenital malformations. Increased rates of prematurity related to severity of maternal disease. In one case report, a baby received maximum of 0.02% of maternal dose via breast milk.</td>
<td>Yes</td>
</tr>
<tr>
<td>Intravenous immunoglobulins</td>
<td>These cross the placenta after 32 weeks but with no adverse effects to fetus.</td>
<td>Yes</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>Increased risk of congenital abnormalities. Enterohepatic recirculation and a long half life.</td>
<td>No (stop six weeks before conception)</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Alkylating agent. Teratogenic and fetotoxic. Risk of suppression of neonatal haemopoiesis.</td>
<td>No (stop three months before conception)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Folate antagonist. Teratogenic and fetotoxic.</td>
<td>No (stop three months before conception, and give folic acid 5 mg daily periconceptually and throughout pregnancy)</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Congenital abnormalities in animal studies, and human studies are limited. A long half life of active metabolites.</td>
<td>No (use cholestyramine to increase clearance preconception)</td>
</tr>
<tr>
<td>Biological agents (such as etanercept, infliximab, adalimumab, rituximab)</td>
<td>Limited experience in human pregnancies and breast feeding, but no adverse fetal or neonatal outcomes to date.</td>
<td>Limit to severe disease</td>
</tr>
</tbody>
</table>

Analgesics and non-steroidal anti-inflammatory drugs

Arthralgia is a common symptom in SLE. Paracetamol is usually the first line analgesic as no adverse effects are known to occur in pregnancy.\(^ {w16}\) Aspirin and non-steroidal anti-inflammatory drugs are not teratogenic,\(^ {w17}\) but salicylates (in analgesic doses) and non-steroidal anti-inflammatory drugs may increase the risk of neonatal haemorrhage via inhibition of platelet function.\(^ {w18}\) Non-steroidal anti-inflammatory drugs may be fetotoxic and lead to oligohydramnios via effects on the fetal kidney\(^ {w19}\) and may cause premature closure of the ductus arteriosus.\(^ {w20}\) Such drugs are therefore usually avoided in pregnancy, especially in the last trimester. Although codeine based analgesics are not the most effective analgesics for joint pain, they are safe in pregnancy.\(^ {w21}\)

Immunosuppressants

Most women with a more severe SLE flare will require immunosuppression. Corticosteroids are the drugs of choice for fast relief of symptoms and disease control, and they may be continued or started during pregnancy. Prednisolone is metabolised by the placenta, and very little (10%) active drug reaches the fetus.\(^ {w22}\) Corticosteroids have been associated with a small increase in the incidence of oral cleft,\(^ {w23}\) intrauterine growth restriction,\(^ {w24}\) and premature rupture of membranes.\(^ {w25}\)

However, a recent large nationwide cohort study recorded no increased risk of congenital malformations and preterm birth in those women receiving corticosteroids,\(^ {w26}\) and a small prospective study showed no increase in intrauterine growth restriction and no difference in infant behaviour and stress induced cortisol levels compared with controls.\(^ {w27}\) The more recent data are reassuring, and expert opinion suggests that corticosteroids, and particularly prednisolone, are safe for the fetus. Maternal complications of steroids include an increased risk of gestational diabetes, hypertension, infection, and osteoporosis.\(^ {w11}\)

If a woman is taking long term maintenance steroids (>7.5 mg prednisolone a day for more than two weeks), parental steroids should be administered to cover the stress of labour and delivery. Prednisolone is safe in breastfeeding mothers as less than 10% of the active drug is secreted into breast milk.\(^ {w28}\)

Table 2 lists other immunosuppressants and outlines the evidence for their use in pregnancy and breast feeding.

The case

Our patient (see scenario box at the start of this article) continued with her preconception medication, and folic acid supplementation. She is now 20 weeks pregnant. She has a close follow-up with a rheumatologist who has reviewed her medical history and medications. She has been taking prednisolone 5 mg daily periconceptually and throughout pregnancy. She is well, with no adverse effects to baby or mother. She has not taken any other medication. Her white cell count is normal.

Cutaneous neonatal lupus
acid was added. She had a scan at 20 weeks that showed normal morphology and growth. At 18 and 32 weeks, fetal echocardiography was normal. At 22 weeks she developed severe arthralgia and lethargy, and her serology indicated an SLE flare (increasing double stranded DNA titres and falling levels of complement 3 and 4). She required 40 mg of prednisolone for symptom control. However, home blood glucose monitoring showed a raised blood glucose concentration, and gestational diabetes was confirmed with an oral glucose tolerance test. She required insulin four times a day in a basal bolus regimen until delivery. Prednisolone was reduced slowly to a 20 mg maintenance dose once daily.

Repeat growth scans were adequate, and labour was induced at 38 weeks for worsening arthralgia and hypertension. Urine analysis remained negative. A 2.5 kg live female infant was delivered vaginally, and the patient was discharged on day 3. The postnatal period was uncomplicated, and the mother breast fed her infant. She stopped insulin immediately after delivery, and antihypertensives were stopped 10 days later. Prophylactic low molecular weight heparin was prescribed postpartum for six weeks in view of the presence of anticardiolipin antibodies and SLE flare. Prednisolone was slowly reduced to 4 mg daily over three months.

**Conclusion**
Systemic lupus erythematosus and the overlap condition of the antiphospholipid syndrome present several challenges in managing a pregnant woman and her fetus. A successful pregnancy outcome depends on stratification of risk at the outset (ideally before pregnancy) and careful and appropriate monitoring during the pregnancy. Should the disease flare up, aggressive but considered management is advocated to reduce maternal and fetal morbidity.

**Contributors:** LHM had the idea for the article. LHM and SJG prepared the first draft and did the literature search. LHM and CN-P managed the patient, together with Andrew McCarthy and Liz Lightstone. All authors contributed to further revisions of the article. CN-P will act as guarantor.

**Competing interests:** None declared.

**Provenance and peer review:** Commissioned, externally peer reviewed.


---

**LESSON OF THE WEEK**

**Anal ulceration induced by nicorandil**

Fayyaz Akbar, Andrew Maw, Arnab Bhowmick

In patients with anal fissures or anal ulceration, treatment with the drug nicorandil should be considered as a possible cause.

Nicorandil is widely used to treat angina, particularly in patients with severe coronary vessel disease. Anal ulceration is a recognised side effect of its use, but the association between the two is not widely appreciated. We want to alert primary care practitioners, general physicians, dermatologists, cardiologists, and surgeons who may encounter such cases of the importance of this association.

**Case report**
A 73 year old man was referred to our department with a one year history of rectal bleeding, mucus discharge, and anal pain. Associated conditions included diabetes mellitus, hypertension, hypercholesterolaemia, and severe ischaemic heart disease. Despite two previous coronary artery bypass operations, he continued to have angina. His medication included aspirin, atenolol, amlodipine, simvastatin, allopurinol, gliclazide, and 30 mg nicorandil twice a day.

Initial assessment found a small posterior anal fissure but the anal ulceration is a recognised side effect of its use, particularly in patients with severe coronary vessel disease. Anal ulceration is a recognised side effect of its use, but the association between the two is not widely appreciated. We want to alert primary care practitioners, general physicians, dermatologists, cardiologists, and surgeons who may encounter such cases of the importance of this association.
histological examination of biopsy specimens from the lesion showed simple ulceration only.

We changed the treatment to chemical sphincterotomy with topical application of diltiazem gel 2% for two months and concentrated on tight glycaemic control. Despite this, the ulceration progressed. Addition of glycerine trinitrate ointment 0.2% also failed, as did additional treatment with ciprofloxacin and metronidazole. We undertook further investigations to identify unusual causes of anal ulceration but results were negative, including those for HIV, syphilis, chlamydia, and lymphogranuloma venereum. Magnetic resonance imaging of the perianal region showed a suspected anal fistula associated with the fissure and so we undertook another examination under anaesthesia. We did not find a fistula, but the ulceration had deepened and enlarged to 2-3 cm wide and was eroding into intersphincteric plane (figs 1 and 2).

At this stage we became aware of reports of anal ulceration associated with nicorandil. After consultation with a cardiologist, we stopped the nicorandil and substituted it with isosorbide mononitrate. This resulted in the patient having an immediate episode of severe angina, but he recovered well. When the patient was reviewed in clinic two months later, his anal symptoms had improved considerably and the ulcer had reduced in size by 75%. Further healing continues.

Discussion

Nicorandil, a nicotinamide ester, is a synthetic nicotine derivative that causes opening of potassium channels and reduces cardiac preload and afterload. Nicorandil is an important but poorly recognised cause of anal fissures and ulceration. Failure to recognise this drug as a cause can lead to considerable morbidity and unnecessary major surgery for patients. The required treatment is to stop the nicorandil, though this should always be done in consultation with an experienced cardiologist.

Conclusion

Nicorandil is an important but poorly recognised cause of anal fissures and ulceration. Failure to recognise this drug as a cause can lead to considerable morbidity and unnecessary major surgery for patients. The required treatment is to stop the nicorandil, though this should always be done in consultation with an experienced cardiologist.

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

Competing interests: None.

Funding: None.

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

The price of life

PERSONAL VIEW Brendan D Kelly, Sharon R Foley

On 31 January 2006 Jaime Elizalde Junior, a 34 year old Hispanic man, was executed by lethal injection in Texas. Elizalde, a welder, had been convicted of killing two men in Houston in the mid-1990s. He spent eight years on death row before being given an injection of thiopental sodium (to sedate him), pancuronium bromide (to collapse his lungs and diaphragm), and potassium chloride (to stop his heart beating). The injection cost $86.08 (£42; €60).

In 2005 at least 2148 people were executed and another 5186 were sentenced to death in various countries around the world. Four countries were responsible for 94% of executions: China, Iran, Saudi Arabia, and the United States. Those put to death included children, and individuals with intellectual disabilities. The prevalence of psychological distress and mental illness is high among prisoners on death row, who may have to wait for more than 20 years for their death sentence to be carried out.

In Texas the average time spent on death row is just over 10 years, and the average age of executed prisoners is 39. Each prisoner is invited to make a last statement, which is then published, along with a photograph and details of their conviction, on the website of the Texas Department of Criminal Justice. At first glance we were astonished that the intimate, tragic last statements of executed prisoners were publicly available. On reflection, however, we realised that these were the last words that these prisoners would ever share, and from that perspective publication seemed not only intellectually defensible but, possibly, morally imperative. This added to our determination to complete our study.

We printed out 100 last statements and spread them across the floor. We printed out the photograph of each prisoner along with details of their crime. Some colleagues happened on us, asked what we were doing, and immediately sat down with us. As we read through successive last statements we became increasingly intrigued, appalled, and affected. At times our study felt like an exercise in morbid voyeurism, modulated only by our increasing empathy for all involved.

We also realised that it is impossible to remove all traces of personal views from a paper dealing with a topic as emotive as capital punishment. One of us, for example, wanted to use the term “state sponsored killing” in place of “capital punishment,” but the more moderate coauthor warned (rightly) against excess emotionalism in a scientific paper. But it still seemed wrong to let such an important issue pass without comment. In the end we agreed that after our research paper was published we would write this essay to highlight the dilemmas we faced and to present in stark and—yes—emotive terms the unvarnished truth about state sponsored killing in the US and beyond.

At the end of 2005 a total of 3254 prisoners were under sentence of death in 38 US states. Mr Elizalde was one of these prisoners, in Texas. Some months later, on the day of his execution, Mr Elizalde, like most prisoners facing execution, chose to make a last statement. And, like most last statements, his contained strong references to God, love, and hope. After thanking his friends and urging remaining prisoners to be strong, Mr Elizalde concluded his short, tragic life with these final words: “We talk about a reprieve or stay from the Supreme Court, but the real Supreme Court you must face up there and not down here. Keep your heads up and stay strong. I love you all. That is it. Stay strong. Thank you.”

Brendan D Kelly is consultant psychiatrist and senior lecturer in psychiatry, Department of Adult Psychiatry, University College Dublin, Mater Misericordiae University Hospital, Dublin, Ireland
brendankelly35@gmail.com

Sharon R Foley is research registrar, DETECT Service, Dun Laoghaire, County Dublin, Ireland
sharonrchelfoley@gmail.com

To what extent should we permit our views about capital punishment to shape the writing of our paper?

simple question: moments before the end of life, what does a person choose to say? We then examined the central themes and psychological constructs in all last statements made by 100 prisoners executed in Texas between 2002 and 2006. Having completed our analysis, however, we were troubled by the depth of our interest in the topic and puzzled about the best way to present our results. Two specific issues presented particular concern. Firstly, what were our true motives for performing this study? To what extent should we permit our personal views about capital punishment to shape the writing of our paper? Our motives were particularly difficult to untangle. We are two practising psychiatrists living and working in one of the 122 countries worldwide that do not practise capital punishment (Ireland). No one in our families or extended families has been directly affected by capital punishment. By chance we had come across a newspaper story about death row in Texas and subsequently looked up the website of the Texas Department of Criminal Justice. At first glance we were astonished that the intimate, tragic last statements of executed prisoners were publicly available. On reflection, however, we realised that these were the last words that these prisoners would ever share, and from that perspective publication seemed not only intellectually defensible but, possibly, morally imperative. This added to our determination to complete our study.

We printed out 100 last statements and spread them across the floor. We printed out the photograph of each prisoner along with details of their crime. Some colleagues happened on us, asked what we were doing, and immediately sat down with us. As we read through successive last statements we became increasingly intrigued, appalled, and affected. At times our study felt like an exercise in morbid voyeurism, modulated only by our increasing empathy for all involved.

We also realised that it is impossible to remove all traces of personal views from a paper dealing with a topic as emotive as capital punishment. One of us, for example, wanted to use the term “state sponsored killing” in place of “capital punishment,” but the more moderate coauthor warned (rightly) against excess emotionalism in a scientific paper. But it still seemed wrong to let such an important issue pass without comment. In the end we agreed that after our research paper was published we would write this essay to highlight the dilemmas we faced and to present in stark and—yes—emotive terms the unvarnished truth about state sponsored killing in the US and beyond.

At the end of 2005 a total of 3254 prisoners were under sentence of death in 38 US states. Mr Elizalde was one of these prisoners, in Texas. Some months later, on the day of his execution, Mr Elizalde, like most prisoners facing execution, chose to make a last statement. And, like most last statements, his contained strong references to God, love, and hope. After thanking his friends and urging remaining prisoners to be strong, Mr Elizalde concluded his short, tragic life with these final words: “We talk about a reprieve or stay from the Supreme Court, but the real Supreme Court you must face up there and not down here. Keep your heads up and stay strong. I love you all. That is it. Stay strong. Thank you.”

Brendan D Kelly is consultant psychiatrist and senior lecturer in psychiatry, Department of Adult Psychiatry, University College Dublin, Mater Misericordiae University Hospital, Dublin, Ireland
brendankelly35@gmail.com

Sharon R Foley is research registrar, DETECT Service, Dun Laoghaire, County Dublin, Ireland
sharonrchelfoley@gmail.com
Eight UK doctors have been followed by a camera crew for the past 20 years. Has anyone’s life gone to plan? Amy Davis watches the latest documentary series.

Back in 1984 a BBC camera crew filmed eight medical students from St Mary’s Hospital Medical School, as it was then called, in west London. In several programmes broadcast during the 1980s and three separate series screened in 1992, 1998, and 2002, viewers saw the student doctors progress through medical school to their final examinations and on to the early years of their medical career. This latest series of eight documentaries catches up with the same doctors 20 years since they were first filmed.

Today Nick Hollings is a consultant radiologist in Truro, Cornwall. In footage from 20 years ago we see Nick as a student being interviewed about working with patients. He says, “I’m not the kind of person that gets latchedin to things emotionally too tightly, when they’re not for my own personal gain—which sounds dreadful but you’ve got to be slightly callous in a way and cut yourself off before you get hurt, otherwise you can’t carry on working.” In a 1991 interview Nick, this time working as a junior doctor, is feeling disillusioned by 52 hour shifts and bed shortages. “Am I actually living or am I just a machine?” he wonders. “It’s just bloody misery, this is. Be better off as a dustman.”

But, 20 years on, was the hard work worth it? Once you became a consultant you had “made it,” so to speak, and you had a job for life. Or had you? The outsourcing of radiological scanning to the private sector in an attempt to reduce waiting lists and achieve government targets has left Nick unsure of his future.

“Times are very uncertain in the health service at the moment, and we’re certainly feeling that in radiology we’re starving down the barrel of a gun.” Nick is so concerned for the safety of his consultant job that he has a back-up plan “to keep the wolf from the door”: he is learning web design.

Back in 1984 Jane Gilbert’s ambition was to become a consultant in obstetrics and gynaecology, but her career hasn’t turned out as expected. Although described by the programme as “one of the brightest medical students” from her intake at St Mary’s, Jane (whose programme, one of the last in the series, will be aired on 29 November) has left the NHS after working as a general practitioner and now works as an agony aunt for a teen magazine and also works in child health promotion. Ten years after breaking from work to have her first child, Gilbert shows no sign of returning to medicine. Back in 1997 she spoke of how the job left her emotionally exhausted: “It gets to the stage where I get six or seven people who’ve got emotional problems, and some evening surgeries I just feel completely drained.”

Gilbert now works from home, where we see her replying to an email from a 16 year old girl: “If your boyfriend is too immature to cope with the squelches and sounds of sexual contact and too insensitive to be kind and gentle with you, maybe you should look for someone better,” she writes. Of her lost medical career she says, “There is a price to pay when you train in medicine. It is a job that becomes your life. For me that was a price too high to pay.”

Modernising Medical Careers, although not mentioned by name, doesn’t escape a bashing by Fey Probst, who is now an accident and emergency consultant. She talks of the problems created by speeding up doctors’ training, combined with the reduction in hours brought about by the European Working Time Directive. “The fact that consultants will have had, let’s say, six years of training at 48 hours a week, rather than 12 years of training at 100 hours a week, means they won’t have the experience,” she says.

Among all the doom and gloom is Mark George, whose life turned out exactly how he wanted it to. From the age of 9 he wanted to be a surgeon, and he is currently one of the UK’s leading colorectal surgeons, with a thriving private practice. “Being a consultant is probably how I thought it would be,” he says. “You’re responsible for the patients who come to see you. You make decisions and hope you get them right. It’s fantastic.”

With all the change in the NHS at the moment, the new doctors’ hours, and Modernising Medical Careers, I wonder what today’s cohort of newly qualified doctors will be doing 20 years from now. Nick Hollings is gloomy: “The NHS is now being run as a business and not as a healthcare organisation.” He also warns junior doctors to take a look at the NHS now and think what it will be like in five years’ time before choosing a specialty. Wise words.

Amy Davis is the Roger Robinson editorial registrar, BMJ. a.davis@bmjgroup.com
The baby shambles

The baby monitors looked mournfully back at me from inside the wheelie bin as I slammed the lid. Then I had a series of flashbacks: the crinkle of a baby’s cry; the whiff of stale vomit on my clothes; the breastfeeding propaganda, and the health visitors’ ‘support’—a tick list questionnaire on depression, domestic abuse, and ‘concerns’ about seemingly everything (my wife took to hiding from them in her subsequent pregnancies). Thus we were sucked into the parental collective. Smoking might be dangerous, but becoming a parent seemed lethal.

In the past, having children involved two teenagers falling in love, having sex, then being forced to marry at the age of 20. Life was straightforward, with clearly defined roles and a script. The children tumbled out, and parents just muddled through— their reward a ruby or even a diamond wedding celebration attended by nine kids and countless grandchildren.

But life has changed. We now have children at an age at which in the past we would have been grandparents. There are fewer children and they are more ‘precious’ than the hordes of the past. Cast adrift in a great sea of parental indifference yesterday’s children generally taught themselves to swim, but now we have stagnant pools of poisonous introspection in which we are all drowning, cold dark pools fed by television programmes, magazines, and so many expert books: Dr Spock, conscious parenting, attachment parenting, authoritative parenting, and all the rest. All this is cookbook parenting, selling complex recipes with exotic ingredients and glossy pictures of the future, success guaranteed. In reality the ingredients are impossible to find, the recipes are pointlessly time consuming, and the final result has a bitter aftertaste.

So what should we doctors tell patients? Should we tell them to trust and draw on their own childhood experiences and that there are no perfect parents or children, just different ones? And yes, rely on experts, but let these be family and friends educated at the school of life, not childless, fakely tanned Californians with unlikely sounding degrees from unheard-of universities. And tell them that childhood is by its nature conformist, for we must teach social rules, but that this is not repression, as it is the very soil from which individuality grows. And lastly, say that childhood should be seen not as separate from adult life but as part of a continuum. If nothing else, tell parents to throw all the parenting theories into life’s wheelie bin, to raise their heads and trust intuition, and even enjoy being parents again.

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

Crown of thorns

The crown of thorns starfish (Acanthaster planci), a voracious predator of coral, is present normally in small numbers on reefs. Extensive and devastating epidemics can occur on reefs when the population of these sinister, grey spiny creatures episodically explodes; they munch through every bit of coral in sight, secreting chemicals as they do so that attract more starfish. The result is total battlefield devastation. There are two types of trigger: pesticides and overfishing kill off the tritons, sea snails, and reef fish that prey on these starfish; and agricultural run-off and warming of the oceans lead to algal blooms that nourish the larval form of A Planci. After a few years of mayhem, life settles back to normal, and the starfish are again corralled in their ecological niche.

In human warfare megalomaniac, usually male, lunatics prevail—tinspot dictators who hold people to ransom. Those men who use rape and mayhem as tools of war are ordinary and mostly well behaved in peace time. The dogs of war are timid creatures; but change the conditions, remove the controlling factors, add in a liberal helping of arms and the ecosystem runs out of control. When the war ends they tuck their tails between their legs, and go back to their ordinary and usually small lives.

After several years mopping up the damage caused by the last outbreak of human starfish in the Balkans, I have a second coral reef analogy. To make a new artificial reef you identify the right place on the sea floor, with the right water temperature, depth, particle level, nutrients, and currents. Then you sink an old ship or a pile of concrete blocks and let it sit. Lo and behold, the structure in a few years’ time will support a perfectly functioning little ecosystem, its rough edges buried by a myriad of ordinary, busy little fish, sponges, and plankton who like nothing better than to get on with things and build something lovely.

In recent years I have seen initially hopeless or tiny international development projects flourish while some major ones leave nothing more than a big pile of embarrassing rubbish. The difference was usually the location—and the timing.

Human society is like the coral reef: resilient yet fragile. There will always be wannabe master of the universe starfish waiting for a chance to run wild. There will always be lots of ordinary creatures wanting to build and repair. We know that getting the conditions in any ecosystem right can prevent disaster and speed up rebuilding, which is why we need democracy, a strong civil society, transparency in government and business, social justice, and an end to the arms trade. This will stop starfish, whether human or A planci, from getting away with it.

Mary E Black is a public health physician, Belgrade, Serbia drmaryblack@gmail.com
The therapy of obedience

It is more difficult these days than ever before to be a literary doctor, what with continuing medical education, revalidation, 360 degree appraisal, the research assessment exercise, and other hobgoblins of the bureaucratic mind, to say nothing of the increase in the actual work to be done.

Time was, however, when even the busiest doctors could retire to their studies and write occasional essays. One such was the Edinburgh physician John Brown, who was born in 1810 and died in 1882. He was famous for his Horae Subseci-vae, that is to say Idle or Stolen Hours, a collection of miscellaneous essays that were reprinted many times, but are now forgotten except, perhaps, by the silverfish and other small creatures that inhabit the less frequented parts of second hand bookshops.

Dr Brown was strongly of the opinion that a man should not write anything unless he had something to say, a dangerous principle that, if taken seriously, would denude the world of much, perhaps most, of its printed matter, not least a good proportion of the medical journals.

My favourite among his essays is entitled “The Doctor—our Duties to him.” This was one of his series of lectures on matters of health to the working men of Edinburgh, and contains four duties of patients to their doctors that, I think, would now cause howls of rage among medical ethicists and other right minded people.

They are as follows: “First, It is your duty to trust the Doctor. Secondly, It is your duty to obey the Doctor. Thirdly, It is your duty to speak the truth to the Doctor, the whole truth, and nothing but the truth; and Fourthly, It is your duty to reward the doctor.”

We must not imagine by this last duty of the patient to his doctor that Dr Brown was an avaricious man; on the contrary, he was universally loved and respected in the Edinburgh of his time, which I am sure would soon have sniffed out any tendency on his part to greed or illicit enrichment.

While Dr Brown explicitly counted the gratitude of patients among the rewards a doctor could reasonably expect, he thought that payment was good for patients, and he provided reasons for this opinion that are not negligible, but are alien to most modern sensibilities:

“Now, I know that few if any of you can pay your Doctor . . . but let me tell you—try and pay him, be it ever so little. It does you good as well as him; it keeps up your self-respect; it raises you in your own eye, in your neighbour’s and, what is best, in your God’s eye, because it is doing what is right.”

Dr Brown would no doubt think we, for our part, had fostered dependence in our patients, and in compensation had returned to them a kind of querulous autonomy. Self importance, not self respect, is what we value now.

As for obedience, Dr Brown illustrates its therapeutic virtues by recounting the case of a man who was given a prescription by his doctor with the order to “Take this,” and who subsequently returned to the doctor completely cured. It turned out that he had eaten the piece of paper on which the prescription was written, and felt much the better for it.

It is more difficult these days than ever before to be a literary doctor, what with continuing medical education, revalidation, 360 degree appraisal, the research assessment exercise, and other hobgoblins of the bureaucratic mind, to say nothing of the increase in the actual work to be done.

Time was, however, when even the busiest doctors could retire to their studies and write occasional essays. One such was the Edinburgh physician John Brown, who was born in 1810 and died in 1882. He was famous for his *Horae Subseci-vae*, that is to say *Idle or Stolen Hours*, a collection of miscellaneous essays that were reprinted many times, but are now forgotten except, perhaps, by the silverfish and other small creatures that inhabit the less frequented parts of second hand bookshops.

Dr Brown was strongly of the opinion that a man should not write anything unless he had something to say, a dangerous principle that, if taken seriously, would denude the world of much, perhaps most, of its printed matter, not least a good proportion of the medical journals.

My favourite among his essays is entitled “The Doctor—our Duties to him.” This was one of his series of lectures on matters of health to the working men of Edinburgh, and contains four duties of patients to their doctors that, I think, would now cause howls of rage among medical ethicists and other right minded people.

They are as follows: “First, It is your duty to trust the Doctor. Secondly, It is your duty to obey the Doctor. Thirdly, It is your duty to speak the truth to the Doctor, the whole truth, and nothing but the truth; and Fourthly, It is your duty to reward the doctor.”

We must not imagine by this last duty of the patient to his doctor that Dr Brown was an avaricious man; on the contrary, he was universally loved and respected in the Edinburgh of his time, which I am sure would soon have sniffed out any tendency on his part to greed or illicit enrichment.

While Dr Brown explicitly counted the gratitude of patients among the rewards a doctor could reasonably expect, he thought that payment was good for patients, and he provided reasons for this opinion that are not negligible, but are alien to most modern sensibilities:

“Now, I know that few if any of you can pay your Doctor . . . but let me tell you—try and pay him, be it ever so little. It does you good as well as him; it keeps up your self-respect; it raises you in your own eye, in your neighbour’s and, what is best, in your God’s eye, because it is doing what is right.”

Dr Brown would no doubt think we, for our part, had fostered dependence in our patients, and in compensation had returned to them a kind of querulous autonomy. Self importance, not self respect, is what we value now.

As for obedience, Dr Brown illustrates its therapeutic virtues by recounting the case of a man who was given a prescription by his doctor with the order to “Take this,” and who subsequently returned to the doctor completely cured. It turned out that he had eaten the piece of paper on which the prescription was written, and felt much the better for it.

**Theoren Dalrymple** is a writer and retired doctor.

---

**Medical Classics**

**The Doctor, his Patient and the Illness**

By Michael Balint

First published 1957

This book arose out of a series of seminars that the author, a psychotherapist, conducted with general practitioners at the Tavistock Clinic in London in the 1950s. At these seminars the GPs presented case reports to discuss aspects of the doctor-patient relationship. What became of interest was those patients who presented repeatedly to GPs with psychological or physical complaints but whose investigation findings were often normal and who were difficult to treat satisfactorily. About such patients Balint came to the conclusion that “some of the people, who for some reason or other, find it difficult to cope with the problems of their lives resort to becoming ill.”

The Doctor, his Patient and the Illness documents the case histories of several of these patients in detail, including their GPs’ attempts at treatment, and the subsequent group discussions. Balint discusses several themes arising from the seminars, such as the idea of the doctor as “drug”—in particular how a doctor’s actions influence how a patient responds to illness and treatment.

These patients seemed harder to help because GPs had to rely on the standard medical model (“elimination by physical examination”), learnt from hospital consultants (“perpetuation of the teacher-pupil relationship”). In many cases where a patient passes through the hands of several specialists, each looking only at one aspect of a problem, a diffusion of responsibility can arise, even for important decisions (“collusion of anonymity”). Balint goes on to discuss ways in which GPs could help such patients, including through psychotherapy.

Balint’s book remains known among most GPs, even if they have not read it. Are its themes still relevant, given the changes in society and medicine, a half century after it was published? Some are directly relevant. How the “drug” (doctor) is prescribed still remains important, and a “collusion of anonymity” would seem to be enshrined in protocols. Many patients still come to their GPs with recurring complaints that have no obvious physical cause but with underlying psychosocial problems. Are GPs now better able to deal with such patients? Vocational training has ensured that GPs can assess patients from more than just a medical model, but how GPs could (and indeed whether they should) try to intervene in treating what may be deep seated personal psychological or social issues continues to be debated, and it is unlikely that many GPs attempt psychotherapy.

So, although this book is still important for the way it opened the lid on doctor-patient interactions, and because many of its messages are still relevant today, the ideas it contains need to be continually re-evaluated and added to.

James Curran, GP locum, Glasgow jdcur@dircon.co.uk

---

**BETWEEN THE LINES**

**Theodore Dalrymple**

It turned out that the man had eaten the piece of paper on which the prescription was written, and felt much the better for it.
OBITUARIES

For the full versions of articles in this section see bmj.com

John Douglas Andrew

Former consultant paediatrician
Bishop Auckland, County Durham (b 1925; q St Andrews 1947; FRCP), d 26 August 2007.

After national service with the Royal Air Force, Douglas Andrew trained in paediatrics in Dundee, Inverness, and Newcastle before being appointed the first paediatrician in Bishop Auckland. Here he built up a unit which was renowned for its clinical care and for the quality of training. While in Newcastle he had become involved in the Thousand Families Study, taking a particular interest in respiratory disease.

Douglas was a keen photographer and used his skills to complement his teaching with his interests in travel, history, and gardening. He made several teaching visits to Libya, during which he also extended his interests in ancient history, becoming an expert on the Romans. He leaves a wife, Megan, and two daughters.

Alan Cottrell

Andrew Cottrell

Rex Penry Edward Barton

Former consultant ear, nose, and throat/head and neck surgeon
Leicester Royal Infirmary (b 1917; q Leeds 1940; MC), d 23 September 2007.

After house jobs, Rex Barton undertook specialist training in ear, nose, and throat surgery at St Mary’s Hospital, Paddington, while being sponsored by the Medical Research Council and LEPRO to research nasal involvement in leprosy at a hospital in central southern India. In Leicester, Rex was instrumental in establishing the multidisciplinary head and neck oncology service, having helped to set up the Temporal Bone Laboratory. He trained medical students and junior staff, many on short term secondments from overseas, and published many papers on head and neck oncology and leprosy. He retired early because of ill health in 1994. He leaves a wife, Nicola; three children; and two grandchildren.

Nicola Barton

Edwin Melville Mack Besterman

Honorary consultant cardiologist
University of West Indies (b 1924; q Cambridge/Guy’s Hospital 1947; MD, FRCP), d 3 September 2007.

For 22 years Edwin Besterman was visiting cardiologist in Malta, selecting patients for cardiac surgery at St Mary’s. He also showed the relation between prebeta lipoproteins and coronary artery disease. His last of over 100 papers was in 2000, a chapter on rheumatic fever in British Cardiology in the 20th Century. Edwin took early retirement to do voluntary work in Jamaica. He reported on electrocardiograms for the Jamaica Heart Foundation—100 000 after 15 years. He was a qualified photographic judge and president of the German Shepherd Club of Jamaica. Predeceased by a son, he leaves a third wife, Perri; three sons from his first two marriages; and eight grandchildren.

E M M Besterman

Anne Gall (née Kirkby)

Former general practitioner
Downham, Bromley, and Southampton (b 1922; q Oxford 1947), died from cerebrovascular disease on 6 February 2007.

Having started at Oxford reading politics, philosophy, and economics, Anne switched to medicine, achieving a string of distinctions and an appointment in neurology. By 1947 she was off with her husband to Kaduna, Nigeria, where she combined raising a family with setting up child welfare clinics. On her return to the United Kingdom in 1956 she started in infant health clinics before joining a general practice in Bromley. She then practised in Southampton followed by a post in psychogeriatrics at Moorgreen Hospital. When this ended, Anne preferred locum work in several local practices to retirement. Predeceased by her husband, David, in 1993, she leaves four daughters and seven grandchildren.

Jean McMillan

Joanna Gall

Geoffrey Brooke Hirst

Former general practitioner Stockport (b 1917; q Leeds 1940; MC), d 23 September 2007.

After qualifying, Geoffrey Brooke Hirst was posted to West Africa. He ran the tropical medicine clinic serving the local population of Soccato. He moved to Suez as the medical officer of the 7th Battalion Rifle Brigade, which moved across the desert to Tripoli, thence to Sicily, Italy, and Rome. On returning to the United Kingdom he became a general practitioner, trainer, and police surgeon. He was made a life member of the local medical committee. Predeceased by a daughter, he leaves a wife, Joyce Mary.

J Hirst

Andrew Wilson Lees

Former consultant chest physician
Ruchill and Stobhill Hospitals, Glasgow (b 1916; q Glasgow 1939; MD, FRCP, FACCP), died from cerebrovascular disease on 2 August 2007.

Andrew Lees was a leading figure in respiratory diseases. His early work entailed evaluating ethanalamine, ethambutol, and rifampicin, his unit being the first to prove rifampicin’s hepatotoxic effects, and he reported the first case of indigenous legionnaires’ disease in Scotland. Latterly, he studied chronic obstructive pulmonary disease, asthma, and lung cancer, as well as writing on the pulmonary effect of rheumatoid diseases. After house jobs Andrew served with the army in North Africa and the Chindits in Burma. He was consultant at Ruchill and Stobhill from 1953 until he retired in 1981. He also studied law, becoming a barrister at Gray’s Inn. He leaves a wife, Nancy; four children; and five grandchildren.

Andrew Dickie

Anne Gall (née Kirkby)

Former general practitioner
Downham, Bromley, and Southampton (b 1922; q Oxford 1947), died from cerebrovascular disease on 6 February 2007.

Having started at Oxford reading politics, philosophy, and economics, Anne switched to medicine, achieving a string of distinctions and an appointment in neurology. By 1947 she was off with her husband to Kaduna, Nigeria, where she combined raising a family with setting up child welfare clinics. On her return to the United Kingdom in 1956 she started in infant health clinics before joining a general practice in Bromley. She then practised in Southampton followed by a post in psychogeriatrics at Moorgreen Hospital. When this ended, Anne preferred locum work in several local practices to retirement. Predeceased by her husband, David, in 1993, she leaves four daughters and seven grandchildren.

Jean McMillan

Joanna Gall

Geoffrey Brooke Hirst

Former general practitioner Stockport (b 1917; q Leeds 1940; MC), d 23 September 2007.

After qualifying, Geoffrey Brooke Hirst was posted to West Africa. He ran the tropical medicine clinic serving the local population of Soccato. He moved to Suez as the medical officer of the 7th Battalion Rifle Brigade, which moved across the desert to Tripoli, thence to Sicily, Italy, and Rome. On returning to the United Kingdom he became a general practitioner, trainer, and police surgeon. He was made a life member of the local medical committee. Predeceased by a daughter, he leaves a wife, Joyce Mary.

J Hirst

Andrew Wilson Lees

Former consultant chest physician
Ruchill and Stobhill Hospitals, Glasgow (b 1916; q Glasgow 1939; MD, FRCP, FACCP), died from cerebrovascular disease on 2 August 2007.

Andrew Lees was a leading figure in respiratory diseases. His early work entailed evaluating ethanalamine, ethambutol, and rifampicin, his unit being the first to prove rifampicin’s hepatotoxic effects, and he reported the first case of indigenous legionnaires’ disease in Scotland. Latterly, he studied chronic obstructive pulmonary disease, asthma, and lung cancer, as well as writing on the pulmonary effect of rheumatoid diseases. After house jobs Andrew served with the army in North Africa and the Chindits in Burma. He was consultant at Ruchill and Stobhill from 1953 until he retired in 1981. He also studied law, becoming a barrister at Gray’s Inn. He leaves a wife, Nancy; four children; and five grandchildren.

Andrew Dickie
William Mathews

Former ear, nose, and throat surgeon Coleraine, Northern Ireland (b 1917; q Queen’s University, Belfast, 1940; FRCSEd), d 20 July 2007. Immediately after qualification, William Mathews (“Bill”) joined the Royal Army Medical Corps and was posted to West Africa before training with the Field Ambulance in Bombay and serving in Burma. He took up his consultant post in 1953, remaining there until his retirement. He joined the St John Ambulance in 1958 and was divisional president from 1980 to 1997. Admitted to the Order of St John as a serving brother in 1987, he became officer brother in 1996. On retirement, he served as a Coleraine borough councillor for 24 years, representing the Alliance Party. He was also a committed Rotarian. He leaves a wife, Hazel; two children; and four grandchildren.

Hilary M L Mathews

Anthony John Membrey

Former general practitioner Tunbridge Wells (b 1932; q Guy’s Hospital, London, 1955; MBE; DObstRCOG), d 5 November 2006. After qualifying, Tony Membrey did his national service as medical officer to the First Malta Artillery Regiment. In 1959 he moved to general practice in Tunbridge Wells. He helped to construct the first purpose built general practice premises there and to set up the first three year vocational training scheme in south east England. Active in the South East Thames Faculty of the Royal College of General Practitioners as secretary, chairman, and provost, he became an examiner for the royal college and helped develop the MRCGP nationally. He was also medical officer for the local Cheshire home for many years, and in retirement did regular locums and headed clinical governance at the Hospice in the Weald in Pembury. He leaves six children and 11 grandchildren.

Helen Membrey

Kusum Mehta

General practitioner Ipswich (b 1949; q Bangalore 1974), d 30 July 2007. Kusum worked in medicine and obstetrics and gynaecology in Bangalore before coming to England in 1976. She worked in several hospitals in the north of England and the Midlands, specialising in paediatrics and anaesthesia, before completing general practice training in 1986. Kusum returned to India but felt she belonged in England and came back to make it her home. She worked in both paediatrics and general practice in Ipswich but decided to confine herself to general practice from 1995, being a partner at the Birches Medical Centre from 1994 to 2007. She was always conscientious despite having ill health for several years. She leaves her mother and six sisters. Moira Pinkney, Nick Edwards, Hanza Mehta

Thilliampalam Paramananthan

Former clinical assistant in psychiatry Darlington (b 1932; q University of Ceylon, Colombo, 1957; MRCP), died from cryptic fibrosing alveolitis on 19 May 2007. Thilliampalam Paramananthan worked in various government hospitals in his native Sri Lanka until 1968 and in forensic pathology until 1972. He passed the MRCP(UK) part one examination held in Colombo in 1971 and came to the United Kingdom in 1973 to pursue postgraduate education. Subsequently he held a senior house officer post in general psychiatry in Bruntwood, Staffordshire, and a registrar post in psychiatry in Burnley, Lancashire. He finally worked as a clinical assistant in psychiatry in Somerset and County Durham. He leaves a wife, Ratna, and a son. B Thalayasingam, Ratna Paramananthan, A D Piyasena

Seyed Abdolmajid Rooholamini

Professor of radiology Olive View-UCLA Medical Center, Sylmar, California (b 1938; q Tehran 1962; FACR, FACP), died from cardiac arrest due to ischaemic heart disease on 1 February 2007. Seyed Abdolmajid Rooholamini left Iran for an additional year’s internship in New York. After appointments at Yale and Stanford in the US and Cambridge in the UK, he returned as assistant professor of radiology, Mashad University Schools of Medicine and Dentistry. Appointed consultant and chairman of the department of radiology at the Queen Pahlavi Foundation and Cardiovascular Medical Centre in Tehran in 1970 and of the department of radiology of the Ministry of Health in 1975, he cofounded the Iranian Radiological Society. In 1984 he left Iran, initially for Sweden and then the US, finally moving to California in 1989 and cofounding the North American Iranian Radiological Society. He leaves a wife, Fatemeh, and a daughter. Bita Manzouri

James Picton Douglas Thomas

Former senior physician University Hospital of Wales (b 1924; q Cambridge/St Bartholomew’s Hospital, London, 1947; MD), d 13 August 2007. James Picton Thomas (“Picton”) established the academic and clinical specialty of endocrinology in Wales. After house jobs and two years’ national service with the Royal Air Force, he was demonstrator in physiology, registrar, and lecturer in medicine at Barts. In 1958 he spent a two year scholarship researching into adrenal steroid hormones at the US National Institutes of Health. Returning as research fellow to Sir John McMichael in London, Picton then became lecturer and senior lecturer in medicine at Cardiff Royal Infirmary and the Welsh National School of Medicine. In 1977 he moved to a full time NHS consultant post until his retirement in 1989. He leaves a wife, Mollie, and her daughter; and his first wife, Jenny, and their three children.

John Peters, M F Scanlon

Maxwell Herman Turner

Former general practitioner Stourbridge (b Wrexham 1924; q Liverpool 1947; MMSA), died from prostate cancer on 14 June 2007. After a house job in Liverpool, Maxwell Turner did national service in the Royal Army Medical Corps. While stationed in Preston he met his future wife, a Sheffield medical student. After several years in general practice in Sheffield and obtaining his MMSA he was appointed, with his wife, to a practice in Stourbridge. He was also an orthopaedic clinical assistant specialising in Perthes’ disease. President of the Dudley, Halesowen, and Stourbridge division of the BMA in 1978 and 1979, he was BMA representative for several years. He leaves a wife, Naomi; two children; and seven grandchildren.

Deborah C Turner
More than 3000 people who had had depression episodes were persuaded to complete an online questionnaire including questions on chocolate consumption and a personality test. Chocolate had been craved by almost half the respondents and by women more than men. Respondents perceived chocolate as good for anxiety and irritability, and it was associated with neurotic behaviour rather than introverted behaviour. The researchers say that simply asking about craving chocolate when depressed seems to be an efficient discriminator of symptoms of DSM-IV atypical depression (British Journal of Psychiatry 2007;191:351-2).

Men who report poor sleep patterns are 18% more likely to have raised concentrations of C reactive protein than men who say they sleep well, according to data taken from the northern Finland 1966 birth cohort study, whose participants were followed up to the age of 31. The same was not observed among women. C reactive protein levels were only mildly raised overall, so it’ll be interesting if these results are replicated in other databases (Psychosomatic Medicine 2007;69:756-61).

Obesity is a risk factor for vitamin D deficiency. A study in the Journal of Nutrition (2007;137:2437-42) assessed the effect of pre-pregnancy body mass index on 25-hydroxyvitamin D concentrations in mothers and their newborn babies. Compared with lean women, obese women had lower serum concentrations of vitamin D in the first half of their pregnancies and a higher prevalence of vitamin D deficiency. Babies of obese women were also more likely to have poor vitamin D status. An increase in body mass index from 22 to 34 was associated with double the risk of vitamin D deficiency. Babies of obese women were also more likely to have poor vitamin D status. An increase in body mass index from 22 to 34 was associated with double the risk of vitamin D deficiency in mid-pregnancy and in neonates.

For people having haemodialysis, distance matters. In Canada, a random sample of more than 18 000 patients was followed up for over 14 years. The risk of death associated with undergoing regular haemodialysis increased the further patients lived from the practice of their attending nephrologist, and the effect of distance was even more evident for deaths from infectious causes (CMAJ 2007;177:1039-4).

A new publication for unpaid carers who lose their role when their loved ones either move to a residential or nursing home or die is called “When Caring Comes to an End.” It highlights the sort of questions and decisions that might need to be made, as well as the actions carers may have to take when their caring responsibilities change. Sections include advance care planning, welfare rights and benefits, hospice care, and ideas about life after caring. The guide can be downloaded at www.carersuk.org or www.timetocare.org.uk.

Skin inflammation induced by ultraviolet radiation can be reduced by an extract of broccoli, say scientists in PNAS (online publication 23 October 2007). The extract, sulforaphane, reduces the skin redness resulting from sun exposure, especially when it’s applied to skin before the exposure has taken place. In six adults, application of the extract cut ultraviolet damage by an average of 37%, with the effect lasting several days. The researchers say sulforaphane works at the cellular level, inducing protective proteins in the skin.

Humans mostly err on the side of optimism, even in the absence of direct evidence to support such expectations. We expect to live longer, and we underestimate the likelihood of getting divorced (Nature 24 October 2007). Functional magnetic resonance imaging shows enhanced activity in the amygdala and anterior cingulate cortex when people imagine positive future events. Function in these areas tends to be disrupted when people are depressed or pessimistic.

Cemented hip prostheses survive longer than the patients who receive them, according to a team from Bristol that analysed their own 10 year survival data on patients. The mean age at the time of surgery for hip replacement was 67, and among the 1154 patients followed for 10 years, 42% aged 65 or over, 56% aged 75 or over, and 77% aged 85 or over at the time of surgery had died. The Bristol team found that 10 year survival for the Exeter hip used for replacement is 98% (Journal of Bone and Joint Surgery 89-B:1299-302).