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Minerva
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Minerva
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Encouraging children and adolescents to be more active

Well evaluated complex interventions are still needed

Physically active children and adolescents are at reduced risk of developing risk factors for cardiovascular disease,1 and they are likely to have enhanced mental and emotional wellbeing.2 However, as with other developed countries, in the United Kingdom, three out of 10 boys and four out of 10 girls are estimated not to take the recommended 60 minutes each day of moderate to vigorous intensity physical activity.3 This is important, because in 2003, 28% of children in the UK were estimated to be overweight or obese.4

In this week's BMJ, Van Sluijs and colleagues report a systematic review of interventions to promote physical activity in children and adolescents.5 The review found weak or inconclusive evidence for the effectiveness of strategies to promote children's physical activity. It confirmed lessons from tobacco control—that at least in adolescents the most effective interventions have many components and are undertaken in multiple settings (school, home, and community).

Randomised controlled trials that focus mainly on education are not sufficient to change behaviour and sustain such changes. This is irrespective of whether interventions target children, adolescents, or parents; low or high socioeconomic groups; or whether they are conducted at school or in the community. Effective interventions are generally those that educate as well as facilitate physical activity by providing opportunities and supportive environments at school, at home, and in the community.

Close examination of the review’s findings5 suggests that it is not all “doom and gloom,” however. More than two thirds of the interventions had a positive effect, and just under half had a significant effect. This is despite the use of, at times, crude self-reporting or proxy reporting of physical activity.

A recent narrative review of physical activity interventions in children and adolescents found that 64% of studies (n=25) that used an objective measure of physical activity reported significant effects compared with only 38% of studies (n=66) that used survey measures.7 This highlights the need to incorporate valid and responsive (sensitive to change) objective measures of physical activity in intervention trials, particularly in studies of children.

Van Sluijs and colleagues’ review also highlights the importance of incorporating a thorough evaluation of the intervention process, which should include measures of fidelity, dose (delivered and received), reach, recruitment, and context. Without this information, it is difficult to determine why an intervention succeeded or failed.

The review5 identifies many gaps in our knowledge about the most effective strategies for promoting physical activity in young people. The authors question whether it is worth pursuing interventions that target boys and girls separately, ethnic minority populations, or those that attempt to change the environment or are delivered via the family or community settings. However, most of these interventions provided education alone, and these interventions are seldom effective. Moreover, few intervention studies have examined the moderating effects of sex, socioeconomic status, or other potentially important factors. Only five studies reviewed focused on environmental interventions. The mediators of change in physical activity behaviour are also rarely assessed or even targeted in interventions to promote physical activity in children. Overall, most interventions reviewed were delivered in schools—very few in other settings—and most involved only education. This suggests that at this stage, there is a lack of available evidence upon which to draw conclusions rather than evidence of a lack of efficacy for interventions targeting subgroups or conducted in various settings.

Future interventions must include parents and families. The review5 confirms findings from previous reviews—that school based interventions that involve families are more likely to be effective than those that do not. Parents are the gatekeepers of children’s physical activity and facilitate adolescents’ physical activity by providing transport to recreational activities.8 They also have an important influence on children’s sedentary behaviours.9 Hence, more interventions delivered in the family setting to promote young people’s physical activity are needed.

Several potentially important physical activity behaviours were not explored in the review. Encouraging active transport is one way to increase overall levels of physical activity.10 This approach also has potential environmental and social benefits. About 20% of all car journeys during the weekday morning rush hour in the UK are thought to be short journeys undertaken by parents taking children to school.11 Children’s independent mobility is greatly influenced by traffic and parents’ real and perceived concerns about safety. Thus, creating environments that support local walking and cycling is a priority. More research is needed for a better understanding of the social and physical environmental determinants of young people’s active transport.

There has been considerable debate about the limitations of randomised controlled trial designs in complex interventions12 and for complex behaviours.
Occlusion therapy for amblyopia
Electronic monitoring of compliance shows that prescribing longer periods of occlusion is not always better

Amblyopia affects about 3.5% of the population. Occlusion therapy using an eye patch to cover the non-amblyopic eye for a couple of hours each day has been the principal means of treatment. The sensitive period in which vision loss can develop and be recovered is generally up to 6 years of age. In many European countries, population based screening and treatment by orthoptists has reduced the proportion of people with untreated or insufficiently treated amblyopia to about 1% of the population. The effectiveness of screening and treatment for amblyopia in the United Kingdom has been questioned because of insufficient evidence from randomised controlled trials, and an effort is now being made to assess its effectiveness and cost. In this week’s BMJ, a randomised controlled trial by Stewart and colleagues compares the effect of prescribing six or 12 hours of occlusion each day in 97 children with amblyopia associated with strabismus, anisometropia, or both. It is the first randomised controlled trial to investigate the relation between the duration of occlusion and visual acuity, and so it greatly contributes to our understanding of the effectiveness of occlusion therapy.

The potential costs that screening and treatment could save in cases where vision in the better eye is lost can be calculated: when amblyopia is insufficiently treated, the duration of bilateral visual impairment (visual acuity 6/12 or less—not being able to read) in later life is 0.6 years longer than in people without amblyopia (average of 1.3 ± 0.7 years). For example, if 1% of the Dutch population had insufficiently treated amblyopia, 1,800 people would be at risk each year for bilateral visual impairment. If a visually impaired person costs society €5,000 (£3,500; $7,000), a conservative estimate, a minimum of €5.4m could be saved annually in the Netherlands. Adding to this, the remaining patients with insufficiently treated amblyopia, who do not lose vision in their better eye, have slightly reduced quality of life. The main cause of insufficiently treated amblyopia is poor compliance. Electronic monitoring of compliance with occlusion therapy is now possible with the occlusion dose monitor. Previous studies using this monitor found that compliance averaged 50%, even though parents knew that compliance was being monitored. Median compliance is 70%, but a considerable number of children do not occlude at all. The most important non-clinical predictor for poor compliance

Some people argue that randomised controlled trials of interventions undertaken in microsettings have little relevance for practitioners who need to deliver population-wide effects. This view was partly supported by van Suijs and colleagues’ review, which found multicomponent interventions more effective in adolescents. Thus, despite the methodological challenges posed, more trials of complex interventions are needed.

Importantly, the interventions themselves need to be subjected to the same level of scrutiny as the study design when assessed for funding and publication, and in systematic reviews. Reviewers need to consider whether the proposed “dose” of intervention is sufficient to produce an effect and how fidelity with the proposed protocol will be (or was) assessed (for example, process evaluation). They also need to consider whether adequate formative research was undertaken or proposed, to ensure that the intervention is suited to the target group and the setting, whether the intervention is based on theory, and whether it included efforts to create a supportive physical or social environment (or both). All of these factors will contribute to the effectiveness of interventions.

In the wake of the obesity epidemic, promising multicomponent interventions need to be disseminated, while the evidence base continues to be built. High quality adequately funded evaluation of programmes based on best practice principles is also needed. Given the complexities involved, partnerships between academics and practitioners are essential.

5 Van Suijs EMF, McMinn AM, Griffin SJ. Effectiveness of interventions to promote physical activity in children and adolescents: systematic review of controlled trials. BMJ 2007 doi: 10.1136/bmj.39320.84.3947.BE.

RESEARCH, p 707
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Mental health in disaster settings

New humanitarian guidelines include the needs of people with severe mental disorders

Guidelines on mental health and psychosocial support in emergency settings were launched in Geneva last week by the Inter-Agency Standing Committee (IASC). They will provide guidance on protecting and promoting the mental and social wellbeing of all people affected by emergencies created by conflict or natural disasters. Among the many topics covered, the guidelines also give special attention to people with severe mental disorders in the community.

Mental disorders account for four of the 10 leading causes of disability worldwide. Yet mental health is one of the most under-resourced specialties, and no country meets its mental health needs even when no emergency exists. In emergencies, the proportion of people with severe mental disorders (such as psychosis or severely disabling moods, anxiety, and stress related disorders) is projected to be about 1% higher than the estimated baseline of 2-3%. In a large emergency this can amount to thousands of people.

People with severe pre-existing mental disorders are particularly vulnerable. A pre-existing disorder may be exacerbated by stressful events, by disrupted supplies of drugs, and by the lack of social support that previously sustained these people. Established traditional means of care, such as those provided by local spiritual healers, may not function. Patients in institutional care may be abandoned by the staff and the institution itself may be targeted, taken over, or destroyed. People with severe mental disorders may not understand the risk of remaining in their surroundings, or they may be abandoned by their families and communities. If they can be persuaded to escape, they may be chained, stoned, and exposed to life threatening situations in refugee camps. They are also without adequate care and protection because of a lack of drugs and trained staff. Stigma may cause families to hide a family member who is mentally ill, so the person is unable to speak for themselves.

Community interventions for people with severe mental disorders in emergencies include assessing existing services and identifying those in need; building a relationship with healers and facilitating the use of supportive traditional healing methods where appropriate; ensuring sustainable supplies of psychotropic drugs; initiating rapid training and ongoing supervision for emergency primary healthcare staff; and establishing an accessible advertised service while avoiding the creation of parallel mental health services focused on specific diagnoses (such as post-traumatic stress disorder) or on narrow groups (such as widows). The service should provide basic biological and psychosocial interventions to relieve symptoms and restore function; educate and support existing carers; work with local community structures and groups to enable protection of people who are severely disabled by mental disorder; plan for the return home of any...
Reform of the coroner system and death certification

Legislation is expected next month

Last year, the UK government published a draft bill to reform the coroner system in England and Wales. The intention is to bring coroner reform legislation to parliament next month.

The draft bill proposed fewer and larger coroner districts, led by full-time legally qualified coroners. A new office of chief coroner would improve consistency of practice between local coroners and deal with appeals. There would be a new emphasis on prompt and sensitive service to bereaved families, and both nationally and locally the new service would have its own medical advice.

In 2006, Baker and Cordner wrote an editorial in the *BMJ* on the government’s approach. They criticised the decision to leave responsibility for the appointment and support of coroners with local authorities and the failure to tackle reform of death certification, as recommended by both the Home Office review and the Shipman Inquiry. These criticisms and others were made in a well researched and strongly argued report from the Parliamentary Select Committee on Constitutional Affairs. There are no indications of a government rethink on the continuing role of local authorities in the coroner service, but a recent consultation document from the Department of Health outlines important changes in death certification now proposed for England and Wales. A uniform certification process would be introduced for all deaths, which would abolish the extra forms and processes currently needed for cremation. A new post of medical examiner would also be introduced. These examiners would be attached to the clinical governance teams of primary healthcare trusts and would scrutinise all deaths after the completion of a medical certificate of the cause of death by the treating doctor.

The medical examiner would have the power to authorise disposal of the body without waiting for registration of the death. Certification by single doctors in burial cases would cease, as would payment of private fees to doctors for the cremation certificate; instead, a fee would be payable in all cases to the medical examiner service. Medical referees at crematoriums would be abolished.

Medical examiners would be doctors with at least five years’ full registration. No specialist background would be required—they would not need to be pathologists and perform autopsies as medical examiners in North America do. Before counter-certifying a death and authorising disposal of the body without waiting for registration of the death, they would talk to the first certifier and see relevant parts of the care record.

They would train local doctors in death certification, audit local standards of death certification, and use information from the medical certificates of the cause of death to analyse local mortality trends. They might be part-time, and might be co-located with...
Diagnosing left ventricular hypertrophy in arterial hypertension

ECG has low sensitivity so further tests are needed to detect organ damage

Arterial hypertension is an important public health challenge—it affects almost one third of the adult population in economically developed countries and is a major contributor of cardiovascular mortality and morbidity. The management of primary hypertension is based on three important principles—diagnosis, treatment, and identifying organ disease and indicators of subclinical organ damage.

In this week’s BMJ, a systematic review by Pewsner and colleagues assesses the accuracy of electrocardiography in screening for left ventricular hypertrophy in people with hypertension.1 It finds that electrocardiography has a low sensitivity for detecting left ventricular hypertrophy compared with echocardiography. Treatment aims for a target blood pressure below 140/90 mm Hg in the general population2 and below 130/80 mm Hg in patients with diabetes and renal dysfunction. A target of ≤130/80 mm Hg should also be considered in patients with cerebrovascular disease, cardiac disease, peripheral artery disease, and advanced retinopathy. Such a target is also advisable when evidence of organ damage is present, because even high-normal blood pressure values increase the risk of complications. Clinical history, clinical examination, and laboratory investigation detect a large proportion of patients who are at high risk. In these patients, intensive modification of risk factors and tight control of blood pressure is needed, but no other routine screening test is...
indicated because the severity of the condition is already established.

Most people with hypertension are not in the high risk categories for left ventricular hypertrophy, but doctors should search for indicators of subclinical organ damage in these patients to identify those at higher risk. For example, electrocardiography and evaluation of microalbuminuria are recommended in all patients with hypertension. About 30% of unselected people with hypertension have microalbuminuria—one of the strongest risk markers for complications in untreated hypertension.\(^3\)\(^4\) A low ankle brachial blood pressure index, although less common, is easy to measure; it indicates advanced atherosclerosis and is also a strong risk marker for complications.\(^5\)\(^6\)

Doctors can request other potentially useful tests, but these are rarely used in clinical practice as they can be expensive, time consuming, and no randomised trials have convincingly shown that they are useful and cost effective. Examples include ultrasound of the carotids\(^7\)\(^8\) or calcium score index of the coronary artery assessed by means of computed tomography, both of which can detect atherosclerosis;\(^9\) or ambulatory electrocardiography, which detects patients with silent ischaemia or increased ventricular ectopic activity, both of which are associated with poor prognosis.\(^10\)

The systematic review by Pewsner and colleagues\(^1\) establishes that electrocardiography cannot rule out left ventricular hypertrophy. None the less, left ventricular hypertrophy assessed by electrocardiography remains a specific sign of organ damage and a marker of increased risk, and it should prompt clinicians to implement a more aggressive course of risk management. The electrocardiographic results may also indicate atrial fibrillation and ischaemic heart disease. Unfortunately, the sensitivity and specificity of electrocardiography is low if interpreted by non-experts, and efforts should be made to arrange expert evaluation of electrocardiograms in general practice.

The review shows that absence of left ventricular hypertrophy on electrocardiography modifies the pre-test probability of left ventricular hypertrophy diagnosed on echocardiography from 33% to 31%, regardless of which electrocardiography criteria are used to detect hypertrophy. This apparently low yield raises the question of whether electrocardiography should be part of a comprehensive assessment of cardiovascular risk in people with hypertension.

About 17% of the population may have increased left ventricular mass by echocardiography, in contrast to just 2-3% with electrocardiography. Left ventricular hypertrophy measured by echocardiography offers prognostic information beyond that provided by the evaluation of traditional cardiovascular risk factors, including electrocardiography.\(^11\)\(^12\) But in clinical practice it may be difficult to measure left ventricular mass in some patients because of poor image quality, an interobserver variation of 15%, and because echocardiography is not routinely recommended.\(^2\)

Echocardiography is always indicated when doctors suspect cardiac dysfunction or structural abnormality on the basis of the patient’s history, electrocardiographic results, and previous diagnoses. In uncomplicated hypertension, echocardiography is comparable to the tests already mentioned for diagnosing organ damage. These tests should be considered in patients otherwise at low risk of cardiovascular disease to determine the treatment target and intensity of risk modification needed. Local tradition and expertise may determine which of the recommended tests to use.

When organ damage is detected it should prompt clinicians to be more aggressive in reaching the target blood pressure and encourage their patients to be more compliant. Doctors should explain to their patients that hypertension has already harmed their organs and optimal treatment can slow down or stop progression.

The presence of left ventricular hypertrophy may also affect the choice of drug. Inhibitors of the renin-angiotensin-aldosterone system, calcium antagonists (amlodipine, felodipine), and probably aldosterone antagonists will reduce left ventricular mass more than other types of drugs.\(^2\)

FAMILIAL HYPERCHOLESTEROLAEMIA

Cascade testing is tried and tested and cost effective

Wald et al suggest that screening children for high cholesterol at the time of immunisation, and then testing the parents of affected children, is an effective screening method for familial hypercholesterolaemia.1

Earlier data from our group showed that universal screening was much less cost effective than cascade testing (family tracing from affected patients). A recent pilot study of cascade testing at five NHS trusts, funded by the Department of Health (www.fhcascade.org.uk), has confirmed cascading to be feasible, cost effective, and acceptable to both patients and clinicians.2

Our recommendations to the department include that, because of the degree of overlap in cholesterol concentrations in affected and unaffected individuals, DNA testing is required to underpin a diagnosis of familial hypercholesterolaemia. The use of cholesterol testing as proposed by Wald et al will lead either to many false positive diagnoses in children, causing unnecessary anxiety, testing, and costs, or to true positives being missed because the cut-off point is set too high.

Around 15,000 patients with familial hypercholesterolaemia (of the estimated 100,000 cases) attend lipid clinics in the United Kingdom and cascading from these known cases should be the first approach as half of their first degree relatives will be affected.3 This has been evaluated and should take priority for resources.4

However, finding more new patients will become important after the cascade work, which is estimated to find half of UK cases. The proposal to screen infants has clinical merit but would need to be piloted carefully. Approaches that circumvent using children as the primary contact warrant further investigation, for example, using data from general practice records, which recent data suggest to be feasible,5 or testing those who have had a heart attack at an early age.

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Child-parent screening may have adverse psychological effects

Wald et al do not mention the potential adverse psychological impact of child-parent screening for familial hypercholesterolaemia.1

No matter how well these issues are communicated, this test will exacerbate the cholesterol neurosis that much of the population already seems to have. General practitioners in particular are aware that a screening programme which sounds fine in theory can translate into anxiety in patients. Throw children into the mix and the anxieties will be even higher.

Telling parents that their child has high cholesterol will worry them, which makes putting things into perspective difficult. It risks casting a shadow over childhood because parents view their progeny as threatened or fragile. This will be compounded by the fact that no immediate therapeutic action can be taken. Parents will feel that their child is vulnerable and that nothing can be done in the immediate term.

At best this will make them uncomfortable, at worst it could blight their parenthood.

Wald et al suggest delaying treatment until adulthood. At which point—after a childhood of being less “well” than their peers and overprotected by their parents—they may or may not decide to be treated and may or may not be happy that this test was imposed on them. Perhaps their thwarted efforts to obtain life insurance will help them make up their minds.

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DIRECT TO CONSUMER ADVERTISING

The world of the market place

Magrini and Font discuss direct to consumer advertising,1 but drug promotion at an earlier stage may have already influenced the views of the public and patients.

Current European legislation on drug promotion makes it difficult to define what promotion by a pharmaceutical company before market authorisation entails. Many drug companies employ marketing companies to promote new drugs. The recent premature promotion of Herceptin for early breast cancer is viewed as exemplary by the industry and to be copied.

Releasing early results from high profile trials at major cancer conferences can gain worldwide publicity. When supported by website press releases to inform the stock market, one sided information is freely available in the market place.

The small patient group “Women Fighting for Herceptin” was supported by a leading marketing company.2 The ensuing national media campaign pushed politicians into supporting the unlicensed use of Herceptin and hence undermined the UK Medicines Act and the role of the National Institute for Health and Clinical Excellence (NICE).3 Many healthcare commissioners caved in under the subsequent pressure and agreed early funding.
LETTERS

The drive for pharmaceutical company profits is changing the tactics of information use. This is more likely to undermine public trust in the industry than help patients. Jonathan V Howell consultant in public health West Midlands Specialised Commissioning Team, Edwin House, Burton on Trent DE14 2SW jonathan.howell@lycos.com

Competing interests: JVH advised healthcare commissioners about the funding of unlicensed Herceptin. His complaint about the promotion of Herceptin was upheld.

1 Magrini N, Font M. Direct to consumer advertising of drugs in Europe. BMJ 2007;335:526. (15 September.)
2 Boseley S. The selling of a wonder drug. BMJ 2007;335:526 (15 September.)
3 Department of Health. Speech by Rt Hon Patricia Hewitt MP, Secretary of State for Health, 25 October 2005:
4 www.dh.gov.uk/en/News/Speeches/Speecheslist/DH_4121929

MEDICAL MIGRATION

Full house

Winyard argues that the BMA is being “ambiguous” in criticising both the medical training application service (MTAS) fiasco and the changes in immigration policy.1 He implies that it is incongruent to do so, as stopping immigration is necessary for the system to run adequately. Although this is somewhat true, the BMA is not lobbying for the rights of future immigrants, but for the rights of current immigrants who have been unfairly forced into exile by the new immigration rules. The BMA desires nothing but praise for this.

He also mentions that the United Kingdom currently has “the worst of all worlds,” as it invests in expanding medical schools but still recruits people from overseas, only to fail to give them all a job down the line. But this is actually quite clever. In the end, what you get is a surplus of intelligent, well intentioned, overqualified people with no transferable skills, thousands of pounds in debt, desperately looking for a job in the one company that has the monopoly for employing their services. It’s the best of all worlds, and any company in the private sector would kill for this.

The way forward is clear. The house is full, so please shut all the doors. All of them. Not only permit-free training, but highly skilled migrant programmes, professional and linguistic assessment board tests, and all entry to UK medical schools by overseas students aspiring to stay in the UK. The fact that all these structures still offer false hope (and charge heavily for the privilege) is nothing but cruel. But what about those already inside? Would it be too much to let them stay? Even if it means a little more competition? After all, they did help to build the house. Jorge Zimbron academic foundation year 2 Institute of Psychiatry at the Maudsley, King’s College, London SE5 8AF jorgezimbron@doctors.net.uk

Competing interests: JZ is an overseas UK graduate unlikely to be able to apply for specialist training next year.
1 Winyard G. Medical immigration: the elephant in the room. BMJ 2007;335:593-5 (22 September.)

The real elephant in the room

Winyard has missed the issue of non-European Union UK medical graduates.1 These students make up about 15% of medical undergraduates, and UK medical schools depend on their financial backing to survive. Each student would have forked out at least £80 000 (£114 000; $162 000) by year 5, excluding the cost of living. When these students first chose to study in Britain, the rules would have allowed them fair access to postgraduate training.

Since April 2006, with the abolition of permit-free training, these students are left in limbo, with a strong feeling of breach of moral contract. I fail to understand why these non-EU students are included in the figures used by the Department of Health and the Foreign Office when accounting for UK graduates but are judged as “international medical graduates” when applying for jobs.

Also it costs the taxpayer about £250 000 to train each one. Mohammad Farhad Peerally fourth year medical student University of Sheffield, Sheffield S10 2TN mada04mfp@shef.ac.uk

Competing interests: MFP is an international medical student in a British medical school.
1 Winyard G. Medical immigration: the elephant in the room. BMJ 2007;335:593-5 (22 September.)

“BARE BELOW THE ELBOWS”

A cheap soundbite

We were astounded to read that the Department of Health plans to ban doctors from wearing white coats because of the risk of cross infection.1 2 The package describes a “bare below the elbows” dress code (short sleeves, no wrist watch, no jewellery, no ties when carrying out clinical activity).

What is the evidence for this? It is impossible to say because this policy is based on two as yet unpublished reviews. Surely, they should have been made available first for discussion. We doubt that evidence is convincing as the working group’s first conclusion is that there is no conclusive evidence that work clothes are a significant risk in terms of spreading infection, and the policy document ends with, “it seems unlikely that uniforms are a significant source of cross-infection.”

The document considers it good practice for medical staff to wear short sleeved garments and not white coats because “cuffs become heavily contaminated and are more likely to come into contact with patients.” Presumably this conclusion is based on bacteria such as Staphylococcus aureus being found on a quarter of white coats.3 But these coats were worn for up to eight weeks and not changed daily. Why? Because hospitals no longer provide clean white coats.

But maybe we should not be astounded. Dirty hospitals are expensive to sort out, whereas “bare below the elbows” is a cheap soundbite that saves money. But the policy ignores the advantages of white coats and name badges—ease of identification and cleaning, protection, and usefulness for carrying things. Most patients in the UK prefer doctors to wear white coats,1 and doctors wear white coats in most countries.5

White coats should not be banned. Yes, use plastic aprons when examining patients, but insist that you are provided with a clean white coat every day.

Competing interests: None declared.
Adam Magos, consultant gynaecologist a.magos@medsch.ucl.ac.uk
Allan Maclean professor of obstetrics and gynaecology Darylil Baker consultant vascular surgeon Nicholas Goddard consultant orthopaedic surgeon Olagunju Ogunbiyi consultant colorectal surgeon
Royal Free Hospital, London NW3 2QG

1 White coats to go in cleanliness bid. BMJ 2007;335:582 (22 September.)
Africans die in pain because of fears of opiate addiction

Dorothy Logie NAIROBI

Attempts to improve palliative care services in Africa are being hampered by the fear that many African professionals have of using morphine therapeutically and by poor access to the drug, a conference was told last month.

Many countries in Africa have no access to morphine so that palliative care is reduced to the level of supportive care without pain relief, delegates from 35 countries heard. They were attending the second palliative care conference for Africa, in Nairobi.

While the world's 20 richest countries consume 86% of global therapeutic morphine, countries such as Rwanda use just 0.039 mg per capita, one of three lowest users in the world.

Opiophobia—the fear of using morphine therapeutically—is a big obstacle facing palliative care services in the continent, the conference heard.

Fear of addiction, excessive bureaucracy, inadequate requisitioning, and a reluctance to use oral morphine outside hospital are widespread throughout Africa. In addition, the lack of doctors, especially in rural areas, makes nurse led prescribing essential, but there is an unwillingness to encourage nurses to take on the prescribing of morphine. At the same time the need for palliative care services is growing.

Cecelia Sepulveda, head of the cancer control programme at the World Health Organization, said that cancer is generally a neglected area in resource poor countries.

United States

DEAMONTE DRIVER, right, who died in February after a dental abscess spread to his brain

Future of US children’s health insurance still uncertain

Janice Hopkins Tanne

NEW YORK

The US State Children’s Health Insurance Program, subject of a fight between President George Bush and Congress, was extended to 16 November.

The programme was to expire on 30 September, the end of the government’s fiscal year and the end of the programme, which began 10 years ago and needs renewal every five years.

Congress passed a “continuing resolution” to extend it and several other programmes.

The current programme, funded partly by the federal government (about 70%) and partly by the states (about 30%), covers more than six million children. The expansion would cover another four million. Last month Congress voted to renew and expand the programme to cover more children in families with incomes too high to qualify for Medicaid insurance, but too low for them to afford private health insurance.

The Congressional plan would cost an additional $35bn (£17bn; €25bn) over the next five years. Proposing a more modest expansion, Mr Bush said that he would veto the bill as it stood, but he had not done so as the BMJ went to press.

A presidential veto can be over-ridden by a two thirds vote in both houses of Congress. A combination of Democrats and Republicans who support the Bill have enough votes to over-ride a veto in the Senate, but they are about 24 votes short in the House. The fight for children’s health insurance became emotional in the media last week. The BBC described Deamonte Driver, who died from a tooth infection that spread to his brain. His mother couldn’t find a dentist who would accept Medicaid payment and couldn’t afford to pay for the extraction herself (http://news.bbc.co.uk, 28 Sep, “Boy’s death highlights US health debate”).

The American Medical Association and AARP (formerly the American Association of Retired Persons), supported expanding the programme, to be funded by an increase in the cigarette tax.
Netherlands considers introducing preconception care

Tony Sheldon UTRrecht

The Health Council of the Netherlands, a scientific advisory body, has recommended that the Dutch government introduce an integrated programme of preconception care, to reduce perinatal mortality, miscarriage, premature birth, and congenital abnormalities.

The Dutch government commissioned the council to draw up its advice because the Netherlands has lost its pre-eminent position on perinatal mortality compared with other European Union countries, partly because of a higher proportion of older mothers and mothers belonging to ethnic minorities (Ned Tijdschr Geneeskr 2004;148:1855-60).

The council’s key message is that current antenatal care, which starts at the eighth week of pregnancy, can miss chances to improve the health of the mother and child. Information on health interventions should be brought forward until at least a month before any planned conception to allow the health benefits a chance to have effect, it says.

The proposal also advocates an “integrated, multidisciplinary approach,” in which all existing individual strands of care would be brought together with the same staff. These strands would include advice on diet, alcohol, and tobacco; genetic factors; chronic health conditions; current medication; and occupational health.

The measures recommended range from abstaining from tobacco, alcohol, and other recreational drugs to ensuring adequate intake of folic acid and vitamin D. Health professionals will also check for rubella antibodies; ensure diabetic women’s blood sugar is under control; recommend that women with epilepsy adjust or phase out drugs completely; and treat any sexually transmitted infection.

Some measures, such as campaigns for the use of folic acid, would target all women of child bearing age; others would target individual prospective parents.

Preconception Care: a Good Beginning is available at www.gr.nl.

UK does well on giving information to patients but poorly on access to new treatments

Rory Watson BRUSsels

The United Kingdom ranks only 17th out of 29 countries in the latest edition of the Euro Health Consumer Index of public healthcare systems—one place behind Ireland and narrowly ahead of Italy and Portugal. It has slipped from 15th position last year.

The rankings, now in their third year, were produced by the Brussels based analysis and information organisation, Health Consumer Powerhouse. They are based on 27 indicators grouped into five categories—patients’ rights and information, waiting times, outcomes, the generosity of public healthcare systems, and access to medication.

The UK, with its electronic patient records, quality ranking of hospitals provided by the Healthcare Commission, and 24 hour telephone healthcare information system provided by NHS Direct is in the forefront of patient access to information. However, it scores badly on access to new treatments and long waiting times, receiving only 381 points out of a potential 1000.

Arne Björnberg, the index’s director, said that “Patients in the UK have the right to expect more. Despite substantial funding increases, the UK is still a mediocre overall performer.”

Top slot with 806 points went to Austria, which scored consistently well across the five categories. The Netherlands, which topped the league in 2006, is in second place, closely followed by France, Switzerland, and Germany. At the bottom of the table are Latvia, Bulgaria, and Poland.

In the individual categories Denmark was the winner on patients’ rights and information; Belgium on waiting times; Sweden on outcomes; Finland, France, Hungary, and Sweden on generosity of systems; and Denmark, Ireland, the Netherlands, Spain, Sweden, and Switzerland on access to medicines.

In general, the survey found that increasing attention is being paid to patients’ rights and that healthcare provision is improving. However, it notes that methicillin resistant Staphylococcus aureus infections in hospitals seem to be spreading and that half of the health services delay consumer access to new medicines.

In the debate between the Bismarck healthcare system, based on social insurance with many insurance organisations, and the Beveridge variety, where financing and provision are handled in one organisational system, as in the UK, the survey indicates that the former delivers better value.

“It is very hard to avoid noticing that the top five countries, which fall within 36 points on a 1000 point scale, all have dedicated Bismarckian healthcare systems,” the report says.

Commenting on the table, John Appleby, chief economist at the King’s Fund, said, “These composite performance tables are problematic. One of the problems is that different weighting has to be given to different components, according to what is thought to matter to patients. But that is often hard to know.”

Court upholds demand for preimplantation genetic diagnosis

Fabio Turone MILAN
The battle on assisted reproduction and prenatal diagnosis in Italy took a new turn last week, when the gynaecologist Giovanni Monni, head of the obstetrics and gynaecology department in the Ospedale Microcitemico in Cagliari, Sardinia, was ordered by the local court to provide preimplantation genetic testing to a couple carrying the gene for β thalassaemia, which is common on the island.

Dr Monni, the current president of the Italian Association of Hospital Gynaecologists, had unwillingly obeyed the controversial law approved in 2004, which, through guidelines, forbids preimplantation genetic diagnosis, even though he personally supported the couple’s request for it (BMJ 2004;328:9). “I am very glad of the court’s decision,” he told the BMJ.

The law contains several points that have been opposed from the beginning by almost all gynaecologists. These include the stipulations that assisted reproduction techniques can be used only by sterile heterosexual couples in a “stable relationship”; that embryos cannot be frozen, which means that a maximum of three fertilised eggs must be immediately implanted in the womb; and that sperm and eggs cannot be donated. In addition only the non-invasive “observation at the microscope” is allowed as a form of preimplantation testing.

The court found that the ban on genetic testing was in guidelines not in the law itself

The constitutional court had rejected in November 2006 a similar request for preimplantation genetic diagnosis by the same couple. The ban on genetic testing, the court argued, was contained in the guidelines defined by the health ministry and not in the law itself. Consequently the law itself was not at variance with the constitutional right to health. After that pronouncement the couple went back to the lower court and sued Dr Monni and the hospital and received the recent favourable judgment.

Meanwhile, the couple at the centre of the controversy started treatment for in vitro fertilisation and preimplantation diagnosis at a private centre in Istanbul, with expenses paid for by two anonymous donors.

Now the woman, Simona, who had two abortions in the past, is already pregnant, but she has said that she will implant the embryos frozen in Italy as soon as possible, after the end of her present pregnancy, if they do not carry the genes for β thalassaemia.

Many specialists have predicted that the law would have several adverse consequences. They said it would reduce success rates, increase the number of multiple pregnancies, and result in many Italian couples travelling abroad for treatment. The first official data support these predictions (BMJ 2007;335:62).

Moreover, many couples seem to be circumventing the ban on the freezing of embryos. According to journalistic reports, more and more couples are being allowed to freeze their embryos by refusing to implant them all in a written statement to the hospital.

The next step will be the publication of new guidelines.

African-American leaders call for action on AIDS in US

Bob Roehr WASHINGTON, DC
African-American leaders launched a call to action to address HIV/AIDS in the black community at a Capitol Hill news conference last month. The aim is to halve the rates of new infections, reduce the stigma of AIDS, increase by a half both the number of people who know their HIV status, and who are receiving care for HIV infection.

“AIDS is a black disease no matter how you look at it—through the lens of gender, or sexual orientation, or age, socioeconomic class, education, or region of the country—black people bear the brunt of the epidemic,” said Phill Wilson, executive director of the Los Angeles based charity the Black AIDS Institute.

“Some 30% of new cases among gay men are among black men; 40% of new cases among men are black; 67% of new cases among women are black; and 70% of new cases among youth are black. That is why we are calling on this mobilisation.”

“Why are more than 50% of new HIV cases occurring within the African-American community when we are only 13% of the people?” asked Mohammad Akhter, executive director of the National Medical Association, which serves doctors and patients in the black community.

“We need to reassess the national strategy on HIV/AIDS to see why it is not working. If 50% of the new cases of HIV are in the African-American community, shouldn’t that be where 50% of the resources should be going?” Dr Akhter said.

Mr Wilson acknowledged that earlier efforts to rally the black community to fight HIV/AIDS have fallen short.

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GMC guidance on conscience goes too far, says BMA

Clare Dyer BMJ

The BMA has clashed with the UK General Medical Council about draft guidance from the GMC for doctors who object to providing certain medical services on the ground that they conflict with their personal beliefs.

In its response to the draft of Personal Beliefs and Medical Practice the BMA argues that the guidance goes beyond doctors’ widely accepted right to opt out of certain procedures that involve matters of life and death, such as abortion, contraceptive services, and the withdrawal of life prolonging treatment. The association claims it could confuse patients and give doctors a licence to discriminate.

But the GMC insists that the draft guidance does not contradict current guidelines in its core text, Good Medical Practice, which does not limit conscientious objections to life and death matters. It says that the new guidance is intended to supplement Good Medical Practice by giving more detailed and practical information in response to growing numbers of inquiries about matters of faith and other areas of personal belief.

The BMA said the draft advice seemed “to extend the right of conscientious objection to any procedure with which doctors have a moral, cultural, or religious disagreement.” The association called for a limited list of clearly defined procedures to which doctors would be entitled to conscientiously object.

Tony Calland, chairman of the BMA’s medical ethics committee, said, “Doctors are not there to judge patients but to treat them.”

The BMA’s response is at www.bma.org.uk

Medical Research Council appoints new chief executive

Roger Dobson ABERGAWNYY

Sir Leszek Borysiewicz, who was knighted for his research into developing vaccines, is the new chief executive of the UK Medical Research Council (MRC).

The deputy rector of Imperial College, London, is to take over from the current holder, Colin Blakemore, whose term of office finishes at the end of this month.

“I’m excited by the chance to work across the whole spectrum of biomedical science and to help to make a difference in relation to healthcare for individuals in the UK and globally,” said Professor Borysiewicz.

He joined Imperial College London in 2001 as principal of the faculty of medicine before becoming deputy rector three years later. His research interests are in viral immunology, infectious diseases, cell mediated immunity, virus associated malignancy, and vaccine development. He was knighted in 2001 for his research into developing vaccines, including one to stop the development of cervical cancer.

He holds a number of appointments in higher education and science and was recently made a governor of the Wellcome Trust. He is also the chairman of the UK Clinical Research Collaboration’s integrated academic training committee and chairman of the joint scientific advisory board of the MRC and the UK Stem Cell Foundation. He is a founder fellow of the Academy of Medical Sciences.

Sir Leszek’s appointment comes in the wake of Sir David Cooksey’s recommendation last year of a single strategy for health research in the UK and the formation of an Office for the Strategic Coordination of Health Research (OSCHR) to oversee this strategy.

“What the Cooksey report has done is to open the door on a plethora of opportunities that exists. It’s not just an opportunity on the translation side, people forget that Sir David’s review also very firmly identified the need to maintain the basic research agenda as the seed corn from which all future proposals are going to flourish.”

He added, “We have a lot of work to do with the Department of Health’s National Institute for Health Research to build up the applicability of discovery into changes both in clinical practice and in drugs or other health interventions.”

Sir Leszek studied medicine at the Welsh National School of Medicine and took his first consultant’s post at Hammersmith Hospital, London. He has had a long association with the MRC. Early in his career he completed an MRC Clinical Training Fellowship, and between 1995 and 2000 he chaired the MRC Molecular and Cellular Medicine Board and served on the MRC Council.

Patients win right to have their

Clare Dyer BMJ

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 new advance decisions to refuse treatment (ADRTs) or risk criminal or civil proceedings in the courts.

The measure forms part of the Mental Capacity Act 2005, which from October 1 also gives individuals the right to create a lasting power of attorney by appointing a trusted friend or relative to take healthcare decisions for them in the event that they become incapacitated.

Advance directives or “living wills” to refuse treatments are already binding under common law, but the act sets up a statutory framework that

The new law should prevent disputes over the wishes of incapacitated patients, like the one that occurred in the Terri Schiavo case in Florida.
Trusts face spot checks if their treatment of elderly people gives cause for concern

Jacqui Wise LONDON

NHS trusts in the United Kingdom must ensure that older people are given care in a way that respects their dignity, and trusts will face spot checks where there is evidence for concern, the healthcare watchdog for England has warned.

The Healthcare Commission compiled a report from assessments at 23 NHS hospitals, surveys of 80,000 NHS inpatients, and nearly 130,000 NHS staff, the commission’s analysis of 10,000 complaints, and information on safety incidents from the National Patient Safety Agency.

The 23 hospitals inspected were chosen because of concerns about levels of care. Although no serious breaches of government standards were found, only five of the trusts were found to have fully complied with all the standards relating to dignity, privacy, and nutrition.

Eight trusts were given letters warning them that they were at risk of not meeting the standards and that they would be scrutinised carefully again next year. The remaining 10 trusts were told to make improvements.

The commission found that in some cases there were inadequate arrangements for providing privacy, such as curtains and locks on toilets and washing facilities. And although hospitals tried to avoid placing patients in mixed sex wards this still occurred, especially at busy times.

One in four complaints received by the Healthcare Commission was about poor nutrition.

See Observations p 698

Caring for Dignity is available at www.healthcommission.org.uk.

GMC says hospital at fault for failing to provide support

Owen Dyer LONDON

A consultant radiologist who failed to carry out breast examinations according to NHS guidelines was last week allowed to continue working under conditions, after a General Medical Council fitness to practise hearing found his employer had failed to provide adequate resources and support.

Lan Keng Lun missed warning signs and failed to carry out standard procedures on Ms A, a patient referred to him after an abnormal mammography result in March 2003. She was diagnosed as having breast cancer seven months later.

The Epping NHS Breast Screening Service in Essex also failed to meet national standards in the breast screenings of eight other women, the GMC found.

But an external review commissioned by the GMC found that the Princess Alexandra Hospital NHS Trust, which oversaw the facility, shared much of the responsibility for the serious service failure in their breast screening service.

advance decisions honoured by medical staff

An ADRT can be oral or written but if it is refusing life sustaining treatment, the law requires it to be in writing, signed and witnessed, and to include a statement that it is to apply even when life is at risk.

Ben Lobo, a consultant physician and community geriatrician who chairs the East Midlands ADRT Project Team and has been asked to help produce national guidance, said, “A valid advance decision has to be respected and acted upon by anybody including doctors, nurses, and ambulance staff. This new law will help to reduce stressful discussions between professionals and carers in times of medical crisis when the patient might be too ill to tell people. It will help people to die with dignity on their own terms.”

Paul Farmer, chief executive of the mental health charity Mind, said, “The Mental Capacity Act is an important development, introducing new safeguards to protect the rights of some of the most vulnerable people in our society. It gives people with mental health problems more control over their lives.”

Guidance on ADRTs is available on the BMA’s website and at www.adrt NHS.co.uk.
NHS continues to flout rights of disabled people to health care

Zosia Kmietowicz LONDON

Campaigners have repeated their call for more to be done to meet the health needs of people with learning disabilities and mental health problems—who, they say, continue to be failed by the NHS in England and Wales.

One year after its damning report into the delivery of health care to disabled people, the Disability Rights Commission, the statutory watchdog organisation for people with disabilities in England, Wales, and Scotland, says in a new report that little has changed to bridge the gap in health care.

Only two strategic health authorities in England—North East and South West—have developed adequate schemes to comply with new laws on disability equality that came into force in December 2006, says the report. Of the remaining eight, six have schemes that are unacceptable and two have failed to address the issue at all.

The report recommends that the Equality and Human Rights Commission, which took over the role of the Disability Rights Commission on 1 October, take legal action against those authorities that fail to produce acceptable schemes.

Equal Treatment: Closing the Gap—One Year On is available at www.drc-gb.org.

Doctors who give lethal injections should be punished, says Amnesty

Caroline White LONDON

Doctors and other healthcare staff who take any part in executions by lethal injection should be punished by their professional bodies, says the human rights organisation, Amnesty International.

In a report published to mark 25 years of the use of this method of execution, Amnesty says that leading professional organisations should push harder to outlaw the practice. The organisation opposes any form of capital punishment.

The practice is condoned in only six countries. But despite an overall fall in the numbers of lethal injections in four of these, it has become the execution method of choice in the United States, says the report.

There have been 919 such executions in the US since the method became legal in 1977 to the end of July this year. More prisoners are executed in China than anywhere else in the world, and the country increasingly views lethal injection as a more modern approach than death by shooting, says the report.

There are no official figures, but about 40% of executions are thought to use this method, with possibly thousands carried out to date, says the report.


Smoking rises as a risk factor in cot deaths:

The prevalence of smoking during pregnancy among mothers of babies who suffered sudden infant death syndrome rose from 50% in the late 1970s to 80% in the period 2003-6, while the rate among expectant mothers in the general population fell from 30% to 20%, a new report says (Early Human Development 2007 Sept 18 doi:10.1016/j.earlhumdev.2007.07.011).

Congo struggles with Ebola virus:

International efforts continued last week in the Democratic Republic of Congo to try to halt the spread of Ebola haemorrhagic fever. Of 24 confirmed cases, six people have died.

Global Fund donors pledge $9.7bn:

Donors to the Global Fund to Fight AIDS, Tuberculosis, and Malaria have given initial pledges worth $9.7bn (£4.7bn; €6.8bn) in new funds—including $1.27bn by France and $729m by the United Kingdom—to combat the three diseases over three years.

France acts on benefit deficit:

A non-reimbursable charge of €0.50 (£0.35; $0.70) will be added to every box of drugs in France in a series of measures to reduce a predicted social security deficit of €11.7bn in 2007 and €12.7bn in 2008.

Litigation payments for breast cancer care average £38 000:

About 2.4% of the total clinical claims received by the English National Health Service Litigation Authority relate to care of patients with breast cancer, according to a study covering 1995 to 2005. The highest payment was £634 194 (€911 575; $1 293 782) and the average £37 928 (Breast 2007 Sep 24 doi:10.1016/j.breast.2007.08.003).

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Eisai to appeal against court ruling on NICE:

Eisai, the company that holds the licence for donepezil (Aricept), announced last week that it would appeal against an English High Court ruling that upholds guidance from the National Institute for Health and Clinical Excellence (NICE) that denies the drug to NHS patients with mild Alzheimer’s disease (BMJ 2007;335:319).

IN BRIEF

Red Cross director acquitted of giving tainted blood: The former director of the Canadian Red Cross, Roger Perrault, and three other doctors were acquitted on Monday after a criminal trial in which they were accused of giving tainted blood to thousands of people with haemophilia who became infected with HIV or hepatitis C.

Eisai to appeal against court ruling on NICE: Eisai, the company that holds the licence for donepezil (Aricept), announced last week that it would appeal against an English High Court ruling that upholds guidance from the National Institute for Health and Clinical Excellence (NICE) that denies the drug to NHS patients with mild Alzheimer’s disease (BMJ 2007;335:319).

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Congo struggles with Ebola virus: International efforts continued last week in the Democratic Republic of Congo to try to halt the spread of Ebola haemorrhagic fever. Of 24 confirmed cases, six people have died.

Global Fund donors pledge $9.7bn: Donors to the Global Fund to Fight AIDS, Tuberculosis, and Malaria have given initial pledges worth $9.7bn (£4.7bn; €6.8bn) in new funds—including $1.27bn by France and $729m by the United Kingdom—to combat the three diseases over three years.

France acts on benefit deficit: A non-reimbursable charge of €0.50 (£0.35; $0.70) will be added to every box of drugs in France in a series of measures to reduce a predicted social security deficit of €11.7bn in 2007 and €12.7bn in 2008.

Litigation payments for breast cancer care average £38 000: About 2.4% of the total clinical claims received by the English National Health Service Litigation Authority relate to care of patients with breast cancer, according to a study covering 1995 to 2005. The highest payment was £634 194 (€911 575; $1 293 782) and the average £37 928 (Breast 2007 Sep 24 doi:10.1016/j.breast.2007.08.003).

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Australian efforts to tackle abuse of Aboriginal children without consultation raise alarm

Melissa Sweet SYDNEY
Aboriginal people in the Northern Territory (NT) are facing considerable changes to their lives, including loss of control of their lands and withheld welfare payments, as part of extensive new policies aimed at tackling the sexual abuse of children.

The Australian government’s “national emergency response” to an inquiry into the sexual abuse of indigenous children in the territory also involves widespread restrictions on alcohol, the abolition of a community employment scheme, and a ban on X rated pornography.

The government initially also announced plans to conduct compulsory checks on the sexual health of Aboriginal children, but after an outcry from health and medical groups it is now organising optional general health checks.

The intervention, announced on 21 June without consultation with indigenous or medical groups, was followed by the rushed passage in August of enacting legislation. It has provoked alarm among many indigenous and public health experts as well as human rights and legal groups.

There is widespread support for some long overdue political attention to the problem of child abuse, which many reports have documented over the past 20 years. Some aspects of the intervention, including the provision of extra police and health services, are also generally supported.

But many experts are concerned that overall the NT intervention, as it is called, may do more harm than good by undermining Aborigines’ control over their lives and connection to their land.

Pat Anderson and Rex Wild, QC, the authors of the report Little Children are Sacred, which prompted the intervention, told a recent forum on indigenous health that their 97 recommendations bore little relation to the government’s response. Indeed their first recommendation emphasises the importance of “genuine consultation” with Aborigines.

Ngiare Brown, a prominent indigenous doctor at the Menzies School of Health Research, in Darwin, told the forum at the Garma festival, in Arnhemland, that the “punitive” intervention had been developed “in a complete policy and strategic vacuum”; violated the principle to first do no harm; and had left many families and communities frightened.

“We don’t empower people by removing their control,” Dr Brown said. “We don’t overcome poverty by stripping them of their land and assets. It is patent fiction to link land rights to child protection.”

A spokesman for the Australian Indigenous Doctors’ Association, which represents indigenous and public health experts as well as human rights and legal groups.

“The report called not for the declaration of war . . . but for a thoughtful consultative process that stands some chance of leading to change”

about 120 doctors and 120 medical students, told the BMJ that the intervention was making many Aborigines “worried sick.”

The Congress of Aboriginal and Torres Strait Islander Nurses also warned that the intervention was creating “fear, confusion, and uncertainty.” It ignored international evidence about the importance of land rights and community controlled services in improving health, tackling social inequality, and developing successful indigenous communities.

“Children are being used as an excuse for an intervention that is disempowering the very communities it purports to assist,” the congress said in a statement issued at its conference in Alice Springs last month.

Fran Baum, a commissioner in the World Health Organization’s Commission on the Social Determinants of Health and professor of public health at Flinders University, in Adelaide, said that the government had used “a report that bravely named and respectfully described the problem of child sexual abuse to launch what is seen as an offensive, an attack, an assault on fragile Aboriginal communities.”

“The report recognised that there has to be change but that this was only likely if Aboriginal people are listened to and respected—the basis of any functional relationship.”

Concerns are widespread that the intervention, announced in a heated pre-election climate, will not translate into long term sustainable solutions despite its likely billion dollar cost.

Oxfam Australia said the lack of consultation raised questions about the intervention’s likely impact. “It would have had a greater chance of sustainable success if there’d been a fuller engagement with Northern Territory Aboriginal people,” the agency’s executive director, Andrew Hewett, told the BMJ.
**SHORT CUTS**

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

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

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**Treating depression is good for business**

About one in six US adults gets depressed at some point in their life. Many of them become ill during their working lives, which costs the US economy billions of dollars a year in lost productivity. Large companies clearly have a financial stake in improving the mental health of their employees, although few take much of an interest at the moment.

A recent trial may help attract their attention. An intervention that screened workers in 16 US companies helped them access treatment for depression, monitored their progress, and provided psychotherapy over the telephone. The intervention had a measurable effect on working hours and job retention as well as symptoms. Employees in the intervention group worked two hours extra a week on average compared with controls who had usual care. They were also more likely to get better (relative odds of recovery 1.4, 95% CI 1.1 to 2.0) and to keep their jobs (92.6% vs 88.0%; odds ratio 1.7, 1.1 to 3.3).

The trial lasted for one year.

The authors have yet to conduct a detailed analysis of costs. But at a glance the sums look favourable. The intervention saved about $1800 (£890; €1270) per worker each year and cost $100-$400 per worker each year. *JAMA* 2007;298:1401-11

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**Too much salt takes its toll in the US**

The US is lagging behind international efforts to reduce the amount of salt in processed foods and restaurant meals, say health policy experts, and the population is paying a high price. Earlier this year the World Health Organization described as “conclusive” the evidence that excessive dietary sodium causes hypertension. In the US, sodium intake has increased by over 50% since 1970, and the lifetime prevalence of hypertension now approaches 90%. The result is a substantial death toll from cardiovascular disease.

Other countries, notably the UK, Ireland, Finland, and Australia have already made a start by setting national targets, educating the public, and using both carrots and sticks to encourage food manufacturers to comply with voluntary regulations. Better food labelling is one common strategy.

US regulators should follow suit urgently, say the experts, preferably by repealing the Food and Drug Administration’s designation of salt as “generally recognised as safe.” If salt lost its privileged status, food manufacturers would have to seek the FDA’s approval to add salt to food, and the FDA would have to set agreed limits.

Experts estimate that if Americans ate 50% less sodium, their systolic blood pressure would drop by a collective 5 mm Hg, which would prevent around 150000 deaths each year from cardiovascular disease. *JAMA* 2007;298:1439-41

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**Heart failure associated with thiazolidinediones doesn’t reduce survival**

A meta-analysis of seven randomised trials has confirmed that rosiglitazone and pioglitazone increase the risk of heart failure in patients with type 2 diabetes (relative risk 1.72, 95% CI 1.21 to 2.42). Fluid retention is the most likely cause, say the authors. Both drugs increase plasma volume. They also speculate that these adverse effects are benign, as they don’t seem to reduce patients’ survival. In this meta-analysis of data from more than 20000 patients, neither drug increased the risk of death from cardiovascular disease compared with placebo or an active control (0.93, 0.67 to 1.29).

**Mercury in thimerosal is unlikely to damage children’s development**

Thimerosal is a preservative used in some vaccines. It contains almost 50% mercury by weight and is at the centre of a long running controversy in the US about the harm it might do to children. In 1999, vaccine manufacturers were asked to phase out thimerosal from their products, but in the meantime researchers have been looking hard for evidence of neurological harm. So far, they have found little.

The latest study analysed multiple neuropsychological tests done by 7-10 year olds after routine immunisation. It found little evidence of a link between thimerosal and any adverse long term effect. (Lancet 2007;370:1129-36)

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**RISK OF CONGESTIVE HEART FAILURE WITH THIAZOLIDINEDIONES**

<table>
<thead>
<tr>
<th>Risk ratio (95% CI)</th>
<th>Weight (%</th>
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<tr>
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<tr>
<td>Rosiglitazone v placebo</td>
<td>7.3</td>
<td>1.81 (0.55 to 6.02)</td>
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<tr>
<td>Pioglitazone v glimepiride</td>
<td>1.1</td>
<td>2.97 (0.12 to 72.63)</td>
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<tr>
<td>Pioglitazone v placebo</td>
<td>49.0</td>
<td>1.31 (1.03 to 1.67)</td>
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<td>2.24 (1.27 to 3.96)</td>
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<td>100.0</td>
<td>1.72 (1.21 to 2.42)</td>
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Adapted from *Lancet* 2007;372:1129-36

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**NEWS**

692 BMJ | 6 OCTOBER 2007 | VOLUME 335
Low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol are both important determinants of cardiovascular risk. Doctors treating patients with heart disease tend to concentrate most of their efforts on bringing down serum concentrations of LDL cholesterol with statins. But HDL cholesterol matters too, even in patients with LDL cholesterol concentrations below the recommended targets.

In a reanalysis of data from one statin trial, researchers found a clear inverse relation between the risk of serious cardiovascular events and HDL cholesterol concentration in patients with heart disease who were taking atorvastatin. Patients were divided into five groups according to HDL concentration. Patients in the highest fifth were significantly less likely to have heart attacks or strokes or to die from coronary disease than those in the lowest fifth. The inverse relation persisted across all concentrations of LDL cholesterol and in a subgroup of patients with concentrations of LDL cholesterol below 1.8 mmol/l (hazard ratio 0.61; 95% CI 0.38 to 0.97 when comparing the highest fifth with the lowest fifth).

These findings suggest that the two types of cholesterol can independently predict serious cardiovascular events in patients treated with statins, say the authors. The 9770 patients in this trial took either 10 mg or 80 mg atorvastatin a day. *N Engl J Med* 2007;357:1301-10

**Bird flu can cross the placenta in pregnant women**

The avian flu virus H5N1 tends to target the lungs, causing overwhelming and often fatal alveolar damage in infected humans. Researchers using sensitive molecular techniques have also found traces of the virus in other organs, most recently in the brain, intestines, and lymph nodes of two Chinese patients. One of them, a 24 year old woman, was four months pregnant when she died. At autopsy, the researchers found evidence of the virus in the baby’s lungs, circulation, and liver. Vertical transmission from the mother is the likeliest explanation, and it sets H5N1 apart from common human flu viruses, which are thought to be harmless to the fetus.

The presence of H5N1 in the intestine fits well with the diarrhoea that often accompanies the infection, says a linked comment (p 1106). Others have already reported viral RNA in faecal samples from infected people, with obvious implications for controlling spread of the disease.

It now seems clear than H5N1 spreads far beyond the lungs in humans and may even cross the blood-brain barrier. We still don’t know why the infection is so lethal, but it may be something to do with our immune response. The immunologically naive fetus in this report was infected but had no organ damage. *Lancet* 2007;370:1137-45

**Coronary heart disease and colorectal lesions often coexist**

Coronary artery disease and colorectal neoplasms share several risk factors including poor diet, obesity, smoking, and the metabolic syndrome. So it makes sense that the two diseases might coexist. In a cross sectional study from Hong Kong, Chinese researchers found more cancers and adenomas in adults with coronary heart disease than in controls who were clear of the disease. The link persisted when they compared patients with coronary artery disease with age and sex matched controls from the general population.

The researchers started with a group of men and women who needed coronary angiography for suspected coronary artery disease. All of them then had a colonoscopy. Just over a third of the 206 adults with a positive angiogram had either an adenoma or a cancer (34%, 70/206) compared with 19% of those with a negative angiogram (39/208) and 21% (43/207) of population controls (P<0.001 for both comparisons). For cancer alone the figures were 4% (9/206), 0.5% (1/208), and 1% (3/207) (P=0.02).

In this study, the link between heart disease and colonic neoplasms was strongest in patients who smoked or had the metabolic syndrome, a well defined cluster of at least three cardiovascular risk factors. *JAMA* 2007;298:1412-9

**Risk of venous thromboembolism after a long haul flight is less than one in 5000**

Long haul flights roughly triple travellers’ baseline risk of a symptomatic venous thrombosis. But for most people the absolute risk remains low—less than one event for every 5000 flights, according to a study of international corporate employees.

The researchers used records of business travel kept by international companies, combined with a web survey of 8755 employees, to calculate the risks associated with flights longer than four hours.

As expected, the incidence of deep vein thrombosis or pulmonary embolus was three times higher during the eight weeks after a long haul flight than at other times (incidence rate ratio 3.2, 95% CI 1.8 to 5.6). The absolute risk of an event was one for every 4656 flights, but the authors found a clear dose response effect—the longer the flight, the higher the risk. Frequent flying was also associated with a greater likelihood of venous thrombosis. The risks were highest in women—especially those taking oral contraceptives—short people, and tall people. Perhaps airlines should be encouraged to fit adjustable seats, say the authors, so tall people don’t have to sit with their legs dangling off the floor. Both problems could conceivably put pressure on the poplitial vein. *PloS Med* 2007;4:1508-14
Industry funded patient information and the slippery slope to New Zealand

Industry funded health information campaigns could become common on our screens if European Commission proposals are passed. Les Toop and Dee Mangin warn that Europe could end up with similar problems to those in their country.

The European parliament is considering allowing the drug industry to have a much greater role in providing information to patients, with no restriction on the type of media. After direct to consumer advertising was rejected in 2002, industry and the commercial arm of the European Commission submitted a new proposal to allow communication between industry and patients that deliberately leaves out the word advertising and replaces the term independence (freedom from commercial influence) with objective. Information can be entirely objective and yet still mislead through incompleteness or lack of balance and context. Opponents believe that industry will not, and cannot be expected to, provide balanced, comparative, and comprehensive information, and that the proposals amount to advertising by stealth.

In New Zealand and the US, the only two developed countries that allow direct to consumer advertising of prescription medicines, opposition has grown steadily from both the public and doctors. New Zealand’s health system is much closer to those in Europe than the US system. So what can we learn from its experience?

Rise of advertising
Unlike most other developed countries, New Zealand never enacted pre-emptive legislation to prevent direct to consumer advertising. The adverts started appearing in the early 1990s, and steadily increased. But the US Food and Drug Administration’s relaxation of regulatory requirements for broadcast advertising in 1997, unleashed an explosion in both the US and New Zealand. Last year drug companies spent over $5bn (£2.5bn; €3.6bn) on direct to consumer advertising in the US and tens of millions of dollars in New Zealand.

Opposition grew alongside the advertising, particularly in the women’s movement as many of the promoted products were fertility and hormonal preparations. By 2000 New Zealand and US health watchdog groups were becoming more vocal. Doctors were slower to react, probably because initially there was not enough advertising to have a great impact on them.

A limited review of advertisements in 2000 showed poor compliance with the guidelines. The rising concern led the New Zealand Ministry of Health to start a public consultation in the same year. The responses were predictable: independent consumer groups against, those with a vested interest supporting its continuation. But because the analysis was based purely on numbers—and there were many more submissions from advertisers and drug companies than from consumer voices—the advertising was allowed to continue with self regulation. This comprised industry vetting of adverts for format and style and a complaints systems that could recommend withdrawal of objectionable or misleading advertisements. The central regulator Medsafe effectively distanced itself from day to day monitoring with no responsibility and at no cost to the state. A promised further review of compliance with the rules never took place.

Adverts are not independently assessed for balance or the scientific validity of the claims unless someone complains

Adverts are not independently assessed for balance or the scientific validity of the claims unless someone complains. As an example, a few brief television commercials for the antifungal terbinafine (promoted for onychomycosis) resulted in a doubling of national prescriptions. Refecoxib and celecoxib were heavily and effectively promoted to the public in New Zealand, despite the awareness of their cardiac risks. The adverts targeted specifically at elderly people with osteoarthritis. As it turned out, this was the group most at risk of the harmful cardiac adverse effects that eventually led to the withdrawal of refecoxib.

In 2002 the marketing arm of Glaxo ran a major television campaign which “informed” people taking the popular branded beclomethasone inhalers that the medicine was to be withdrawn and they should visit their doctors to ask to switch to fluticasone. Doctors and New Zealand’s health funding agency (PHARMAC) thought that the campaign contained several misleading elements and distressed many patients. The unnecessary additional workload and difficult consultations infuriated many general practitioners. Nevertheless, the campaign was highly effective and sales of the more expensive fluticasone skyrocketed. An unintended consequence was an almost twofold increase in the doses of inhaled steroids prescribed.

Spurred by the professional outcry, a group of academic general practitioners assessed the literature on the public health effects of direct to consumer advertising. It presented the conclusions to government, with a further call for a ban on advertising. As part of this advocacy the report’s authors also canvassed the views of all New Zealand general practitioners on direct to consumer advertising. Such was the strength of feeling that within 10 days, half of
them had responded to a single mailing. Four fifths of the 1600 respondents were critical of consumer advertising, believing it harmed the doctor-patient relationship and public health. The report drew a swift and forceful reaction from the drug and advertising industries, resulting in several complaints to ethics committees and to the host university. None of these complaints were upheld.

Between 2002 and 2004 almost all health professional groups in New Zealand (including academic pharmacy) issued position statements calling for a ban of direct to consumer advertising and the provision of centrally funded independent consumer health information. But while the New Zealand government was considering its position, a wave of surveys broke out, with marketing academics producing evidence that consumers and doctors liked the advertising and opponents producing evidence to the contrary. As always these surveys triggered criticism and counter criticism of sample sizes and response rates and accusations of bias. An almost identical debate has played out in the US, where successive consumer surveys by the FDA show an increasingly negative attitude to drug advertising. The surveys all show that consumers prefer to get information from health professionals and that they dislike being misled. Worryingly, although consumers mistrust advertising, they still act on it. A survey in the US showed many erroneously assume that some state agency ensures that information in advertisements is balanced, accurate, and truthful and that only medicines that are 100% safe are allowed to be advertised.

Even some prominent New Zealand marketing academics who have studied the effects of advertising on consumer knowledge have moved from initial support to opposition: “The advertising and pharmaceutical industries’ failure to respond to well-documented concerns about DTCA raises serious questions about the power of policy refinements to control advertisers’ conduct.”

Back tracking
In response to evidence of mounting concern from the public and the professions, the New Zealand government resolved to ban direct to consumer advertising in late 2003. The easiest mechanism seemed to be to include a ban in the omnibus legislation being drafted to set up a joint Australia-New Zealand Trans Tasman agency for the regulation of all therapeutic goods. Advertising of drugs to the public is prohibited by law in Australia. To date the government has been unable to pass the necessary legislation.

In early 2006 the New Zealand Ministry of Health decided to run a further round of public consultation canvassing the views of consumers and other stakeholders. Analysis of the individual submissions obtained under the official information act shows the political mandate for a ban on direct to consumer advertising was clearer than ever. There is almost complete (90%) opposition from independent consumer and patient organisations. Nearly two thirds of all submissions oppose advertising. And two thirds of the supporting submissions were from groups who profit from drug sales (drug companies, pharmacists, advertisers, marketers) while an additional 5% were from groups that have publicly declared receiving funding from the drug industry.

The lesson from the New Zealand experience for Europe is clear. Pandora’s irresistible jar contained within it the misfortunes of mankind. Europe is staring at the lid of pharma’s jar and, once opened, hope alone will not be enough to undo the damage. Having seen what lies inside, Europe should find nothing in there to tempt it to take this risk. Allowing industry funded objective information will serve only to manipulate consumer choices. It will not help consumers make better decisions about medicines but will increase the pharmaceuticalisation of health and will expose more of the population to new medicines (many of which offer little benefit over existing medicines) at a time when long term safety is unknown. It will also rapidly drive up drug costs with major implications for already stretched health budgets—all of which will be of net harm to the overall public health.

If the driver for the European legislation was truly the information needs of patients, rather than the needs of industry to boost sales, the recommendations might have been different. The goal should be a global collaborative commitment to facilitate access to the independent information prescribers and consumers need to be able to make decisions about medicines.

Les Toop, professor, Dee Mangin, senior lecturer, Department of Public Health and General Practice, University of Otago, Christchurch, New Zealand

Correspondence to: L Toop les.toop@otago.ac.nz

Competing interests: LT and DM have both received funding from PHARMAC and from general practitioner organisations for organising and speaking at seminars on rational prescribing and innovative models of extended primary care. LT has received funding for speaking on DTCA to the National Prescribing Service in Australia. DM is a member of the Healthy Skepticism management group. Both have actively campaigned for the provision of independent consumer health information and the banning of direct to consumer advertising in New Zealand.
Should general practitioners resume 24 hour responsibility for their patients?

Roger Jones  Wolfson professor of general practice, Department of General Practice and Primary Care, King’s College London, London SE1 6SP  roger.jones@kcl.ac.uk

YES

New contractual arrangements to encourage practices to opt back into 24 hour responsibility and to support general practitioners who choose to discharge this responsibility personally would have many benefits. The change would begin to redress the increasing separation of daytime, surgery based care from out of hours care provided by deputising services. These arrangements would also improve general practice training; greatly increase the quality and appropriateness of out of hours care, particularly in terms of hospital admissions and appropriate use of services by patients; and enhance patient safety by improving the communication of important clinical information. They would be widely welcomed not only by patients but also by other sectors of the medical profession, and are also likely to be cost effective.

Sick system

The background to this debate is the new contract for general practitioners introduced in 2004, which allowed practitioners to opt out of 24 hour responsibility. In a recent article suggesting that out of hours primary care in the UK was becoming a shambles, Heath pointed out that the new contract provided little money for practices that wanted to continue to cover out of hours care, effectively forcing them to opt out. This has led to a situation in which the best trained general practitioners concentrate their efforts on daytime care, while patients who become ill at night risk being seen by less experienced doctors without the depth of background knowledge needed to make the most appropriate decisions about management, including hospital admission. Not only does a parallel out of hours service lead to fragmentation of care and potentially dangerous communication errors, it is likely to be more expensive, in terms of both running costs and unnecessary inpatient costs.

Complaints about out of hours general practice care have risen sharply in the past two years. The Medical Protection Society opened 30 cases related to out of hours care in 2003 and 100 in 2006 (personal communication). Many of these complaints relate to poor doctor-patient communication (including rudeness) and to diagnostic delay and error. The second Wanless report has linked a recent steep rise in accident and emergency attendances to changes in general practice out of hours arrangements. Audit Scotland has recently declared the out of hours services in that country to be financially unsustainable.

International experience

These difficulties are not restricted to the UK. Six years ago Dutch general practitioners gave up personal responsibility for out of hours services, many with mixed feelings, and now a subgroup of patients is emerging who use the service for routine primary care consultations. Patients are often seen by recently trained doctors with little experience and no personal connection to their general practitioner. In Australia and New Zealand general practitioners are still responsible for 24 hour cover, which is usually contracted to out of hours services of varying quality. Some cover is provided by doctors who have made career decisions to work in out of hours services, avoiding the responsibilities of practice management and long term patient care. The Royal Australian College of General Practitioners has set out detailed requirements for the arrangements that practices are required to make when delegating their 24 hour responsibility, including stringent guidelines for the communication of essential clinical information. There is evidence that in the UK quality assurance arrangements of this kind do not always work well, and that patient satisfaction is often not assessed.

I am not suggesting that all general practitioners resume out of hours responsibility for their entire professional life. And I am certainly not supporting the view that surgeries should be open at all hours for routine care—this entirely misses the point. However, during vocational training and in the early years of practice, seeing patients in their homes, assessing acute medical problems—particularly in areas where paramedical services are not readily available—and making appropriate decisions about treatment and hospital referral should be regarded as core aspects of training and professional development, just as they are in hospital medicine. Younger doctors, more able to tolerate broken sleep, may also be more interested in earning additional income by taking part in out of hours rotas for their practices, and more senior doctors may also wish to maintain patient contact.

In parts of Canada, regional health authorities help general practitioners to form networks in which out of hours care is shared between practices, and in which trainees in family medicine, supervised by experienced primary care doctors, are first on call. Heath suggested that the NHS should be able to devise and fund a system of out of hours care based on smaller rotas of general practitioners covering smaller populations, so that the possibility of some sort of continuity—of hearing a familiar voice or seeing a familiar face—is enhanced.

I have covered my practice at night in the rural south of England and in inner city areas of Southampton, Newcastle, and London. I have sometimes been concerned for my safety. I do not underestimate the difficulties of re-engaging with personal out of hours care but am convinced that for many doctors and patients a return to a more personal approach to 24 hour responsibility would reap enormous benefits.

Competing interests: None declared.
Complaints about the care provided by out of hours services in the UK are growing. Roger Jones thinks that general practitioners should take back the role, but Helen Herbert believes their efforts would be better focused on improving current systems.

The question should not be whether general practitioners should take 24 hour contractual responsibility for their patients; rather we should be calling on primary care organisations to take creative and innovative action to engage providers, including general practices, to provide good local solutions. Several organisations have done this already so why not the rest? Access to good quality care should be the preserve of all, not just the lucky few.

Danger of long hours
The relinquishing of out of hours responsibility has led to accusations that general practitioners do not care about their patients. But it is precisely because we want the best care for patients that the change was made. Surely it cannot be in the interests of patients for doctors to work all day, be up most of the night on call, and then work through another full day in surgery. Sleep deprived people should not be making life threatening decisions. Lorry drivers and airline pilots would not be allowed to do that. Sleep deprivation on performance the next day.2 When I began in my practice 25 years ago, I worked a one in three rota, caring for 6000 patients covering an area of over 200 square miles. During the long periods on call, I worked alone without any team support. Often in a state of exhaustion, I would be called time and time again from my barely warm bed. Understandably, patients preferred the immediate contact with a known and trusted general practitioner, but many needed direction in the appropriate use of services and the system was open to abuse.

General practitioners are blamed unfairly for the state of out of hours services when the responsibility for commissioning and providing these services resides with primary care organisations. Although many do provide an excellent out of hours service, some services are confusing and fragmented and patients are often unable to determine the most appropriate service to access. The lack of clear signposting is a big problem, and we must urge primary care organisations to take action. As experts in providing out of hours care, general practitioners are the solution to improving urgent care services, not the problem.

Delegation not abdication
Recognising this, the Royal College of General Practitioners has published a position statement on urgent care, recommending that services are designed around the clinical needs of patients.3 It states that patients should expect to receive a consistent and rigorous assessment of their needs and an appropriate and prompt response to that need—regardless of who is administering their care. Crucially, the action plan calls for better signposting for access.

WHERE DO YOU STAND ON THE ISSUE?
Tell us on bmj.com

Sleep deprived people should not be making life threatening decisions.

Where out of hours care is properly organised and resourced, it works well, and many studies have shown high satisfaction with the care provided.4 5 However, we must not be complacent when this care does not come up to the standards that our patients deserve. It is necessary to continually monitor not only the process but the outcome of the care, including patient satisfaction and effect on other services such as the ambulance service, accident and emergency departments, and social and secondary care.6 7

Nowhere is the need for good out of hours care better exemplified than for patients requiring end of life care. Being ill in the middle of the night can be a frightening and lonely experience for patients and carers alike. There are many excellent models facilitating systematic, anticipatory care in primary care and nursing homes8 with evidence of positive measurable outcomes such as the doubling of home death rates and reduction in hospital deaths. General practitioners continue to use their professionalism by identifying those patients likely to require out of hours care and anticipating their needs: providing drugs in the patients’ homes, communicating with the out of hours providers, possibly sharing personal telephone numbers, and following up relevant consultations the following morning.9

Continuity and accessibility remain important professional values of general practitioners. The profession made the difficult decision to withdraw provision of out of hours care to ensure the safety of our patients and recruitment of future generations of doctors, but we must maintain responsibility for these values by providing excellence in anticipatory care and by influencing the providers, commissioners, and policy makers to ensure provision of the high standards of care that we expect for our patients. Our advocacy role remains as important as ever, and we must champion optimal standards of out of hours care for our patients.

Competing interests: None declared.
All references are on bmj.com

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An age old problem

New treatment, new laws—but will either help elderly people?

“How a society treats its elderly people is a yardstick of its civilisation,” said the world’s oldest man, who celebrated his 112th birthday last month. Inevitably, Tomoji Tanabe (one of Japan’s 30 000 centenarians) was asked about the secret of his longevity. “Avoiding alcohol and maintaining a daily regime to keep me young” was his reply. Dying was not on his agenda, he said; he wanted to live indefinitely.

If most of us experienced old age in such a positive way we could perhaps simply sit back and marvel at our species’ increasing longevity. Sadly, this is not the case, and governments in nearly all countries are waking up to the fact that their ageing populations pose formidable economic, social, and health challenges.

The latest UN Report on World Ageing (executive summary www.un.org/esa/population/publications/WPA2007/wpp2007.htm) shows the scale and pace of what some term the demographic tsunami. World population is increasing at 1.1% a year, but the number of people over 60 is increasing at 2.6%. The number of people over 60 tripled between 1950 and 2000, and it is projected to triple again by 2050. The fastest growing sector is the “oldest old,” defined as 80 and over.

A figure that worries economists is the dependency ratio—the number of people aged 15-64 for each person aged over 65. Between 1950 and 2007, this declined from 12:1 to 9:1; the projected figure for 2050 is 4:1. These statistics are worrying politicians. Vladimir Putin has described demographic change as “Russia’s biggest problem”; Jose Manuel Barroso, president of the European Commission, says it is one of Europe’s major challenges.

Amid the discussions on how global ageing will affect economic growth, labour markets, migration trends, pensions, housing demand, health services … the list goes on, is a fascinating one on the potential of regenerative research to “combat” it. In a thought provoking paper in the Scientist (March 2006; www.g3.org/resources/TheScientist.html) the authors, which include Jay Olshansky, professor of public health at the University of Illinois, present readers with two scenarios: carry on as we are and be overwhelmed by increases in frailty, disability, and costly age related diseases such as Alzheimer’s, cardiovascular disease, and diabetes—or invest (hugely more) in research into ageing in the hope that it will deliver a new treatment to delay and compress morbidity and mortality.

Recent advances in biogerontology research indicate that this may well be achievable. The goal we should be striving for, Olshanksy told me when we talked at last month’s World Ageing Congress (http://tinyurl.com/ym7qau), is a treatment that will result in people aged 50 having the health profile and disease risk of today’s 43 year olds. This “longevity dividend” would bolster the economy: fit people spend longer as producers and consumers, and they demand less from health services.

Interestingly, in the animal experiments that extended the disease-free life of rats by 40%, the intervention included calorie restriction along with gene manipulation and changes to cell signalling pathways. The message for the obesity tsunami could scarcely be clearer.

Most medical research is focused on individual diseases. What gerontologists are calling for is a new paradigm where comparable effort and investment are put into investigating how ageing predisposes only some of us to develop chronic and disabling diseases. Their argument has persuaded the US budget appropriations committee to put pressure on the National Institutes of Health to increase funding for research into the biology of ageing. It’s not hard to see why: the committee estimates that the medical cost of chronic illness in the US will reach $16 trillion a year by 2030. Having an effective treatment to achieve what disease prevention and health promotion programmes are largely failing to do is an appealing idea. Baby boomers, who currently spend billions of dollars on ineffective anti-ageing products, will doubtless flock to buy it. But what about poor countries? These countries are “growing old before they grow rich.” For many, access to even essential medicines is limited. The prospect of people in poor countries benefiting from breakthroughs in ageing research seems vanishingly small.

Nor is it much comfort to those currently suffering from neglect and discrimination by virtue of their age. Their number is not captured in any global report, but insight into their plight comes from stories in the press and a steady stream of reports. One last week from the Healthcare Commission showed just how poorly NHS hospitals protect the privacy and dignity of elderly people (p 689).

Urging healthcare providers in either the public or private health sector to do better by elderly people is easy; finding a mechanism to ensure they do is harder. Some believe that the opportunity to seek legal redress under a new extension of the Human Rights Act may help. Among them is Trevor Phillips, head of the new Commission for Equality and Human Rights (Daily Telegraph 29 September 2007 www.telegraph.co.uk/news/main.jhtml?xml=/news/2007/09/29/nrights229.xml). How this will work will be discussed at a conference on health rights and human ageing on 16 October in London.

How a society treats its elderly people is a yardstick of its civilisation. The law seems a blunt weapon to counter the effects of societal breakdown, dislocation, and a lack of intergenerational respect and solidarity, but it might help a bit. That said, I think I’ll give my money to the researchers, not the lawyers. One spin-off of healthy ageing is that you can fight your corner for longer.

Tessa Richards, assistant editor, BMJ trichards@bmj.com
Adding fluoride to water supplies

Adding fluoride to water supplies to prevent dental caries is controversial. K K Cheng, Iain Chalmers, and Trevor A Sheldon identify the issues it raises in the hope of furthering constructive public consultation and debate.

Several countries add fluoride to water supplies to prevent dental caries (boxes 1 and 2). Since the 2003 Water Act, water companies are required to add fluoride to supplies when requested—after public consultation—by a health authority in England or the Welsh Assembly in Wales. Plans to add fluoride to water supplies are often contentious. Controversy relates to potential benefits of fluoridation, difficulty of identifying harms, whether fluoride is a medicine, and the ethics of a mass intervention. We are concerned that the polarised debates and the way that evidence is harnessed and uncertainties glossed over make it hard for the public and professionals to participate in consultations on an informed basis. Here, we highlight problems that should be confronted in such consultations and emphasise the considerable uncertainties in the evidence.

Known benefits of adding fluoride to water

In 1999, the Department of Health in England commissioned the centre for reviews and dissemination at the University of York to systematically review the evidence on the effects of water fluoridation on dental health and to look for evidence of harm. The review was developed with input from an advisory committee, which included members who supported and opposed fluoridation, or who had no strong views on the matter. Exceptional steps were taken to avoid bias and ensure transparency throughout.

Given the certainty with which water fluoridation has been promoted and opposed, and the large number (around 3200) of research papers identified, the reviewers were surprised by the poor quality of the evidence and the uncertainty surrounding the beneficial and adverse effects of fluoridation.

Studies that met the minimal quality threshold indicated that water fluoridation reduced the prevalence of caries but that the size of the effect was uncertain. Estimates of the increase in the proportion of children without caries in fluoridated areas versus non-fluoridated areas varied (median 1.5%, interquartile range 5% to 22%). These estimates could be biased, however, because potential confounders were poorly adjusted for.

Water fluoridation aims to reduce social inequalities in dental health, but few relevant studies exist. The quality of research was even lower than that assessing overall effects of fluoridation. The results were inconsistent—fluoridation seemed to reduce social inequalities in children aged 5 and 12 when measured by the number of decayed, missing, or filled teeth, but not when the proportion of 5 year olds with no caries was used.

Potential harms of fluoridation

The review estimated the prevalence of fluorosis (mottled teeth) and fluorosis of aesthetic concern at around 48% and 12.5% when the fluoride concentration was 1.0 part per million, although the quality of the studies was low. The evidence was of insufficient quality to allow confident statements about other potential harms (such as cancer and bone fracture). The amount and quality of the available data on side effects were insufficient to rule out all but the biggest effects.

Small relative increases in risk are difficult to estimate reliably by epidemiological studies, even though lifetime exposure of the whole population may have large population effects. For example, an ecological study from Taiwan found a high incidence of bladder cancer in women in areas where natural fluoride content in water is high. The authors attributed the finding to chance because multiple comparisons were made. Testing the hypothesis that drinking fluoridated water increases the risk of bladder cancer would need to take account of errors in estimating total fluoride exposures; potential lack of variation in exposure; the probable long latency between exposure and outcome; the
Box 1 | Dental caries
What is dental caries?
Dental caries is a process of demineralisation of dental hard tissue caused by acids formed from bacterial fermentation of sugars in the diet. Demineralisation is countered by the deposit of minerals in the saliva—remineralisation. Remineralisation is a slow process, however, which has to compete with factors that cause demineralisation. If remineralisation can effectively compete the enamel is repaired. If demineralisation exceeds remineralisation a carious cavity finally forms. Fluoride prevents caries by enhancing remineralisation.

How common is caries?
The figure shows the average numbers of decayed, missing, and filled teeth in 12 year old children for several European countries. In most countries this number is around 1.5 and 50% of children have no caries. Although the prevalence of caries varies between countries, levels everywhere have fallen greatly in the past three decades, and national rates of caries are now universally low. This trend has occurred regardless of the concentration of fluoride in water or the use of fluoridated salt, and it probably reflects use of fluoridated toothpastes and other factors, including perhaps aspects of nutrition.

Box 2 | Exposure to fluoride
How common are water supplies containing fluoride?
About 9–10% of water supplies in England and Wales contain 0.5–1 mg/l fluoride, either naturally or as an additive.2–4 Limited fluoridation trials were introduced in England from the mid-1950s, but resistance by water companies curtailed their spread. Currently, 1.5 million people receive water containing fluoride drawn from ground that is relatively high in the mineral. Another five million people in parts of the West Midlands, Yorkshire, and Tyneside receive water with added fluoride (1 mg/l). Fluoride is not added to water supplies in Scotland, Wales, or Northern Ireland. In Western Europe 12 million people receive water with added fluoride, mainly in England, Ireland, and Spain.1 In the United States, just under 60% of the population receive fluoridated water.4 Water fluoridation has also been introduced in Australia, Brazil, Chile, Colombia, Canada, Hong Kong Special Administrative Region of China, Israel, Malaysia, and New Zealand. Worldwide, about 5.7% of people receive water containing fluoride to around 1 mg/l.5 In some countries such schemes have been withdrawn. These include Germany, Finland, Japan, the Netherlands, Sweden, and Switzerland. Systematic information on the rationale behind these decisions is not available. In the Swiss canton of Basel-Stadt, the fluoridation scheme was withdrawn in 2003 after 41 years of operation because other measures were of “comparable effectiveness” to “compulsory medication”.7

What are the sources of fluoride exposure?
Before the widespread use of fluoride containing toothpastes, fluoride in water (natural or fluoridated) was the main source of exposure in adults and children.6 Although the relative contribution from toothpaste has increased, in fluoridated areas drinking water remains the main source of exposure. Young children are more likely to ingest fluoridated toothpaste, so its relative importance as a source of exposure is higher in children than in adults.
should be aware of the limitations of evidence about its potential harms and that it would be almost impossible to detect small but important risks (especially for chronic conditions) after introducing fluoridation.

**Alternative ways to prevent caries**

The evidence from systematic reviews of randomised trials is strong for alternative ways of preventing caries—mainly toothpastes containing fluorides. Analysis of 70 randomised trials of 42,300 children yielded a pooled preventive fraction for decayed, missing, or filled teeth of 24% (21% to 28%). However, the use of toothpaste depends on individual behaviour, which has implications for reducing inequality.

**Is fluoride added to water supplies a medicine?**

Fluoride is not in any natural human metabolic pathway. Because it mainly reduces caries by remineralisation of demineralised enamel (box 4), some people regard water fluoridation as a form of mass medication. Other people point out that fluoride occurs naturally at concentrations comparable to those used in fluoridation programmes and is therefore not a medicine. If viewed as a medicine, water fluoridation would require approval from a relevant authority.

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**Box 3 | Key recommendations for future research on water fluoridation**

- “Studies are needed to provide estimates of the effects of water fluoridation on children aged 3-15 years against a background of widespread use of fluoride toothpaste, and to extend knowledge about the effect of water fluoridation by... (socio-economic status), taking into account potentially important effect modifiers such as sugar consumption and toothpaste usage"13
- “A robust evaluation of the benefits of water fluoridation, as well as the potential risks of fluorosis... should be a health priority"15

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The legal definition of a medicinal product in the European Union (Codified Pharmaceutical Directive 2004/27/EC, Article 1.2) is any substance or combination of substances “presented as having properties for treating or preventing disease in human beings” or “which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action.” Furthermore, in 1983 a judge ruled that fluoridated water fell within the Medicines Act 1968, “Section 130 defines ‘medicinal product’ and I am satisfied that fluoride in whatever form it is ultimately purchased by the respondents falls within that definition.”16

If fluoride is a medicine, evidence on its effects should be subject to the standards of proof expected of drugs, including evidence from randomised trials. If used as a mass preventive measure in well people, the evidence of net benefit should be greater than that needed for drugs to treat illness.17 An important distinction also exists between removing unnatural exposures (such as environmental tobacco smoke) and adding unnatural exposures (such as drugs or preservatives).18 In the second situation, evidence on benefit and safety must be more stringent. There have been no randomised trials of water fluoridation.

**Ethical implications**

Under the principle of informed consent, anyone can refuse treatment with a drug or other intervention. The Council of Europe Convention on Human Rights and Biomedicine 199719 (which the UK has not signed) states that health interventions can only be carried out after free and informed consent. The General Medical Council’s guidance on consent also stresses patients’ autonomy, and their right to decide whether or not to undergo medical intervention even if refusal may result in harm.20 This is especially important for water fluoridation, as an uncontrollable dose of fluoride would be given for up to a lifetime, regardless of the risk of caries, and many people would not benefit. The convention makes provision for exceptions to the principle of informed consent if necessary for public safety, to prevent crime, or to protect public health (article 26).20 Potential benefit must therefore be balanced against uncertainty about harms, the lower overall prevalence of caries now than a few decades...
Contributors and sources: All authors contributed to the original idea of the paper and its writing. TAS chaired the CRD fluoride review advisory panel. IC was a member of the same panel. KKC lives in Birmingham where the water is fluoridated. The sections on potential benefits and harms of water fluoridation are largely based on a systematic review and recent materials identified through Medline searches. The rest of the paper reflects the authors’ opinion. KKC is guarantor.

Competing interests: Please see the Contributors and sources section.

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

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Box 4 | Effect of fluoride on the association between sugar and caries

Fluoride is the main factor that alters the resistance of teeth to acid attack and interacts with sugars in plaque. Fluoride affects tooth structure during and after development. It reduces caries in three ways:

- It reduces and inhibits dissolution of enamel
- It promotes remineralisation; remineralisation in the presence of fluoride not only replaces lost mineral but also increases resistance to acids and to subsequent demineralisation
- It affects plaque by altering the ecology of the dental plaque and reducing acid production

Fluoride is most effective when used topically, after the teeth have erupted.

SUMMARY POINTS

Water fluoridation is highly controversial

Evidence is often misused or misinterpreted and uncertainties glossed over in polarised debates

Problems include identifying benefits and harms, whether fluoride is a medicine, and the ethical implications

This article provides professionals and the public with a framework for constructive public consultations

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2 WHO. WHO oral health country/area profile programme. www.who.int/ednt/regions.html.
Effectiveness of interventions to promote physical activity in children and adolescents: systematic review of controlled trials

Esther M F van Sluijs, investigator scientist, Alison M McMinn, PhD student, Simon J Griffin, group leader

ABSTRACT

Objective To review the published literature on the effectiveness of interventions to promote physical activity in children and adolescents.

Design Systematic review.

Data sources Literature search using PubMed, SCOPUS, Psychlit, Ovid Medline, Sportdiscus, and Embase up to December 2006.

Review methods Two independent reviewers assessed studies against the following inclusion criteria: controlled trial, comparison of intervention to promote physical activity with no intervention control condition, participants younger than 18 years, and reported statistical analyses of a physical activity outcome measure. Levels of evidence, accounting for methodological quality, were assessed for three types of intervention, five settings, and three target populations.

Results The literature search identified 57 studies: 33 aimed at children and 24 at adolescents. Twenty four studies were of high methodological quality, including 13 studies in children. Interventions that were found to be effective achieved increases ranging from an additional 2.6 minutes of physical education related physical activity to 283 minutes per week of overall physical activity. Among children, limited evidence for an effect was found for interventions targeting children from low socioeconomic populations, and environmental interventions. Strong evidence was found that school based interventions with involvement of the family or community and multicomponent interventions can increase physical activity in adolescents.

Conclusion Some evidence was found for potentially effective strategies to increase children’s levels of physical activity. For adolescents, multicomponent interventions and interventions that included both school and family or community involvement have the potential to make important differences to levels of physical activity and should be promoted. A lack of high quality evaluations hampers conclusions concerning effectiveness, especially among children.

INTRODUCTION

The prevalence of childhood obesity and related health problems is increasing in many Western countries and is anticipated to continue to increase. Evidence of an association between physical activity and weight gain remains sparse. Nevertheless, in an effort to halt or reverse trends in obesity, promotion of physical activity in children and adolescents has been identified as a key focus of efforts to promote health. Physical activity among children and adolescents is believed to be insufficient, and low levels of activity seem to persist into adulthood. This makes physical inactivity among young people a risk factor for cardiovascular disease, cancer, and osteoporosis in later life. The development and evaluation of interventions to promote physical activity in young people is therefore a priority.

METHODS

We carried out a literature search of papers on interventions to promote physical activity in young people using six electronic databases (Pubmed, Psychlit, SCOPUS, Ovid Medline, Sportdiscus, and Embase) from the year of their inception up to and including December 2006. The search strategy focused on four key elements: population (for example, youth, children), study design (for example, controlled trial, random), behaviour (for example, physical activity, walking, exercise), and intervention (for example, health education, behaviour change). The full list of terms is available at www.mrc-epid.cam.ac.uk/Publications/Supplementary_Material/VanSluijsBMJ2007/.

We also carried out a citation search of included papers and published relevant reviews.
speakers translated potentially relevant foreign language papers.

Inclusion criteria
We restricted the review to published trials, applying the following inclusion criteria: children and adolescents (≤18 years), not selected on the basis of having a specific disease or health problem; interventions in which the main component or one of the components was aimed at promotion of physical activity through behaviour change in any setting (we excluded interventions to reduce sedentary behaviour, or structured exercise programmes to prevent obesity); inclusion of a non-physical activity intervention for the control group; and reported statistical analyses of an outcome measure related to physical activity (self reported or objectively measured).

Two reviewers (EMFvS, AMMcM) independently reviewed the results from the initial search of the title then the abstract and finally the full paper. When opinions differed consensus was reached through discussion.

Assessment of methodological quality
We assessed methodological quality using a 10 item quality assessment scale derived from previously used quality criteria and we focused on internal validity and analyses (table 1). Two reviewers (EMFvS, AMMcM) independently assessed for each study whether its score on an item was “positive,” “negative,” or “not, or insufficiently, described.” In cases of disagreement, consensus was reached by discussion. We accumulated the positive scores and defined quality as high when a randomised controlled trial scored six or more or a controlled trial scored five or more. We analysed the level of agreement between the two reviewers using Cohen’s κ, with agreement assessed on a dichotomous scale (negative and not described versus positive).

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Table 1: Criteria for assessment of methodological quality

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Groups comparable at baseline on key characteristics (positive if stratified baseline characteristics were presented for age, sex, and at least one relevant outcome measure; for cluster randomised controlled trials and controlled trials, positive if this was statistically tested; and for all studies only positive when differences observed were controlled for in analyses)</td>
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<tr>
<td>B</td>
<td>Randomisation procedure clearly described and adequately carried out</td>
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<tr>
<td>C</td>
<td>Unit of analysis was individual (negative if unit of analysis was school level or school level randomisation not accounted for in individual level analyses)</td>
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<tr>
<td>D</td>
<td>Validated measures of physical activity used (positive if validation of measures of physical activity was reported or referred to)</td>
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<tr>
<td>E</td>
<td>Dropout described and not more than 20% for studies with follow-up of six months or shorter and 30% for studies with follow-up of more than six months</td>
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<tr>
<td>F</td>
<td>Timing of measurements comparable between intervention and control groups</td>
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<td>G</td>
<td>Blinding outcome assessment (positive if those responsible for assessing physical activity at outcome were blinded to group allocation of individual participants)</td>
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<td>H</td>
<td>Participants followed up for a minimum of six months</td>
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<td>I</td>
<td>Intention to treat analysis used</td>
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<td>J</td>
<td>Potential confounders accounted for in analyses</td>
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</table>

Data extraction
Data extraction on to standardised forms was undertaken separately for studies including children (<12 years, AMMcM) and adolescents (≥12 years, EMFvS). We included interventions in high schools and American middle schools (6th to 8th grade, ages 11 to 14) in the adolescent category. Data extracted included project title, country, study design, inclusion criteria, baseline descriptive data, randomisation procedure, descriptions of intervention and control conditions, length of follow-up, losses to follow-up, selective drop out (observed differences between drop outs and study completers), physical activity measures used, secondary outcome measures, and results. In addition both reviewers (EMFvS, AMMcM) extracted information on the specifics of the intervention (setting, target population, and intervention type), size of the baseline sample, and the overall effectiveness of the study for the main physical activity outcome measure (a measure of individual physical activity was used when available). We scored the size of the study as positive if there were more than 250 participants or if a power calculation was provided justifying the sample size (large) and as negative if there were 250 or fewer participants (small).

Studies used a wide range of methods to assess effectiveness and reported a variety of different outcome measures. We considered devising a common outcome metric for interpretational purposes, similar to a previous review focusing on interventions promoting one particular behaviour, walking. Although the studies included in this review assessed walking in different ways, it is a relatively homogeneous behaviour. In contrast, physical activity is more complex and consists of various domains, making it difficult to compare the results of the various measures used to assess this behaviour or particular sub-domains (for example, during breaks, out of school). Consequently because of the heterogeneity of the behaviour of interest and the outcome measures used we decided that calculating one common
Table 2 | Intervention characteristics of included studies aimed at increasing physical activity in children (named reference is main reference)

<table>
<thead>
<tr>
<th>Study</th>
<th>Design; country</th>
<th>Setting</th>
<th>Target population</th>
<th>Participants</th>
<th>Intervention description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christodoulus 2006**</td>
<td>Randomised controlled trial (school); Greece</td>
<td>School plus†</td>
<td>None</td>
<td>n=78; mean age 11.2 (SD 0.4) years; 54% boys</td>
<td>Intervention group: 1 year's duration, two 45 minute classes of physical education per week. Focus on cooperative activities, including individual goal setting and three minute talk on physical activity and health. Weekly classroom lecture with focus on physical activity knowledge and health education integrated into other subjects. Physical education teachers and classroom teachers received training. Children got homework assignments with family activities; parents received educational material and were advised to encourage children to incorporate physical activity into daily lives. Control group: usual physical education programme, two 45 minute classes per week</td>
</tr>
<tr>
<td>Fitzgibbon 2006** (Hip-hop to health Jr)</td>
<td>Randomised controlled trial (school); USA</td>
<td>School plus†</td>
<td>Ethnic minority</td>
<td>n=401; mean age 51 (SD 7) months; 50% girls; 81% Latino</td>
<td>Intervention group: 14 weeks’ duration, three 40 minute sessions per week. Focus on healthy eating and exercise, specific topics changed each week. Each session included 20 minutes to introduce new topic and 20 minutes physical activity. Parents received weekly newsletter to match curriculum, including homework assignment. Control group: “general health” intervention for 14 weeks, no information on diet or physical activity included, one 20 minute session per week</td>
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<tr>
<td>Harrison 2006* (Switch off—get active)</td>
<td>Controlled trial (school); Ireland</td>
<td>School plus†</td>
<td>Low SES</td>
<td>n=312; mean age 10.2 (SD 1.0) years; 43% girls</td>
<td>Intervention group: 16 weeks’ duration, ten 30 minute lessons. Focus on minimising television and computer use and increasing physical activity. Health education approach targeting self esteem, decision making skills, and personal development. Included self monitoring, budgeting, and goal setting techniques. Parents encouraged to support children and to verify children’s behaviour. Control group: usual curriculum</td>
</tr>
<tr>
<td>Manios 2006**</td>
<td>Controlled trial (area); Greece</td>
<td>School plus†</td>
<td>None</td>
<td>n=1046 (subsample of 579 selected for cohort analyses); aged 5.5-6. 5 years; 53% boys</td>
<td>Intervention group: 6 years’ duration. Health and nutrition component (15-17 hours over academic year), physical fitness, and activity component (2×45 minute physical education sessions per week and 4-6 hours of classroom sessions per year), and homework. Parents given booklets on nutrition and physical activity. Control group: standard physical education classes.</td>
</tr>
<tr>
<td>Fairclough 2005**</td>
<td>Randomised controlled trial (class); UK</td>
<td>School-only</td>
<td>One sex</td>
<td>n=33, mean age 12.4 (SD 0.4) years, girls only</td>
<td>Intervention group: 5 weeks’ duration, curriculum based. Weekly two hour physical education classes taught by usual physical education teacher. Teacher given objectives to work by to increase physical activity during class. Control group: usual curriculum</td>
</tr>
<tr>
<td>Fitzgibbon 2005** (Hip-hop to health Jr)</td>
<td>Randomised controlled trial (school); USA</td>
<td>School plus†</td>
<td>Ethnic minority</td>
<td>n=409; mean age 49.7 (SD 7.0) months; 50% girls; about 90% African American</td>
<td>Intervention group: 14 weeks’ duration, three 40 minute sessions per week. Focus on healthy eating and exercise, specific topics changed each week. Each session included 20 minutes to introduce new topic and 20 minutes’ physical activity. Parents received weekly newsletters to match curriculum, including homework assignment. Control group: “general health” intervention for 14 weeks, no information on diet or physical activity included. Weekly 20 minute sessions and newsletter</td>
</tr>
<tr>
<td>French, 2005**</td>
<td>Randomised controlled trial (girl scout troop); USA</td>
<td>Community</td>
<td>One sex</td>
<td>n=322; mean age 10.5 years; girls only</td>
<td>Intervention group: 2 years’ duration, ten 90 minute sessions in each year at troop meetings. Focus on developing behavioural skills to choose calcium rich foods and engage in weighbearing physical activity. Included group goal setting, interactive web based programme, and summer camp for one week. Parents also targeted through web based programme. Troop leaders received training and delivered intervention. Control group: usual troop meeting activities</td>
</tr>
<tr>
<td>Kelder 2005** (CATCH Kid’s Club)</td>
<td>Controlled trial (school); USA</td>
<td>School only</td>
<td>None</td>
<td>n=258, mean age 9 years; both sexes†</td>
<td>Intervention group 1: 5 months’ duration. Physical activity component aimed to involve students in 30 or more minutes of daily physical activity, at least 40% of which should be MVPA, and to provide students with opportunities to practise physical activity skills to carry over to other times of day. Staff given training and “activity box.” Intervention group 2: as above, plus education and snack components, consisting of nutrition activities, modules on health food choices, and increasing MVPA at school and home. Control group: no intervention</td>
</tr>
<tr>
<td>Palmer 2005** (Healthy hearts 4 kids)</td>
<td>Controlled trial (class); USA</td>
<td>School only</td>
<td>None</td>
<td>n=233; 5th grade children; 44% boys</td>
<td>Intervention group: 1 month’s duration. Web based programme consisting of units on cardiovascular function, physical activity, nutrition, and tobacco. Sessions twice a week in computer lab, each lasting up to 50 minutes. Online activities include quizzes, information (such as benefits, physical activity recommendations, how to participate in physical activity), and reporting physical activity and nutrition habits. Participants also received feedback on their reported physical activity. Control group: received above intervention after one month (comparison made before control group started intervention)</td>
</tr>
<tr>
<td>Sääkslahti 2004* (part of STRIP)</td>
<td>Controlled trial (family); Finland</td>
<td>Family</td>
<td>None</td>
<td>n=228; mean age 4.5 (SD 0.5) years; 48% boys in intervention group, 55% boys in control group</td>
<td>Intervention group: 3 years’ duration. Annual one hour sessions held with parents, covering importance of sensory integration, motivation through providing information on physical activity and health and previous intervention studies, and options for children's physical activity in Turku. Parents also received printed material twice a year including activity posters, a special physical activity board game, and review articles. Control group: no intervention</td>
</tr>
<tr>
<td>Baranowski 2003** (GEMS FFP)</td>
<td>Randomised controlled trial (individual), pilot study; USA</td>
<td>Community</td>
<td>Ethnic minority &amp; one gender</td>
<td>n=35 (child and family), age 8 years; African-American girls only</td>
<td>Intervention group: summer camp for 4 weeks plus 8 weeks of internet programme at home. Camp mixed usual activities with interactive activities to promote intake of fruit and vegetables and physical activity, including decision making, problem solving, and goal setting. Participants asked to log on to internet programme once a week after summer camp. Control group: summer camp for 4 weeks, containing usual camp activities only. Internet programme contained links to general health and homework websites. Participants asked to log on once a month</td>
</tr>
</tbody>
</table>
Environmental interventions:

- **Verstraete 2006**
  - Randomised controlled trial (school), Belgium
  - School only, None
  - n=249; mean age 10.8 (SD 0.7) years; 51% boys
  - Intervention group: 3 months' duration. Classes provided with game equipment and activity cards with examples of games and activities. Teachers asked to encourage children daily to play with equipment during morning, lunch, and afternoon breaks. Control group: no provision of equipment or cards

- **Stratton 2005**
  - Controlled trial (area), UK
  - School only, None
  - n=120; aged 4-11 years; 50% boys
  - Intervention group: playground painted during school holidays according to school preference to encourage play. Also small pieces of sports equipment allowed in playgrounds. Control group: no playground markings

- **Stratton 2002**
  - Randomised controlled trial (school); UK
  - School only, None
  - n=60; 5-7 years; 50% boys
  - Intervention group: painted playground markings to encourage play. Control group: no playground markings

- **Stratton 2000**
  - Controlled trial (school); UK
  - School only, None
  - n=60; aged 5-7 years; 50% boys
  - Intervention group: playground painted according to children's designs to encourage play. Children also allowed a football in playground but no other play equipment. Control group: no playground markings but allowed limited equipment into playground

Multicomponent interventions:

- **Jung 2006**
  - School plus†, Low SES
  - n=510; grades 4-6 (9-12 years)
  - Intervention group: 6 years' duration (this paper reports results at 1 year). Composed of six programme components: school sports activities (during and after school), pupil
Controlled trial (city district); Netherlands

48.5% boys; 71% of intervention group and 94% of control group of foreign origin (P<0.01)

Follow-up system (yearly monitoring of pupils’ physical activity levels by physical education teacher), in-class exercises, lessons on awareness, parental information services, and an activity week (once a year, involving parents, the schools, and local sports clubs). Control group: usual curriculum

Reilly 2006w27

Randomised controlled trial (nursery); UK

School plus† None

n=545; mean age 4.2 (SD 0.3) years; 50% boys

Intervention group: three 30 minute physical activity sessions per week over 24 weeks delivered by nursery staff who attended three training sessions. Aim to increase physical activity and fundamental movement skills. Families received resource pack with guidance on linking physical activity at nursery and home and opportunities for increasing physical activity and reducing time spent watching television. Control group: usual curriculum

Coleman 2005w28†

Controlled trial (school); USA

School only Ethnic minority and low SES

n=366; aged 8-9 years, 52% boys

Intervention group: 1 year curriculum based intervention consisting of EL Paso coordinated approach to child health (CATCH) education classes, Eat Smart, classroom curriculum, and home team components (implemented in stages). Schools given funding for physical education equipment, training staff for intervention and promotion of CATCH. Control group: also received funding (although lesser amount) as incentive to participate. Schools received summary results after one year. Otherwise usual curriculum

Paradis 2005w30 (El Paso CATCH)

Controlled trial (area); Canada

School plus† None

n=443, aged 6-7 years (for longitudinal comparison); both sexes‡; Native American community

Intervention group: 6 years’ duration (grades 1-6), consisting of ten 65 minute sessions per year for each grade. Curriculum included type 2 diabetes, nutrition, physical activity and fitness, and other healthy lifestyles. Also had community activities, ban on junk food at school, and construction of walking and cycling paths in the community. Control group: non-equivalent comparison group

Caballero, 2003w31†w32

Randomised controlled trial (school); USA

School plus† Ethnic minority

n=1704; mean age 7.6 (SD 0.6) years; 52% boys; Native American

Intervention group: 3 years’ duration (grades 3-5). Included classroom curriculum (two lessons per week for 12 weeks in grades 3 and 4, 8 weeks in grade 5), physical activity (minimum of three 30 minute sessions per week of MVPa), family involvement (nine events at school plus information sent home), and changes to food service (to promote healthy eating). Control group: usual curriculum

Pate 2003w37 (Active winners)

Controlled trial (area); USA

School plus† Ethnic minority

n=436; mean age 10.8 (SD 0.7) years; 49% boys; 87.4% African-American in intervention group, 59.8% in control group

Intervention group: 18 months’ duration: 1 year of primary intervention, follow-up activities for 6 months. Four components; active kids (after school and summer programme), active home (newsletter, home assignments, and family activity nights), active school (activities to make physical activity more accessible and attractive), active community (features in local newspaper and incorporation of physical activity into existing events). Control group: no intervention

Van Beurden 2003w38†w39

Randomised controlled trial (school); Australia

School only None

n=1045; aged 7-10 years; 53% boys

Intervention group: 1 year’s duration. Consisted of five strategies to support teachers and create supportive environments, and healthy school policies to improve fundamental movement skills and increase physical activity. Strategies were school project teams, buddy programme, professional development for teachers, project website, and funding for purchase of equipment. Control group: no intervention

Sahota 2001w40

Randomised controlled trial (school); UK

School only None

n=636; mean age 8.4 (SD 0.63) years; 51% boys in intervention group, 59% in control group

Intervention group: one (academic) year’s duration. Consisted of teacher training, modifications of school meals, and development and implementation of school action plans to promote healthy eating and physical activity. Control group: usual health curriculum

Sallis 1999w41†w42

Randomised controlled trial (school); USA

School plus† None

n=1538; mean age range 9.49 to 9.62 years in three study groups; 53% boys

Intervention group 1: 2 years’ duration (grades 4 and 5). Specialist led physical education classes three 30 minute sessions per week and weekly self management session (30 minutes) to teach behaviour change skills to help generalise to regular physical activity outside school. Included homework and monthly newsletters. Specialists received ongoing training and supervision from investigators. Intervention group 2: as above but teacher led. Teachers received extensive in-service training programme, which decreased in frequency over the intervention group period. Also had consultations with physical education specialists, ranging from biweekly to bimonthly during the intervention period. Control group: usual physical education programmes but schools provided with sufficient physical education equipment to carry out sports, play, and active recreation for kids (SPARK) programme, as with intervention schools

McKenzie 1996w43†w44

Randomised controlled trial (school); USA

School plus† None

n=5106; mean age 8.7 years; 52% boys

Intervention group 1: 3 years’ duration (grades 3-5). School based programme: ≤ 90 minutes of CATCH physical education per week over a minimum of three sessions per week, taught by either physical education specialists or classroom teachers. Also food service modifications and CATCH curriculum focused on eating habits, physical activity, and smoking. Intervention group 2: school based and family based interventions as above plus home activity curriculum and family fun nights. Control group: usual health curriculum, physical education, and food service programmes. Required to give ≤ 90 minutes of physical education over a minimum of three sessions per week

SES=socioeconomic status; MVPa=moderate-vigorous or vigorous physical activity.

*Level of randomisation or group allocation given in brackets.
†No further descriptive data available on baseline sample.
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measure of outcome would not be valid or informative. Alternatively we used scores to indicate effectiveness—that is, whether there was no difference in effect between control and intervention group (0 score), a positive or negative trend (+ or −), or a statistically significant difference (P<0.05) in favour of the intervention or control group (+ + or − −, respectively). In cases of disagreement, consensus was reached by discussion.

Strength of the evidence
We thought a formal meta-analysis inappropriate owing to the heterogeneity of the interventions, settings, participants, and outcome measures. Instead we used a rating system of levels of evidence to draw conclusions on effectiveness, based on previously used best evidence syntheses.16,31 We defined five levels on the basis of study design, methodological quality, and sample size: strong, moderate, limited, inconclusive, or no evidence for effect (see www.mrc-epid.cam.ac.uk/Publications/Supplementary_Material/VanSluijsBMJ2007/), and conclusions were drawn on the basis of the consistency of results of studies with the highest available level of quality. If at least two thirds (66.6%) of the relevant studies were reported to have significant results in the same direction then we considered the overall results to be consistent. In a stratified analysis we assessed levels of evidence for studies according to setting, target population, and type of intervention (educational only, environmental or policy based only, or a combination of both, “multicomponent”).

RESULTS
Overall, 3045 references were retrieved from the database search (PubMed, n=2000; Psychinfo, n=340; Scopus, n=692; Ovid Medline, n=591; Sportdiscus, n=472; Embase, n=400). Fifty one studies met the inclusion criteria, a further six were added after searching the citations (figure). Thirty three included children1–17 and 24 included adolescents.18–77 Tables 2 and 3 show the characteristics of the studies.

Methodological quality
Agreement was 85.9% on the 570 items scored during the quality assessment (κ=0.72, substantial agreement); full consensus was reached after discussion. Overall 24 studies (42%) exhibited high methodological quality, of which 15 (25%) had more than 250 participants (see www.mrc-epid.cam.ac.uk/Publications/Supplementary_Material/VanSluijsBMJ2007/). Most studies applied intention to treat analyses and measured all study groups at similar times, but only 10 studies (18%) had a follow-up of six months or longer. Insufficient information was provided to score the adequacy of the randomisation procedure for 34 studies (60%), and 33 studies (58%) lacked information on allocation concealment at outcome assessment.

Study characteristics
Eighteen of the 33 studies in children were carried out in the United States, seven in the United Kingdom, and the remainder in other countries. Most of the child studies (82%) evaluated school based interventions, 14 of which included a community or family component. Around half of the child interventions were educational whereas a third used a multicomponent approach. Jointly over half of the studies relied on child reported or parent reported questionnaires or diaries as the main measure of physical activity (see www.mrc-epid.cam.ac.uk/Publications/Supplementary_Material/VanSluijsBMJ2007/). Twelve studies used an objective measure of physical activity whereas three used observation methods. Only five of these assessed overall physical activity; the remainder mostly assessed activity during physical education or playtime. Nineteen of the studies assessed overall physical activity, eight measured school based physical activity only, and six assessed out of school physical activity.

Eighteen of the 24 studies in adolescents were carried out in the United States and six in other countries. Almost all evaluated school based interventions, six of which included involvement of the family or community. Five studies included a follow-up measurement of six months or more (see www.mrc-epid.cam.ac.uk/Publications/Supplementary_Material/VanSluijsBMJ2007/). Measurement of physical activity was mostly focused on non-school related activities and carried out with self reported questionnaire or recall instruments. Four studies used an objective measure as the main measure of physical activity, all assessing total physical activity, and one study used direct observation to assess physical education related physical activity.

Evidence of effect on physical activity
Thirty eight studies reported a positive intervention effect (67%), achieving statistical significance in 27 (47%). This included 14 studies in children (42%) and 13 in adolescents (54%). Significant results ranged from an increase of 2.6 minutes during physical education classes to a 42% increase in participation in regular physical activity and an increase of 83 minutes per week in moderate to vigorous physical activity.

Table 4 summarises the stratified levels of evidence for the effectiveness of interventions to promote physical activity in children and adolescents.

Intervention types in children
Nineteen studies evaluated education only interventions, including one large high quality randomised controlled trial,11 two large high quality controlled trials,13,14 four small high quality randomised controlled trials,15–17,23 and seven low quality randomised controlled trials.1,12,19–21 Four of these reported a statistically significant intervention effect, therefore no overall evidence of an effect of education only interventions was identified. Four studies evaluated changes in the school
### Table 3 | Intervention characteristics of included studies aimed at increasing physical activity in adolescents (named reference is main reference)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design*; country</th>
<th>Setting</th>
<th>Target population</th>
<th>Participants</th>
<th>Intervention description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Educational interventions:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Jago 2006w48 (Fit for life)</td>
<td>Randomised controlled trial (boy scout troop); USA</td>
<td>Community</td>
<td>One sex</td>
<td>n=473; mean age 13 (SD 0.1) years; males only; 16 troops started in spring, 26 in autumn</td>
<td>Intervention group: 9 weeks' duration: troop meetings (once weekly) and internet intervention (asked to log on twice weekly) aimed at increasing physical activity skills, physical activity self efficacy, and goal setting. Troop meetings included 20 minute activity sessions. Internet based programme focused on role modelling, goal setting, goal review, and problem solving. Badge could be earned, with points for goal setting and achievement, and attending troop meeting. Control group: fruit and vegetable intervention, as above</td>
</tr>
<tr>
<td>Patrick 2006w49 (PACE+ for adolescents)</td>
<td>Randomised controlled trial (individual); USA</td>
<td>Primary care</td>
<td>None</td>
<td>n=819; mean age 12.7 (SD 1.3) years; 46.5% males</td>
<td>Intervention group: 12 month programme, one stage based computer tailored intervention with endorsement of primary care provider. Focus on diet and physical activity (MVPA and sedentary behaviour). After initial consultation, participants received manual and 11 telephone based follow-up sessions. Parents were targeted to help them encourage attempts at behaviour change. Control group: sun protection intervention, as above</td>
</tr>
<tr>
<td>Robbins 2006w50 (Girls on the move)</td>
<td>Randomised controlled trial (grade); USA</td>
<td>School plus†</td>
<td>One sex and low SES</td>
<td>n=77; 11-14 years; females only; sedentary (ready to change physical activity behaviour)</td>
<td>Intervention group: 9 week programme set in school wellness centre. Included three individually tailored computer sessions with face to face feedback from school paediatric nurse, and two telephone calls with research assistant, focusing on agreed goals. Parents were posted tip sheets to support girls to achieve goals. Control group: one page leaflet with age specific recommendations for physical activity</td>
</tr>
<tr>
<td>Frenn 2005w51</td>
<td>Controlled trial (class); USA</td>
<td>School only</td>
<td>None</td>
<td>n=132; 12 and 13 years; both sexes†</td>
<td>Intervention group: eight session blackboard based intervention (Internet) in science classes (40 minutes per class). Individually tailored feedback on basis of stage of change to increase physical activity and improve diet. Control group: usual curriculum</td>
</tr>
<tr>
<td>Schofield 2005w52</td>
<td>Controlled trial (school); Australia</td>
<td>School only</td>
<td>One sex</td>
<td>n=68; mean age 15.8 (SD 0.8) years; females only; inactive</td>
<td>Intervention group 1: twelve weekly sessions, with pedometer based self-monitoring and educative meetings encouraging daily increases in steps until 10 000/day. Intervention group 2: twelve weekly sessions, with self monitoring by recording daily minutes of MVPA and educative meetings encouraging daily activity by 10-15 minutes per week until 30-60 minutes per day. Control group: no intervention</td>
</tr>
<tr>
<td>Tsombatzoudis 2005w53</td>
<td>Controlled trial (school); Greece</td>
<td>School only</td>
<td>None</td>
<td>n=366; mean age 14.2 (SD 0.7) years; 52% females</td>
<td>Intervention group: 12 week educational programme, three sessions per week. Aim to support cognitive, emotional, and behavioural components of student’s attitude to physical activity to change behaviour. In addition, three 45 minutes lectures given on effective behaviour change, goal setting, and health and exercise. Weekly posters on announcement board. Control group: usual curriculum</td>
</tr>
<tr>
<td>Wilson 2005w54</td>
<td>Controlled trial (school); USA</td>
<td>School only</td>
<td>Low SES</td>
<td>n=48; mean age 11.0 (SD 0.6) years; 71% females</td>
<td>Intervention group: after school programme with three 2 hour meetings per week during 4 weeks. Programme emphasised increasing intrinsic motivation and behaviour skills to increase MVPA to 60 minutes per day. Each session included a one hour activity component chosen by the students. Control group: after school programme providing information on general health</td>
</tr>
<tr>
<td>Bayne-Smith 2004w55 (PATH)</td>
<td>Randomised controlled trial (individual and class); USA</td>
<td>School only</td>
<td>One sex</td>
<td>n=442; mean age 16.0 (SD 1.3) years; females only</td>
<td>Intervention group: 12 week, physical education curriculum based programme. Daily 30 minute classes (five days per week); classes consisted of 5-10 minute lecture and 20-25 minutes of vigorous physical activity, with additional homework assignments. Control group: normal curriculum (no lecture, so about 5 minutes more physical activity per class)</td>
</tr>
<tr>
<td>Hsu 2004w56</td>
<td>Randomised controlled trial (class); Taiwan</td>
<td>School only</td>
<td>One sex</td>
<td>n=188; mean age 16.45 (SE 0.31) years; females only</td>
<td>Intervention group: 12 week intervention. Usual physical education plus education based programme focusing on physical activity knowledge, self efficacy, and attitudes. One 50 minute seminar held then regular discussions in small groups (10 or 11), led by peer leaders, to encourage and support physical activity. Control group: usual curriculum</td>
</tr>
<tr>
<td>Ortega-Sanchez 2004w57</td>
<td>Randomised controlled trial (individual); Spain</td>
<td>Primary care</td>
<td>None</td>
<td>n=448; mean age 17.0 (SD 2.4) years; 58% males</td>
<td>Intervention group: two 5-10 minutes of counselling by doctor (baseline and 6 months) on basis of current activity level (either initiation, increase, reinforcement counselling). Based on ask-assess-advice principle. Control group: no advice</td>
</tr>
<tr>
<td>Prochaska 2004w58</td>
<td>Randomised controlled trial (class); USA</td>
<td>School only</td>
<td>None</td>
<td>n=138; mean age 12.1 (SD 0.9) years; 65% females</td>
<td>Intervention group 1: 30 minute computer based health education session, stages of change based health assessment with tailored feedback with individual plans for behaviour change or relapse prevention. Intervention group 2: same as above, including nutrition intervention. Control group: no intervention</td>
</tr>
<tr>
<td>Frenn 2003w59</td>
<td>Controlled trial (class); USA</td>
<td>School only</td>
<td>None</td>
<td>n=178; age 12-15 years; both sexes†</td>
<td>Intervention group: four internet or video delivered health education sessions (stage of change based), setting up of gym lab run by active students (duation one month). Control group: usual curriculum</td>
</tr>
<tr>
<td>Gortmaker 1999w60 (Planet Health)</td>
<td>Randomised controlled trial (school); USA</td>
<td>School only</td>
<td>None</td>
<td>n=1560; age 11 and 12 years; both sexes‡</td>
<td>Intervention group: 2 year programme, 32 classroom based sessions taught by regular teachers. Interdisciplinary intervention for prevention of obesity aimed at decreasing television viewing, making space for activity, with focus on &quot;lifestyle&quot; changes in behaviour. Control group: usual curriculum</td>
</tr>
<tr>
<td>Perry 1994w61 w62 (Class of 1989)</td>
<td>Controlled trial (class), (3 year of 7 year community intervention); USA</td>
<td>School plus†</td>
<td>None</td>
<td>n=2406; age 13 and 14 years§; both sexes$</td>
<td>Intervention group: classroom based intervention using peer leaders; self monitoring intervention FM250 in year 8 (hypothetically cycle 250 miles between two towns in 4 weeks, based on daily energy expenditure). Control group: no intervention</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample</td>
<td>Intervention</td>
<td>Findings</td>
<td></td>
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<td>-----------------------------------------</td>
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<tr>
<td>Nader 1992*</td>
<td>Randomised controlled trial (school); USA</td>
<td>Family None</td>
<td>Intervention group: 12 after school sessions, with family attendance. Each session included aerobic exercise, education (separate for children and adults), behaviour management, and heart healthy snacks (duration 3 months); also six maintenance sessions over following 9 months. Control group: no intervention.</td>
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<tr>
<td>Killen 1988**†</td>
<td>Randomised controlled trial (school); USA</td>
<td>School only None</td>
<td>Intervention group: 7 week classroom based educational programme (three 50 minute sessions per week) taught by special teachers in five modules (physical education, diet, smoking, stress, problem solving). Each module contained health benefits, skills acquisition, resisting social influence, and skills practice. Control group: usual curriculum.</td>
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<tr>
<td>Perry 1987††</td>
<td>Randomised controlled trial (school); USA</td>
<td>School only None</td>
<td>Intervention group: 10 sessions of peer led classroom based educational intervention with focus on changing environmental, personality, and behavioural attributes to behaviour change (including videotaped instructions and goal setting, self monitoring, social support, and how to change environment). Control group: usual curriculum.</td>
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<tr>
<td>Environmental interventions:</td>
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<tr>
<td>Salvis 2003*</td>
<td>Randomised controlled trial (school); USA</td>
<td>School only None</td>
<td>Intervention group: 2 year programme based on ecological model focused on physical activity and nutrition. Physical activity intervention included changing content and structure of physical education, increasing choice for physical activity during leisure periods and environmental changes (increased supervision, equipment, and activities). No health promotion. Control group: usual curriculum (schools received $1000 ($500; $700) for physical education equipment)</td>
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<tr>
<td>Multicomponent interventions:</td>
<td></td>
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<tr>
<td>Young 2006*</td>
<td>Randomised controlled trial (individual); USA</td>
<td>School plus† One sex</td>
<td>Intervention group: one school year programme focusing on social independence, environmental factors, and problem solving skills. Delivery during class lectures, small group discussions, and homework activities. Included physical activity monitoring and strategies to maximise physical activity during physical education classes. Families were invited for workshop and received newsletters and parent-child homework. Control group: usual curriculum.</td>
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<tr>
<td>Haerens 2005‡</td>
<td>Randomised controlled trial (school); Belgium</td>
<td>School plus‡ None</td>
<td>Intervention group 1: 2 year intervention implemented by school staff. Focus on creating opportunities for physical activity during breaks, lunch, and after school. Provision of extra sports material and setting up of variety of (non-competitive) activities. Computer tailored intervention (once in year 2) providing feedback on physical activity levels and determinants. Intervention group 2: intervention group 1 plus parents invited to interactive meeting on physical activity, diet, and health. Parents received CD with similar computer tailored intervention and regular newsletters. Control group: usual curriculum.</td>
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<tr>
<td>Pate 2005*</td>
<td>Randomised controlled trial (school); USA</td>
<td>School plus‡ One sex</td>
<td>Intervention group: one year multicomponent intervention with emphasis on enhancing physical activity self efficacy through successful experiences of physical activities and skill development. Focus on six components: changing physical education, providing health education, creating supportive school environment, school health services, staff health promotion, and family based and community based activities. Control group: regular physical education classes.</td>
<td></td>
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<tr>
<td>Jannner 2004*</td>
<td>Controlled trial (school); USA</td>
<td>School only One sex</td>
<td>Intervention group: 4 months' intervention. Additional classes (five 60 minutes per week), four activity based classes with female targeted activities, one discussion class on health benefits from physical activity and strategies to increase physical activity. Control group: usual curriculum.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simon 2004*</td>
<td>Randomised controlled trial (school); France</td>
<td>School plus‡ None</td>
<td>Intervention group: 4 years' duration, in partnership with families and community groups. Focus on three areas: increasing knowledge, attitudes, beliefs, and motivation for physical activity through debates and providing information; social support form parents, peers, teachers, and physical activity instructors; and changing environmental conditions for physical activity. Educational component and new opportunities for physical activity. Control group: usual health curriculum and physical education.</td>
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<tr>
<td>Neumark-Sztainer 2003*</td>
<td>Randomised controlled trial (school); USA</td>
<td>School only One sex</td>
<td>Intervention group: 16 week programme, five classes per week. Females only additional physical education classes four times weekly and one educational session per week (either discussing social support or nutrition). Aimed to create environment in which larger girls could feel comfortable being physically active. Control group: usual curriculum.</td>
<td></td>
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</tbody>
</table>

SES=socioeconomic status; MVPA=moderate-vigorous or vigorous physical activity. *Level of randomisation or group allocation given in brackets. †Includes involvement of family or community. ‡No further descriptive data available on baseline sample.
environment, including two low quality randomised controlled trials. Both of these reported a significant intervention effect, providing limited evidence of an effect of environmental interventions.

Ten studies evaluated multicomponent interventions in children, including three large high quality randomised controlled trials. Only one of these high quality trials reported a significant positive effect, equating to inconclusive evidence of effectiveness.

### Intervention types in adolescents

Seventeen studies evaluated education only interventions in adolescents, including four large high quality randomised controlled trials. No evidence of an effect was found, with only one of the large high quality trials reporting statistically significant positive results. Only one study, a low quality randomised controlled trial, evaluated the effect of an environmental intervention, providing inconclusive evidence of an effect.

Six studies evaluated multicomponent interventions, all in the school setting. Three were large high quality randomised controlled trials, which all showed significant positive results, providing strong evidence of an effect of multicomponent interventions.

### Settings in studies of children

Twenty seven studies evaluated school based interventions. Thirteen of these were restricted to the school setting only, including five randomised controlled trials, one of high quality, and four of lower quality. Three of these randomised controlled trials reported significant positive intervention effects, resulting in the classification of inconclusive evidence of an effect of school only interventions. The other 14 school based interventions also included family or community components, such as homework assignments to do with parents or incorporation of physical activity into existing community events. Two large high quality randomised controlled trials were identified, one of which showed a significant positive intervention effect, suggesting inconclusive evidence of an effect.

### Settings in studies of adolescents

Of the 20 studies that evaluated school based interventions, 14 were restricted to the school setting, including two large high quality randomised controlled trials, one of which reported a statistically significant intervention effect. This represents inconclusive evidence of an effect. Six studies evaluated school based interventions also including family or community involvement, three of which were large high quality randomised controlled trials. Two of these large high quality trials showed statistically significant positive results suggesting strong evidence of an effect of school based interventions including family or community involvement.

The only study evaluating a family based intervention, a high quality randomised controlled trial, did not report a positive effect, as did the high quality randomised controlled trial evaluating a community based intervention. One of the two low quality randomised controlled trials evaluating

### Table 4

<table>
<thead>
<tr>
<th>Variables</th>
<th>Children (33 studies)</th>
<th>Adolescents (24 studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention type:</td>
<td>No of studies</td>
<td>Level of evidence</td>
</tr>
<tr>
<td>Educational</td>
<td>19</td>
<td>No</td>
</tr>
<tr>
<td>Environmental or policy</td>
<td>4</td>
<td>Limited</td>
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<td>Multicomponent</td>
<td>10</td>
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<tr>
<td>Setting:</td>
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<tr>
<td>School</td>
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<tr>
<td>School plus community or family</td>
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</tr>
<tr>
<td>Family</td>
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<td>Community</td>
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<td>Primary care</td>
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<tr>
<td>Target group:</td>
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<tr>
<td>One sex only</td>
<td>5</td>
<td>No</td>
</tr>
<tr>
<td>Ethnic minority populations</td>
<td>10</td>
<td>No</td>
</tr>
<tr>
<td>Low SES populations</td>
<td>3</td>
<td>Limited</td>
</tr>
</tbody>
</table>

Categories are exclusive for setting and intervention type but not for target group. SES = socioeconomic status.

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RESEARCH

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Identification of included studies

primary care based interventions showed a significant positive effect. Consequently evidence of an effect of either family based, community based, or primary care based interventions in adolescents is inconclusive.

Target populations in children

Five studies evaluated interventions targeted specifically at girls: one large high quality randomised controlled trial, two small high quality randomised controlled trials, and two low quality randomised controlled trials. Four reported positive effects but only one was significant. Ten studies evaluated interventions specifically aimed at ethnic minority groups, including four small high quality randomised controlled trials, and four low quality randomised controlled trials. Only one low quality randomised controlled trial reported a significant positive effect. Therefore no overall evidence of an effect for interventions targeting girls or ethnic minority groups was found. Three controlled trials, including two of high quality, assessed the effect of interventions targeting children from low socioeconomic backgrounds. All reported a significant positive effect, resulting in a classification of limited evidence of an effect for these interventions.

Target populations in adolescents

Eight studies evaluated interventions specifically aimed at adolescent girls and one aimed at boys. Three were large high quality randomised controlled trials, of which one showed significant positive results. In two small high quality studies—one randomised controlled trial and one controlled trial—interventions were aimed at low socioeconomic groups, with only one reporting a significant intervention effect. Consequently evidence of an effect of interventions targeting adolescents of one sex or from low socioeconomic groups is inconclusive.

DISCUSSION

We found that in children there is limited evidence of an effect of interventions targeting low socioeconomic populations and environmental interventions and the evidence of an effect for multicomponent interventions and the two types of school based interventions is inconclusive. More adequately powered high quality research is needed to strengthen and confirm these results. In general, interventions achieved important changes, such as a 13% increase in play time spent in moderate to vigorous physical activity. No evidence of effectiveness was observed in six of the intervention categories. This review especially raises questions about the usefulness of targeting interventions at children from ethnic minority populations or carrying out family based or community based interventions, as most of the studies identified did not report positive results. Before pursuing these strategies further, it is necessary to identify and learn from the limitations of these interventions and their evaluations. In addition, no evidence of an effect was found for educational interventions and the interventions targeting females, despite more than 67% of studies evaluating these interventions reporting positive effects. Most of these were low quality studies and did not always achieve statistical significance.

Overall there was more evidence for an effect of interventions among adolescents than among children. However, more studies in adolescents compared with studies in children were of high quality and included a large sample size (33% vs 21%). Adolescents are also known to be less active than children so may exhibit greater potential for change. Effects ranged from increases of three minutes during physical education to a 50% increase in the number of participants being regularly active. Strong evidence was found for the effectiveness of school based interventions including family or community involvement and multicomponent interventions. No evidence of an effect was observed for educational interventions although an overall positive trend was observed. This trend is, however, mainly due to the results of studies with lower methodological quality and should therefore be interpreted with caution. This review also shows inconclusive evidence of an effect in adolescents in other categories, warranting further investigation.

Intervention approaches

Almost a third of the included studies in children were targeted at minority ethnic groups, although the evidence on the association between ethnicity and physical activity in children is fairly inconsistent. In contrast an association has often been reported in adolescents, with levels of physical activity tending to be lower in non-white ethnic groups yet no interventions targeting adolescents from minority ethnic groups were identified. Low socioeconomic status has been identified as a possible determinant of physical inactivity. Recently, trials of interventions targeting socially disadvantaged people
provided some evidence of the potential of this strategy. A higher level of activity in males compared with females is consistently observed throughout childhood and adolescence and evidence also suggests that both sexes tend to become less active with increasing age.\textsuperscript{33,35} This review raises doubts about whether targeting females and males separately is an effective approach, although a positive trend was observed among children. Most of the studies investigating differential response by sex did not find one, casting more doubt on the need for separate approaches for the sexes.

Parental factors and the home environment are believed to influence physical activity,\textsuperscript{14,45} yet few interventions were specifically aimed at the home and those that have been carried out did not show significant positive results. An increasing number of school based interventions do, however, include some parental involvement, although usually limited to newsletters and homework assignments. Evidence of effectiveness of these interventions in adolescents was strong, although in children the evidence is still inconclusive. Whether the strategy of involving parents in interventions will be as effective for children should be the focus of future research.

The conclusion of strong evidence of effect of multicomponent interventions in adolescents and the limited evidence of effect of environmental interventions in children is in keeping with the ecological approach to behaviour change as advocated in recent years.\textsuperscript{46-49} The environmental or policy element of multicomponent interventions mostly consisted of alterations to the physical education programme, such as additional classes, physical education teacher training, or the availability of additional equipment. Observations of physical activity during physical education classes mostly showed some increases, but few effects were observed in overall physical activity. This raises the question of whether children might compensate during the rest of the day. It is therefore important to use objective measures to assess the overall effect of the intervention on total activity levels.

Young children’s activity is typically intermittent\textsuperscript{34} in contrast to that of adolescents, which is more structured and planned. Although traditional cognitive approaches, potentially combined with environmental approaches, may increase activity among adolescents and older children (≥10 years), more structural environmental or policy changes might be needed to change younger children’s physical activity behaviour.\textsuperscript{50} This is supported by the evidence of an effect of environmental interventions, which tended to be evaluated in children in the lower grades (grades 1-4) at primary school. Few studies, however, included preschool aged children.

### Implementation of interventions

Factors that may have limited effectiveness are the levels of exposure to the intervention and adherence. Several papers reported problems in these areas. For example, Pate et al.\textsuperscript{37} described that only 5% of participants attended at least half of the sessions offered. Most papers, however, did not describe attendance, implementation, or quality assurance of the intervention, making it impossible to assess the impact these factors may have had on the overall findings.

Most of the studies included in this review were carried out in the United States, raising questions about the generalisability of these results to other countries. Feasibility and effectiveness of cross national implementation is potentially limited owing to known differences in infrastructure, school systems, environments, and social norms. To assess the usefulness of these strategies across different cultures we would advocate replicating evaluations of previously successful interventions adapted to a specific country.

### Methodological quality

Various limitations in study design and subsequent reporting were identified. In particular, information was lacking on the randomisation procedure and blinding at outcome assessment, limiting the interpretation of the methodological quality. Brief descriptions of interventions hampered stratification of the studies and analyses of potential effective components. Overall, methodological limitations across the studies included short duration of follow-up, inadequate adjustment for potential confounders, and a lack of adjustment for clustering when randomisation was carried out at group level. Another limitation was the lack of precision of the physical activity outcome measures. Eighteen of the studies in children used self reported or parent reported measures (55%), just over half of which were not reported to be previously validated, possibly limiting responsiveness. Studies using observation or objective measures of physical activity were in fact more likely to report significant positive results than studies with a self reported measure, both in children and in adolescents.

### Conclusion

Various policy documents have called for the development of effective strategies to increase physical activity in children and adolescents to help halt or reverse the increase in obesity and to improve other aspects of health.\textsuperscript{4,11,15,32} Based on the published evidence to date it seems that a multilevel approach to promoting physical activity, combining school based interventions with family or community involvement and educational interventions with policy and environmental changes, is likely to be effective among adolescents and should be promoted. For children, there is limited evidence of an effect for environmental interventions and interventions targeting those from low socioeconomic groups. Research should focus on filling the gaps identified in this review, such as the lack of studies among adolescent ethnic minority populations and preschool children, and of interventions outside the school setting. Furthermore,
WHAT IS ALREADY KNOWN ON THIS TOPIC

Children and adolescents are believed to have low levels of physical activity, which is associated with obesity and other health problems.

It is unclear what strategies might be effective to promote physical activity.

WHAT THIS STUDY ADDS

Multicomponent interventions and interventions including school and family or community involvement may make important differences in physical activity levels in adolescents.

For children some evidence of effect was shown for environmental interventions and those involving physical activity interventions in youth: a review. Prev Med 2004;39:157-63.

Future studies should aim to strengthen the evidence with rigorous design, appropriate sample size, follow-up beyond post intervention to assess maintenance, use of objective measures of overall activity, and assessment of factors along the causal pathway. Moreover, studies should include assessment of implementation issues and carry out cost-effective analyses to further inform future public health strategies in this topic.

We thank Stephen Sharp for his help in interpreting the statistical methods applied and results presented in the included papers.

Contributors: EMFvS led the review, identified the research question, and designed the search strategy. She is guarantor for the paper. EMFvS and AMMcM carried out the literature searches and screened the initial results, assessed methodological quality, extracted data, analysed the findings, and drafted the tables. EMFvS drafted the manuscript. All authors contributed to synthesising the results and critical revision of the manuscript, and all approved the final version.

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47 Ball K, Timperio AF, Crawford DA. Understanding environmental influences on nutrition and physical activity behaviors: where should we look and what should we count? *Int J Behav Nutr Phys Act* 2006;3:33.


Accepted: 11 July 2007
Objectively monitored patching regimens for treatment of amblyopia: randomised trial

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ABSTRACT
Objectives To compare visual outcome in response to two prescribed rates of occlusion (six hours a day and 12 hours a day).
Design Unmasked randomised trial.
Setting Research clinics in two London hospitals.
Participants 97 children with a confirmed diagnosis of amblyopia associated with strabismus, anisometropia, or both.
Interventions: 18 week period of wearing glasses (refractive adaptation) followed by occlusion prescribed (“patching”) for six or 12 hours a day.
Main outcome measures Visual acuity measured by logMAR letter recognition; objectively monitored rate of occlusion (hours a day).
Results The mean age of children at study entry was 5.6 (SD 1.5) years. Ninety were eligible for occlusion but 10 dropped out in this phase, leaving 80 children who were randomised to a prescribed dose rate of six (n=40) or 12 (n=40) hours a day. The mean change in visual acuity of the amblyopic eye was not significantly different (P=0.64) between the two groups (0.26 (95% confidence interval 0.21 to 0.31) log units in six hour group; 0.24 (0.19 to 0.29) log units in 12 hour group). The mean dose rates (hours a day) actually received, however, were also not significantly different (4.2 (3.7 to 4.7) in six hour group v 6.2 (5.1 to 7.3) in 12 hour group; P=0.06). The visual outcome was similar for those children who received three to six hours a day or more than six to 12 hours a day, but significantly better than that in children who received less than three hours a day. Children aged under 4 required significantly less occlusion than older children. Visual outcome was not influenced by type of amblyopia.
Conclusions Substantial (six hours a day) and maximal (12 hours a day) prescribed occlusion results in similar visual outcome. On average, the occlusion dose received in the maximal group was only 50% more than in the substantial group and in both groups was much less than that prescribed. Younger children required the least occlusion.
Trials registration Clinical Trials NCT00274664.

INTRODUCTION
The developing visual system is highly sensitive to visual experience.1 2 Interruption by any obstacle, such as blurred vision or strabismus before about 7 years, results in a reduction of visual capacity known as amblyopia.1 3 About 90% of work in the children’s eye services is related to amblyopia,4 and the condition carries an increased lifetime risk (at least three times that of the general population) of serious loss of vision in the other eye.5

In animal models, deficits caused by early monocular deprivation can be corrected to normal or near normal levels if treatment is initiated early in life.6 7 Though such studies have increased our understanding of the sensitivity of the developing visual system, they cannot tell us how children with amblyopia will respond.

Treatment of amblyopia has two main components: refractive correction by glasses and occlusion (by “patching”) or “penalisation” (by pharmacological or optical means) of the other eye. The improvement attributable to wearing glasses (that most children with amblyopia require) takes considerable time,8 9-10 a process we call “refractive adaptation.”11-13 Although wearing glasses and patching may both improve vision, their individual contributions to outcome are not differentiated from each other either in routine clinical practice or research as they are often prescribed together. Understanding of the dose-response of occlusion is further impeded by the failure to monitor how much of the prescribed treatment a child actually receives. The two studies that have used objective monitoring showed that compliance is rarely total and that it differs unpredictably from that prescribed.14 15 Compliance (concordance) with occlusion inflicts a considerable burden on the child and family because of a range of factors including skin irritation, forced use of an eye with degraded vision, poor cosmesis, and lengthy treatment periods.

Though studies have provided good evidence that occlusion therapy can improve the vision of amblyopic eyes,12 13 results suggest that “maximal” doses (12 hours a day) are no more beneficial than “substantial” doses (six hours a day). Despite these important results, many clinicians in the United States think that this new evidence is insufficient to initiate a change from traditional treatment methods that are based on “beliefs, from years of experience.”15 One objection raised is
Children who required correction with glasses (measurable refractive error, defined previously) or who had already been wearing glasses for less than 18 weeks entered the refractive adaptation phase. They were instructed to wear glasses all the time and scheduled to return for assessment of vision every six weeks from week 0 (onset of wearing glasses) until 18 weeks of refractive adaptation had been completed: a period that we have previously established would allow for all measurable improvement attributable to wearing glasses to have occurred. On completion of refractive adaptation, children who still met the study’s operational definition of amblyopia (see below) entered the occlusion phase. Those children who did not require correction with glasses or who had previously worn glasses for 18 weeks or longer entered directly into the occlusion phase. CES allocated children to prescribed dose rates of either 12 hours a day (maximal) or six hours a day (substantial) using a random number generator in the statistical package “R” (www.r-project.org/), stratified, but not blocked, by type of amblyopia and implemented by means of a concealed typed allocation list. Neither investigator nor the parents were masked to group allocation.

The occlusion dose monitor recorded episodes of occlusion to the nearest minute. The monitor consists of an eye patch with two electrodes attached to its undersurface connected by a plastic encapsulated wire lead to a data logger powered by battery. Visual function was recorded every two weeks, at which time we also audited the occlusion dose received between visits. The occlusion phase continued until visual acuity ceased to improve—as evidenced by either two inflexions of change in acuity (for example, improve/decline/improve/decline) or three consecutive measurements of acuity not differing by plus or minus 0.02 log units. On completion of the occlusion phase, children returned to standard clinical care.

Outcome measures
Our primary outcome measure was logMAR visual acuity. To encompass the reading ability and age span of the children, we used three logMAR visual acuity charts: ETDRS (Precision Vision, IL, USA), crowded, and uncrowded (Keeler, Windsor). We used standard protocols for visual acuity testing, scored by letter. The type of chart used for each child did not change during the course of the study.

We expressed visual outcome in three ways: firstly, by calculating the change in visual acuity of the amblyopic eye; secondly, by calculating the amount of residual amblyopia (acuity difference between the amblyopic and fellow eye at outcome); and, thirdly, by calculating the proportion of the visual deficit corrected (proportional improvement). The box gives details of relevant terminology.

Statistical analysis
We used Wilcoxon signed rank analysis to test for significant differences in outcome and dose between the groups and Kruskal-Wallis one way analysis of
variance on ranks to test for significant differences in outcome for participants by objectively monitored dose rate. The statistical power of the analyses (based on the outcome of a previously reported study) ranged from 0.6 to 0.9 to detect a 0.20 difference in logMAR values between groups (for ranges of n=17-41), with \( \alpha = 0.01 \).

**RESULTS**

Ninety seven children with a mean age of 5.6 (SD 1.5) years entered the study. Forty two had amblyopia associated with anisometropia (mean age 6.3 (SD 1.4) years), 21 had strabismus (4.7 (SD 1.3) years), and 34 had mixed anisometropia and strabismus (5.3 (SD 1.5) years). Ninety three children had measurable refractive error, although nine had undergone full refractive adaptation before study entry and progressed directly from baseline to the occlusion phase, leaving 84 (89%) children who underwent refractive adaptation (fig 1). No adverse events occurred.

**Refractive adaptation phase**

The primary purpose of this phase was to ensure that full refractive adaptation was complete before occlusion commenced. The mean (SD) visual acuity of amblyopic eyes improved from 0.55 (0.28) to 0.38 (0.34) logMAR; a mean improvement of 0.17 (95% confidence interval 0.12 to 0.22). In 40 children who had undergone partial refractive adaptation before study entry (with a mean (SD) number of weeks wearing glasses 14 (3)), the mean change in acuity was 0.11 (0.05 to 0.17). The change in acuity in the 44 children who underwent full refractive adaptation monitored in our study was significantly greater (\( P = 0.03 \)) (mean 0.22 (0.16 to 0.28) logMAR units).

During refractive adaptation, visual acuity in seven children improved to an extent that they were no longer eligible to enter the occlusion phase, with mean logMAR visual acuity 0.00 (−0.07 to 0.07) in the amblyopic eye and −0.04 (−0.10 to 0.02) in the fellow eye.

**Occlusion phase**

Though 90 children were eligible for occlusion, 10 left the study. The 80 remaining were randomised to a prescribed occlusion dose rate of six (n=40; age 5.4, SD 1.7) or 12 hours a day (n=40; age 5.6, SD 1.4) (table 1). In the six hour group, the mean (SD) visual acuity in the amblyopic eye improved from 0.45 (0.30) to 0.19 (0.19) logMAR, a change of 0.26 (95% confidence interval 0.21 to 0.31) log units. In the 12 hour group, the mean (SD) improvement was from 0.44 (0.30) to 0.20 (0.24) logMAR, a change of 0.24 (0.19 to 0.29) log units (table 2). There was no significant difference between the two groups for any outcome measure (visual acuity at start and end, magnitude of change in acuity, amount of residual amblyopia, or proportion of the amblyopia deficit corrected) (table 2).

The mean dose rates (hours a day) actually received were not significantly different (4.2 (3.7 to 4.7) in the six hour group \( > 6.2 \) (5.1 to 7.3) in the 12 hour group; \( P = 0.06 \)) (fig 2). Correspondingly, there was no difference in the total (accumulated) dose received by children in either of the two groups (\( P = 0.03 \)) (fig 3). Only nine (23%) and three (7%) children in the two groups, respectively, achieved an average concordance within 10% of their prescribed dose rate. Concordance was 3.6 times more variable in the 12 hour group than in the six hour group.

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**Table 1** Baseline characteristics of children according to two prescribed occlusion

<table>
<thead>
<tr>
<th>prescribed occlusion (hours/day)</th>
<th>6 (n=40)</th>
<th>12 (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) baseline visual acuity</td>
<td>0.45 (0.30)</td>
<td>0.44 (0.30)</td>
</tr>
<tr>
<td>Type of amblyopia:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anisometropia</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Strabismus</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Mixed</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>5.4 (1.7)</td>
<td>5.6 (1.4)</td>
</tr>
</tbody>
</table>

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Fig 1 | Recruitment and retention of participants during three study phases
The mean dose rate and the mean percentage concordance with the prescribed regimen did not differ significantly with age (table 3). Also, the mean dose rate of occlusion did not differ significantly with type of amblyopia, even when we stratified by prescribed dose rate (P = 0.05).

We also analysed the data by objectively monitored dose rate (that is, received rather than prescribed). Children were categorised into three groups according to the dose rate received in hours a day: ≤3 (n=22), ≥3-6 (n=32), and ≥6-12 (n=27). We found a significant difference in visual outcome between children who received less than three hours a day compared with those in the other two groups, with no difference between the latter (table 2). There was a significant trend for improved visual outcome (greater change in visual acuity and proportional improvement, less residual amblyopia) with increasing dose rates up to four hours a day (figs 4).

**Duration of occlusion therapy**

The mean time to achieve best visual acuity was nine weeks (SD 5, range 2-26 weeks). Only 12 children (eight in the six hour group; four in the 12 hour group) required more than 14 weeks of occlusion. The mean time to achieve best visual acuity did not differ significantly between the prescribed groups (10 weeks (SD 6, range 2-26) in the six hour group v eight weeks (SD 5, range 1-18) in the 12 hour group). Most of the improvement occurred in the first six weeks of treatment.

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### Table 2 | Mean (95% confidence interval) visual outcome according to prescribed dose of occlusion (six or 12 hours a day) and actual dose received

<table>
<thead>
<tr>
<th>Prescribed occlusion dose (hours/day)</th>
<th>Change in visual acuity</th>
<th>Proportion of deficit corrected</th>
<th>Residual amblyopia</th>
<th>Cumulative dose (hours)</th>
<th>Dose rate (hours/day)</th>
<th>Time to best visual acuity (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (n=39)</td>
<td>0.26 (0.21 to 0.31)</td>
<td>0.67 (0.57 to 0.77)</td>
<td>0.17 (0.11 to 0.23)</td>
<td>225 (183 to 267)</td>
<td>4.2 (3.7 to 4.7)</td>
<td>59 (49 to 69)</td>
</tr>
<tr>
<td>12 (n=41)</td>
<td>0.24 (0.18 to 0.30)</td>
<td>0.61 (0.50 to 0.72)</td>
<td>0.22 (0.15 to 0.29)</td>
<td>307 (240 to 384)</td>
<td>6.2 (5.1 to 7.3)</td>
<td>54 (44 to 64)</td>
</tr>
</tbody>
</table>

**Difference** 0.02 (0.0 to 0.04) 0.06 (0.03 to 0.09) 0.05 (0.03 to 0.07) 82 (63 to 101) 2.0 (1.7 to 2.3) 05 (1.8 to 8.8)

**P value** 0.64 0.34 0.25 0.30 0.06 0.48

### Fig 2 | Achieved dose rate in children allocated to six or 12 hours of occlusion a day. Vertical lines indicate interquartile range. To enhance clarity, dots have been jittered horizontally

### Fig 3 | Total dose of occlusion actually received in children allocated to six or 12 hours of occlusion a day. Vertical lines indicate interquartile range. To enhance clarity, dots have been jittered horizontally

*One child received dose rate of only 0.2 hours (12.5 minutes a day), an amount with doubtful therapeutic value. Significance values are unchanged with or without this data point.
Table 3 | Mean dose rate and concordance with prescribed regimen with age (years) and type of amblyopia

<table>
<thead>
<tr>
<th>Dose rate (hours/day):</th>
<th>Mean (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 years</td>
<td>4.05 (2.65 to 5.45)</td>
<td>0.48</td>
</tr>
<tr>
<td>4-6 years</td>
<td>4.65 (3.45 to 5.85)</td>
<td></td>
</tr>
<tr>
<td>&gt;6 years</td>
<td>5.55 (4.45 to 6.45)</td>
<td></td>
</tr>
</tbody>
</table>

Percentage concordance in 6 hour group:

<table>
<thead>
<tr>
<th>Dose rate (hours/day):</th>
<th>Percentage concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 years</td>
<td>53 (27 to 79)</td>
</tr>
<tr>
<td>4-6 years</td>
<td>72 (55 to 89)</td>
</tr>
<tr>
<td>&gt;6 years</td>
<td>69 (57 to 81)</td>
</tr>
</tbody>
</table>

Percentage concordance in 12 hour group:

<table>
<thead>
<tr>
<th>Dose rate (hours/day):</th>
<th>Percentage concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 years</td>
<td>41 (24 to 58)</td>
</tr>
<tr>
<td>4-6 years</td>
<td>47 (30 to 64)</td>
</tr>
<tr>
<td>&gt;6 years</td>
<td>58 (46 to 70)</td>
</tr>
</tbody>
</table>

Dose rate (hours/day):

<table>
<thead>
<tr>
<th>Type of amblyopia</th>
<th>Mean (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anisometropia</td>
<td>5.19 (4.19 to 6.19)</td>
<td>0.48</td>
</tr>
<tr>
<td>Strabismus</td>
<td>5.79 (4.39 to 7.19)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>4.56 (3.46 to 5.66)</td>
<td></td>
</tr>
</tbody>
</table>

Factors affecting outcome as a function of dose rate

The proportion of the deficit corrected and residual amblyopia were not significantly different (P=0.46 and P=0.42, respectively) for each type of amblyopia. The mean (95% confidence interval) proportions of deficit corrected were 0.60 (0.48 to 0.72) for anisometropia, 0.67 (0.54 to 0.80) for mixed, and 0.67 (0.52 to 0.82) for strabismus. The mean residual amblyopia was 0.18 (0.13 to 0.23); 0.23 (0.13 to 0.33), and 0.20 (0.07 to 0.32), respectively.

There was a significant difference in the dose rate required to obtain maximum proportional improvement with respect to age (table 4, fig 5). For those children under 4 years of age, we observed significant gains in the proportion of the deficit corrected even at low dose rates (0-3 hours a day) with marginal but not significant (P=0.54) additional gains for doses over three hours a day (table 4). In contrast, children aged 4-6 and over 6 years showed significant differences (P=0.03 and P<0.001, respectively) between none to three hours a day and up to six hours a day but no difference between three to six and six to 12 hours a day. Children aged over 6 who wore a patch up to three hours a day had little deficit corrected. To gain equivalent proportional improvement in children aged under

6, those aged over 6 needed to achieve a dose rate over three hours a day.

DISCUSSION

Substantial (six hours a day) and maximal (12 hours a day) prescribed occlusion regimens provide equivalent visual outcome for the treatment of unilateral amblyopia in children aged 3-8. These findings agree with those from a previous study.13 By objectively monitoring occlusion we showed that the maximal group received only about 50% more occlusion a day, despite being prescribed twice the rate in the substantial group. Furthermore, analysis of dose-response showed that the average amount of occlusion received in each group was sufficient to achieve best outcome. Researchers have previously raised the possibility that similar outcomes seen with different prescribed occlusion rates could be because similar rates were actually received, but the study did not include any objective monitoring.13

Optimum dose rate

We carried out exploratory analyses on the effect of received dose rate and on dose rate and age. The relation between dose rates and outcome showed that

Table 4 | Proportion of deficit corrected (means and 95% confidence intervals) grouped by age at start of occlusion and dose rate received

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>≤3 hours/day (n=22)</th>
<th>&gt;3-6 hours/day (n=32)</th>
<th>&gt;6-12 hours/day (n=27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 (n=20)</td>
<td>0.53 (0.34 to 0.72)</td>
<td>0.66 (0.46 to 0.86)</td>
<td>0.68*</td>
<td>0.54</td>
</tr>
<tr>
<td>4-6 (n=32)</td>
<td>0.49 (0.30 to 0.68)</td>
<td>0.80 (0.67 to 0.93)</td>
<td>0.60 (0.38 to 0.82)</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt;6 (n=17)</td>
<td>0.17 (0.1 to 0.44)</td>
<td>0.83 (0.61 to 1.05)</td>
<td>0.67 (0.45 to 0.89)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P value: 0.03 0.23 0.97 —

*Denotes single data point. P values refer to comparison between ≤3 hours/day and the two other groups (3-6 hours/day and ≥12 hours/day) and between age 6 and 6.5 years.
outcome was similar in children receiving between four and 12 hours a day. We observed a linear relation between improved outcome and increased dose rate for dose rates up to four hours a day (fig 4), and our analysis suggests that achieving an initial dose rate of three to four hours a day should be a clinical priority. The response depends on age, however, so that for those under 4 years this could be reduced. Higher dose rates achieve the best outcome more rapidly but at a risk of accumulating excessive non-therapeutic hours of patching. Thus, patching for all waking hours is almost certainly excessive.

We consider that the observed effect of dose prescribed (that is, in the intention to treat analysis) was not compromised by potential confounding of other variables (for example, type of amblyopia, age of child, visual acuity at start of study). The imperfect adherence to assigned treatment, however, implies that an observational analysis that inspects the effect of dose received may be subject to confounding. A carefully constructed multiple regression analysis of causal inference methods would therefore be required to analyse the data on dose received.23

Concordance

Eye patching can cause considerable distress for both the child and family.21 24 Full concordance with prescribed dose rates is rare; children in our study received on average 66% and 50% of their prescribed occlusion of six and 12 hours a day, respectively. This suggests that these prescribed regimens imposed a considerable burden on our participants and would be expected to do so in routinely treated patients. We observed a plateau of improvement in outcome at about four hours a day. Prescriptions of occlusion should take this into account, minimising the amounts necessary for best expected outcome.

The conventional clinical approach in a child whose vision does not improve with part time occlusion therapy is to prescribe a more intense regimen,16 thus increasing the burden of treatment on the child and family.4 19 21 24 Knowledge of concordance with treatment permits detailed evaluation of treatment strategy. For example, if compliance was low initially then this could be the reason for poor outcome, in which case education25 or different patching strategies may facilitate best outcome. If concordance was high, however, additional occlusion will probably not be beneficial.

Objective monitoring of occlusion

Our study highlights the benefits of objective monitoring of occlusion within routine clinical practice. Firstly, clinicians no longer have to rely on subjective and qualitative feedback from children and parents as to the amount of patching achieved. Secondly, the availability of an objective quantitative record of the occlusion dose and dose rate allows the clinician to tailor advice and prescription to an individual patient. In practical terms, this will reduce the number of patching hours prescribed and clinic visits required. This should result in an improvement in cost effectiveness and potentially a better experience for the child and his or her family.

Although treatment for amblyopia is thought to be more successful at earlier stages of visual development,26 the evidence is unconvincing and contradictory.26-32 We have provided further evidence that age can influence effectiveness. It seems that patching dose rate is the predictive factor of whether younger children (over 6 years) can be treated successfully. Thus the child under 4 years responds both more rapidly and with less occlusion than the older child, but the final level of attainment for all ages between 3 and 8 years is the same. The data provide further evidence of the timing and plasticity within the sensitive period for visual recovery. Towards the end of the visual sensitive period, however, it seems that the deficit becomes more resistant and less plastic, requiring more occlusion to achieve the same outcome.

We did not intend to provide specific evidence based guidelines for the treatment of amblyopia as this would require further accumulation of evidence (such as on the influence of the severity of amblyopia). Our results, however, suggest that a typical amblyopic child (in this study a child with a mean acuity of 0.45 logMAR after refractive adaptation who improved by 0.26 logMAR as a result of occlusion) would require an accumulation in the region of 180-270 received hours of patching at an average dose rate of four hours a day (table 2 and figure 4).

Dose-response analysis of amblyopia therapy is a novel approach that can elucidate the kinetics of the sensitive period in humans. By fine tuning therapeutic strategies it will be possible to facilitate evidence based treatment plans specific for each child. This will reduce the burden of amblyopia treatment for the child and family and, ultimately, for health service providers.

We thank all the children and parents who took part in the study and the members of the ROTAS Cooperative (Tricia Rice, Rowena McNamara, Avril Charmock, Clare Baldwin, Naheem Abbas).

Contributors: All authors contributed to the design. CES was responsible for the day to day management of the study. ARF and CES analysed the data. CES drafted the manuscript, which was revised by all authors. ARF is guarantor.

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Competing interests: None declared.

Ethical approval: Hillingdon and St Mary’s Hospitals London NHS Trusts’ local research ethics committees.

Provenance and peer review: Non-commissioned, externally peer reviewed.

5 Rahl J, Logan S, Timms C, Russell-Eggitt I, Taylor D. Risk, causes and outcomes of visual impairment after loss of vision in the non-BMJ | ONLINE FIRST | bmj.com
Oclusion therapy (patching) is the main treatment for amblyopia. It is an unpleasant procedure and compliance with treatment is often poor. Given the inability to record objectively the amount of occlusion a child actually receives, many practitioners prescribe large doses, above six hours a day.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Occlusion therapy (patching) is the main treatment for amblyopia. It is an unpleasant procedure and compliance with treatment is often poor. Given the inability to record objectively the amount of occlusion a child actually receives, many practitioners prescribe large doses, above six hours a day.

WHAT THIS STUDY ADDS

Results of occlusion do not differ in groups prescribed six or 12 hours of occlusion a day. Objective monitoring shows that the amount of occlusion a child actually receives is substantially less than that prescribed, irrespective of dosing regimen.
Accuracy of electrocardiography in diagnosis of left ventricular hypertrophy in arterial hypertension: systematic review

Daniel Pewsner, senior research fellow in general practice; and general practitioner,1 Peter Juni, reader in clinical epidemiology;2 Matthias Egger, professor;3 Markus Battaglia, senior research fellow in general practice, and general practitioner,1 Johan Sundström, associate professor,4 Lucas M Bachmann, reader in clinical epidemiology and deputy director5

ABSTRACT

Objective To review the accuracy of electrocardiography in screening for left ventricular hypertrophy in patients with hypertension.

Design Systematic review of studies of test accuracy of six electrocardiographic indexes: the Sokolow-Lyon index, Cornell voltage index, Cornell product index, Gubner index, and Romhilt-Estes scores with thresholds for a positive test of ≥4 points or ≥5 points.

Data sources Electronic databases ((Pre-)Medline, Embase), reference lists of relevant studies and previous reviews, and experts.

Study selection Two reviewers scrutinised abstracts and examined potentially eligible studies. Studies comparing the electrocardiographic index with echocardiography in hypertensive patients and reporting sufficient data were included.

Data extraction Data on study populations, echocardiographic criteria, and methodological quality of studies were extracted.

Data synthesis Negative likelihood ratios, which indicate to what extent the posterior odds of left ventricular hypertrophy is reduced by a negative test, were calculated.

Results 21 studies and data on 5608 patients were analysed. The median prevalence of left ventricular hypertrophy was 33% (interquartile range 23-41%) in primary care settings (10 studies) and 65% (37-81%) in secondary care settings (11 studies). The median negative likelihood ratio was similar across electrocardiographic indexes, ranging from 0.85 (range 0.34-1.03) for the Romhilt-Estes score (with threshold ≥4 points) to 0.91 (0.70-1.01) for the Gubner index. Using the Romhilt-Estes score in primary care, a negative electrocardiogram result would reduce the typical pre-test probability from 33% to 31%. In secondary care the typical pre-test probability of 65% would be reduced to 63%.

Conclusion Electrocardiographic criteria should not be used to rule out left ventricular hypertrophy in patients with hypertension.

INTRODUCTION

Arterial hypertension is a major cause of coronary heart disease, stroke, and heart failure. Several studies have shown that left ventricular hypertrophy is an important risk factor in patients with hypertension, leading to a fivefold to 10-fold increase in cardiovascular risk,1,2 which is similar to the increase seen in patients with a history of myocardial infarction.2

The presence of left ventricular hypertrophy, in addition to hypertension, thus has important implications for assessing risk and managing patients, including decisions on interventions other than antihypertensive treatment, such as lipid lowering treatment and lifestyle modifications.7-8 Accurate and early diagnosis of left ventricular hypertrophy is therefore an important component of the care of patients with hypertension.

Decisions about treatment should be based on assessments of hypertensive target organ damage and overall cardiovascular risk. The appropriate diagnostic work-up of suspected left ventricular hypertrophy in patients with hypertension is less clear, however. More than 30 different electrocardiographic indexes for the diagnosis of left ventricular hypertrophy, based on the standard 12 lead electrocardiogram, have been described. Many of the proposed indexes have remained anecdotal, but others are commonly used, including the Sokolow-Lyon index,9 the Cornell voltage index,10 the Cornell product index,11 the Gubner index,12 and the Romhilt-Estes scores.13 However, debate about their comparative diagnostic value continues.14-16 We did a systematic review to clarify the accuracy of different electrocardiographic indexes, with emphasis on their ability to rule out left ventricular hypertrophy in patients with arterial hypertension.

METHODS

Identification of studies

We searched Medline and (Pre-)Medline (PubMed version) from 1966 to present (last update December 2005) and Embase (Ovid version) from 1980 to present (last update December 2005) to identify observational studies that evaluated the accuracy of
electrocardiographic indexes for the diagnosis of left ventricular hypertrophy and established the presence or absence of left ventricular hypertrophy with echocardiography. We restricted our search to papers published in English, German, Italian, Spanish, French, and Portuguese. The search strategies are available on request. Checks of the reference lists of relevant studies and contacts with experts in the field complemented the electronic searches.

Study selection
We included studies in asymptomatic patients with primary arterial hypertension in any type of healthcare setting. Studies included patients on antihypertensive treatment, patients with newly diagnosed hypertension being evaluated for treatment, and patients in whom treatment was withdrawn shortly before evaluation. We selected the studies in a two stage process. Two reviewers (DP and MB) independently assessed the abstracts of all retrieved studies. We ordered all papers considered to be potentially relevant by one reviewer and made the final decision by using a checklist to assess whether the criteria for inclusion had been met. We included all studies that assessed the electrocardiographic criteria in hypertensive adults against echocardiography (left ventricular mass indexed for body surface area) for whom sufficient data to allow the construction of the two by two table was available. We excluded studies that compared patients with known left ventricular hypertrophy with healthy controls (diagnostic case-control studies).17 18 We also excluded studies that used a reference standard calibrated according to heart mass/body height and studies that evaluated patients with concomitant left anterior fascicular block and left bundle branch block.

Data extraction
We extracted data in duplicate, including the number and characteristics of patients (mean age, distribution of sex and ethnic groups, mean body mass index, and smoking status), the healthcare setting (primary care versus secondary care), the prevalence of echocardiographically confirmed left ventricular hypertrophy, the electrocardiographic indexes evaluated, and the definition of the echocardiography threshold. We constructed two by two contingency tables for all electrocardiographic criteria reported in included articles. The data extraction form had been piloted for other diagnostic reviews and is described in detail elsewhere.13 21 We contacted first authors of eligible studies that reported insufficient data and asked them for additional information.

Assessment of study quality
We assessed the methodological quality of papers that met the eligibility criteria. We examined the methods of patient selection and data collection, completeness of descriptions of index and reference tests, completeness of blinding, and the likelihood of verification bias.17 18 20 We ranked studies as high quality if they described the setting (for example, family physicians referring patients to the clinic); collected data prospectively, with enrolment of consecutive patients and follow-up of all patients, including those who did not have echocardiography; and provided details on echocardiography and whether the assessor of the echocardiography was unaware of the electrocardiogram result or vice versa (blinding). We ranked studies as intermediate quality if they met four or five of the six criteria, as low quality if they met only one to three of the six criteria, and as very low quality if they met none of the criteria.

Statistical analysis
We added 0.5 to each cell of all two by two tables that included one or more zero cells. We calculated sensitivities, specificities, and likelihood ratios with their confidence intervals. As the electrocardiogram will mainly be used to rule out the diagnosis of left ventricular hypertrophy, we were particularly interested in the sensitivity and the likelihood ratio of a negative electrocardiogram result. The likelihood ratio of a negative test indicates how likely it is to find a negative result among people with left ventricular hypertrophy compared with those without.21 The negative likelihood ratio is calculated as (1−sensitivity)/specificity. It indicates to what extent the posterior odds of left ventricular hypertrophy would be reduced if the test was negative. If the prior odds is 1 and the negative likelihood ratio is 0.5, the posterior odds will be 1×0.5=0.5. The likelihood ratio of a positive test indicates how likely it is that a positive result will be found among people with left ventricular hypertrophy compared with those without; it is defined as sensitivity/(1−specificity).21 We summarised results by plotting sensitivities and specificities in the receiver operating curve space and

Definitions of six electrocardiographic indexes commonly used in diagnosis of left ventricular hypertrophy
- Sokolow-Lyon index—sum of SV1+RV5 or V6≥3.5 mV
- Cornell voltage index—men: RaVL+SV3≥2.2 mV; women: RaVL+SV3≥2.0 mV
- Cornell product—men: (SV3+RaVL)×QRS duration ≥2440 ms; women: (SV3+(RaVL+8 mV))×QRS duration≥2440 ms
- Gubner—RI+SiII≥25 mV
- Romhilt-Estes scores—excessive amplitude: 3 points (largest R or S wave in limb leads ≥20 mV or S wave in V1 or V2 ≥30 mV or R wave in V5 or V6 ≥30 mV). ST-T segment pattern of LV strain: 3 points (ST-T segment vector shifted in direction opposite to mean QRS vector). Left atrial involvement: 3 points (terminal negativity of P wave in V1≥1 mm with duration ≥0.04 s). Left axis deviation: 2 points (left axis ≥–30° in frontal plane). Prolonged QRS duration: 1 point (≥0.09 s). Intrinsicoid deflection: 1 point (intrinsicoid deflection in V5 or V6≥0.05 s). Two thresholds in use: positive if ≥4 points or ≥5 points

Number of signs and symptoms needed for diagnosis of left ventricular hypertrophy
- Sokolow-Lyon index
- Cornell voltage index
- Cornell product
- Gubner
- Romhilt-Estes scores

Sensitivity and specificity of electrocardiographic indexes
<table>
<thead>
<tr>
<th>Electrocardiographic Index</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sokolow-Lyon index</td>
<td>0.85</td>
<td>0.82</td>
<td>0.36</td>
</tr>
<tr>
<td>Cornell voltage index</td>
<td>0.80</td>
<td>0.85</td>
<td>0.42</td>
</tr>
<tr>
<td>Cornell product</td>
<td>0.85</td>
<td>0.82</td>
<td>0.36</td>
</tr>
<tr>
<td>Gubner</td>
<td>0.80</td>
<td>0.85</td>
<td>0.42</td>
</tr>
<tr>
<td>Romhilt-Estes scores</td>
<td>0.85</td>
<td>0.82</td>
<td>0.36</td>
</tr>
</tbody>
</table>
by calculating medians, ranges, and interquartile ranges.

**RESULTS**

**Literature search**

Our search identified 1761 citations. After exclusion of duplicates and examination of the abstracts we considered 142 as potentially eligible, and after scrutinising the full text articles we included 21 studies. Figure 1 summarises the process of assessing and selecting the studies. First authors provided additional information on nine studies.

Study characteristics

The 21 studies included a total of 5608 (range 30-947) patients. Table 1 details the characteristics and methodological quality of the studies. Ten studies were done in primary care and 11 in secondary care. Three studies included only men; all others examined men and women. The median prevalence of left ventricular hypertrophy was 33% (interquartile range 23-41%) in primary care settings and 65% (37-81%) in secondary care. Three studies met all six methodological criteria and were ranked as high quality. Another 11 studies met four or five criteria and were ranked as intermediate quality, whereas seven studies met two or three quality items and were considered of low quality. Table 1 lists the criteria met by different studies.

**Electrocardiographic indexes**

The 21 articles reported on 12 different electrocardiographic criteria. We analysed in detail the six most commonly used indexes, including the Sokolow-Lyon voltage index, the Cornell voltage and Cornell product indexes, the Gubner index, and the Romhilt-Estes score with two different thresholds. The box shows definitions of these indexes.

**Sensitivity, specificity, and likelihood ratios**

Figure 2 shows the accuracy data for the six electrocardiographic indexes plotted in the receiver operating curve space. For all indexes, most studies are located in the bottom left corner of low sensitivity and high specificity. Table 2 shows, for each of the 21 studies,

### Table 1 | Characteristics of studies of test accuracy of six commonly used electrocardiographic criteria for diagnosis of left ventricular hypertrophy

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Study characteristics</th>
<th>Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clementy, 1982&lt;sup&gt;w1&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men and women ≥120; A, B, E</td>
<td>No of patients: 56; Mean age (years): 47; Men (%): 61; Caucasian: 39</td>
</tr>
<tr>
<td>McLennan, 1988&lt;sup&gt;w2&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥145; women ≥110; A, B, E</td>
<td>No of patients: 100; Mean age (years): 58; Men (%): 65; Caucasian: 69</td>
</tr>
<tr>
<td>Calaca, 1990&lt;sup&gt;w3&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥134; women ≥110; C</td>
<td>No of patients: 56; Mean age (years): 55; Men (%): 52; Caucasian: 52</td>
</tr>
<tr>
<td>Ottestad, 1991&lt;sup&gt;w4&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥124; A, C, E, H</td>
<td>No of patients: 100; Mean age (years): 46; Men (%): 100; Caucasian: 48</td>
</tr>
<tr>
<td>Paladil, 1991&lt;sup&gt;w5&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥131; women ≥110; A, B, C, 2, 3, 4, 5, 6</td>
<td>No of patients: 74; Mean age (years): 49; Men (%): 36; Caucasian: 81</td>
</tr>
<tr>
<td>Vijan, 1991&lt;sup&gt;w6&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men and women ≥115; A, E, K, 1, 2, 3, 4, 5</td>
<td>No of patients: 75; Mean age (years): 54; Men (%): 79; Caucasian: 45</td>
</tr>
<tr>
<td>Lee, 1992&lt;sup&gt;w7&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥131; women ≥110; A, B, C, E, 2, 3, 4, 5</td>
<td>No of patients: 270; Mean age (years): 54; Men (%): 69; Black (US), white (US): 23</td>
</tr>
<tr>
<td>Fragra, 1993&lt;sup&gt;w8&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥125; women ≥112; A, B, C, E, H, I, 1, 3, 4, 5</td>
<td>No of patients: 200; Mean age (years): 51; Men (%): 62; Caucasian: 35</td>
</tr>
<tr>
<td>Fragra, 1994&lt;sup&gt;w9&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥125; women ≥112; A, C, E, H, I, 1, 3, 4, 5, 6</td>
<td>No of patients: 100; Mean age (years): 50; Men (%): 62; Caucasian: 26</td>
</tr>
<tr>
<td>Schillaci, 1994&lt;sup&gt;w10&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥128; women ≥106; A, B, C, E, F, G, H, I</td>
<td>No of patients: 923; Mean age (years): 51; Men (%): 50; Caucasian: 34</td>
</tr>
<tr>
<td>Tomiyama, 1994&lt;sup&gt;w11&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥125; A, C, E</td>
<td>No of patients: 77; Mean age (years): 100; Japanese: 19</td>
</tr>
<tr>
<td>Crow, 1995&lt;sup&gt;w12&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥134; women ≥110; A, C, E, D, 1, 2, 3, 4, 5, 6</td>
<td>No of patients: 834; Mean age (years): 55; Men (%): 61; Black (US), white (US): 15</td>
</tr>
<tr>
<td>Casiglia, 1996&lt;sup&gt;w13&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥134; women ≥110; A, C, E, 1, 2, 3, 4, 5, 6</td>
<td>No of patients: 352; Mean age (years): –; Men (%): –; Caucasian: 73</td>
</tr>
<tr>
<td>Kamide, 1996&lt;sup&gt;w14&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥123; women ≥110; A, E, 1, 2, 3, 4, 5, 6</td>
<td>No of patients: 48; Mean age (years): 70; Men (%): –; Japanese: 65</td>
</tr>
<tr>
<td>Domingos 1998&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥120; women ≥98; A, B, C, E, 2, 3, 4</td>
<td>No of patients: 30; Mean age (years): 57; Men (%): 40; White, Afro-Caribbean: 83</td>
</tr>
<tr>
<td>Verdecchia, 2000&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥125; women ≥125; A, C, E, G, H, 2, 3, 4, 5, 6</td>
<td>No of patients: 947; Mean age (years): 60; Men (%): 59; Caucasian: 27</td>
</tr>
<tr>
<td>Chapman, 2001&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥134; women ≥110; A, C, 1, 3, 4, 5</td>
<td>No of patients: 386; Mean age (years): 48; Men (%): 49; White, Afro-Caribbean, other (UK): 37</td>
</tr>
<tr>
<td>Sundström 2001&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥150; A, C, D, H, 1, 3, 4, 6</td>
<td>No of patients: 212; Mean age (years): 70; Men (%): 100; Caucasian: 41</td>
</tr>
<tr>
<td>Wong 2003&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥134; women ≥110; A, C, D, 1, 3, 4, 5</td>
<td>No of patients: 47; Mean age (years): –; Men (%): –; Caucasian: 51</td>
</tr>
<tr>
<td>Martinez 2003&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Primary care</td>
<td>Men ≥134; women ≥110; C, 1, 3, 4, 6</td>
<td>No of patients: 250; Mean age (years): 49; Men (%): 47; Caucasian: 32</td>
</tr>
<tr>
<td>Salles 2005&lt;sup&gt;21&lt;/sup&gt;</td>
<td>Secondary care</td>
<td>Men ≥116; women ≥104; A, C, D, 1, 2, 3, 4, 5, 6</td>
<td>No of patients: 471; Mean age (years): 60; Men (%): 28; White, Afro-Caribbean: 81</td>
</tr>
</tbody>
</table>

ECG=electrocardiogram; LVH=left ventricular hypertrophy.

<sup>*</sup>ASokolow-Lyon index; <sup>B</sup>Gubner index; <sup>C</sup>sex specific Cornell voltage; <sup>D</sup>sex specific Cornell product; <sup>E</sup>Romhilt-Estes score; <sup>F</sup>Framingham criteria; <sup>G</sup>Perugia score; <sup>H</sup>left ventricular strain; <sup>I</sup>left atrium enlargement; <sup>J</sup>Sokolow-Lyon index and left ventricular strain.

<sup>†</sup>1consecutive enrolment; 2prospective design; 3clear description of technique; 4=clear definition of cut-off levels; 5blinded assessment of electrocardiogram; 6blinded assessment of echocardiography.
was developed in 1949. Irrespective of the index clearly superior to the Sokolow-Lyon index, which the more recent and more sophisticated indexes is hypertrophy is unsatisfactory. In particular, none of diagnostic indexes in the diagnosis of left ventricular diagnostic tests found that the accuracy of electrocardiographic indexes in the diagnosis of left ventricular hypertrophy. This systematic review of studies of the accuracy of electrocardiographic testing for other reasons, electrocardiograms should not be done specifically to exclude left ventricular hypertrophy in patients with hypertension. A comprehensive assessment of cardiovascular risk is important to guide decisions on therapeutic interventions in these patients, and referral for echocardiography may be justified in some patients. Referral for specialist examinations and care is often based on high cardiovascular risk scores, but echocardiography may be more informative in hypertensive patients who, on the basis of age, sex, smoking history, and blood lipids, are at low or intermediate risk. In patients known to be at high risk, echocardiographic findings will often not affect clinical management, because interventions to reduce risk, such as example lipid lowering treatment, smoking cessation, and dietary modification, are already in place.

DISCUSSION
This systematic review of studies of the accuracy of diagnostic tests found that the accuracy of electrocardiographic indexes in the diagnosis of left ventricular hypertrophy is unsatisfactory. In particular, none of the more recent and more sophisticated indexes is clearly superior to the Sokolow-Lyon index, which was developed in 1949. Irrespective of the index used, the electrocardiogram is a poor screening tool to exclude left ventricular hypertrophy in hypertensive patients in primary and secondary care settings. Of note, specificity was reasonably high in most studies, but because sensitivity was low the power to rule in left ventricular hypertrophy was also unsatisfactory, and the electrocardiogram cannot be considered a “SpPI” (specific, positive, in) test for the diagnosis of left ventricular hypertrophy.24

Strengths and limitations
We did a comprehensive literature search, selected studies according to pre-defined criteria, and appraised the methodological quality of studies. We acknowledge that we may have missed some studies, but their inclusion is unlikely to have changed our conclusions: empirical research suggests that unpublished studies of test accuracy are small and show lower diagnostic accuracy.24 We excluded diagnostic case-control studies, which are known to overestimate accuracy,17 18 as well as studies that did not index ventricular mass for body surface area. We also excluded studies that evaluated patients with concomitant left anterior fascicular block and left bundle branch block, because these patients usually need further examinations and referral irrespective of left ventricular hypertrophy. We summarised the evidence by calculating medians, rather than combining data in meta-analysis. We believe that a formal meta-analysis would have added little in this situation. Similarly, we thought that further exploration of potential sources of heterogeneity was not warranted. The published data did not allow direct comparisons of test accuracy between the different indexes. More importantly, we did not identify any randomised comparisons of diagnostic and treatment strategies and assessed clinical end points.

Implications for clinical practice
Although many hypertensive patients have electrocardiographic testing for other reasons, electrocardiograms should not be done specifically to exclude left ventricular hypertrophy in patients with hypertension. A comprehensive assessment of cardiovascular risk is important to guide decisions on therapeutic interventions in these patients, and referral for echocardiography may be justified in some patients. Referral for specialist examinations and care is often based on high cardiovascular risk scores, but echocardiography may be more informative in hypertensive patients who, on the basis of age, sex, smoking history, and blood lipids, are at low or intermediate risk. In patients known to be at high risk, echocardiographic findings will often not affect clinical management, because interventions to reduce risk, such as example lipid lowering treatment, smoking cessation, and dietary modification, are already in place.

Recommendations from current guidelines differ. The 2003 European Society of Hypertension-European Society of Cardiology guidelines recommend echocardiography in patients in whom target organ damage is not discovered by routine
<table>
<thead>
<tr>
<th>Index/authors</th>
<th>True positives</th>
<th>False positives</th>
<th>False negatives</th>
<th>True negatives</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<tbody>
<tr>
<td>Sokolow-Lyon</td>
<td></td>
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<td>Casiglia&lt;sup&gt;13&lt;/sup&gt;</td>
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electrocardiography. The 2004 guidelines from the British Hypertension Society state that echocardiography is not required routinely but is valuable to confirm or refute the presence of left ventricular hypertrophy when the electrocardiogram shows high left ventricular voltage without T wave abnormalities. In the United States, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends routine electrocardiography but makes no mention of echocardiography.

The evidence on the capacity of various antihypertensive agents to decrease left ventricular hypertrophy is limited. Several studies have shown a possible advantage of angiotensin converting enzyme inhibitors and angiotensin II subtype 1 receptor antagonist based treatments in reducing left ventricular hypertrophy and preventing clinical events. However, as most patients need several antihypertensive agents for optimal blood pressure control, the relative merits of each agent may be of lesser importance. In addition to antihypertensive drugs, preventing cardiovascular disease through modifications of other risk factors such as smoking cessation, lifestyle change, or lipid lowering treatment is the most promising approach.

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Future research
Further research is needed to identify cost effective diagnostic strategies in primary care settings, including randomised controlled trials that compare different diagnostic and treatment strategies and assess clinical end points. Such research could inform the development of algorithms to identify patients who should be referred for echocardiography. In the absence of accurate and inexpensive screening tests for left ventricular hypertrophy, research into new diagnostic technologies is also warranted. Of note, electrocardiographic left ventricular hypertrophy and echocardiographic left ventricular hypertrophy have been shown to predict mortality independently of each other and may therefore assess different aspects of the underlying pathology. Alternatively, they may measure the same condition with some imprecision. For example, in echocardiography, distinguishing physiological from pathological left ventricular hypertrophy can sometimes be difficult. Further studies are needed to better define the pathophysiological mechanisms and outcomes in patients with echocardiographically confirmed left ventricular hypertrophy but negative electrocardiograms. Similarly, more data are needed on patients with positive electrocardiographic tests but negative echocardiography.

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Fig 2 | Receiver operating curves of six commonly used electrocardiographic indexes for diagnosis of left ventricular hypertrophy. Each point represents one study.

See box for definitions of indexes.
Fig 3 | Forest plots of negative likelihood ratio from test accuracy studies of six electrocardiographic indexes in diagnosis of left ventricular hypertrophy. Points represent estimates of likelihood ratio; lines represent 95% confidence intervals.
### Electrocardiographic Index

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Echocardiography is needed for a comprehensive assessment of cardiovascular risk in hypertensive patients

WHAT THIS PAPER ADDS

The accuracy of the more commonly used electrocardiographic criteria for ruling out left ventricular hypertrophy is unsatisfactory in both primary and secondary care.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Several indexes calculated from standard 12 lead electrocardiograms are used in the diagnostic work-up of patients with hypertension.

Conclusions

The power of some of the more commonly used electrocardiographic criteria to rule out the diagnosis of left ventricular hypertrophy in patients with hypertension is poor. Further research is needed to assess the cost effectiveness of different diagnostic and treatment strategies and to develop alternative diagnostic technologies for assessment of left ventricular hypertrophy in primary care.

We thank Marc Geritsch, Richard S Crow, Benedict Martina, Fritz Grossenbacher, and Heiner C Bucher for valuable input and for commenting on an earlier draft.

Contributors: DP, ME, PI, and MB initiated the study and wrote the protocol. DP and MB did the searches, screened the literature, and extracted the data. LMB did the analysis, supervised the work, and wrote a first draft, which was subsequently revised by ME. All authors participated in interpreting the data and critically revising the manuscript for important intellectual content. ME is the guarantor.

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Colorectal cancer

Anne B Ballinger, Clive Anggiansah

Colorectal cancer is common, the presenting symptoms are non-specific, and the stage of disease at diagnosis is closely related to survival. In this review we discuss disease presentation, criteria for urgent referral of patients to specialist care, and recent developments in the implementation of national screening programmes, which aim to reduce mortality from this common disease. Many general practitioners will also refer patients with suspected colorectal cancer “direct to test” and this review covers the various modalities for investigation of patients with colorectal symptoms.

Sources and selection criteria
We searched PubMed for recent papers using the keywords “colorectal cancer”, “screening”, “investigation”, and “incidence”. We also searched the Cochrane Database of Systematic Reviews using the search terms “colorectal cancer” and “inflammatory bowel disease”. In addition we used our personal reference archive.

How common is colorectal cancer?
In the Western world colorectal cancer is the second most common cancer in women after breast cancer and the third most common in men after lung and prostate cancer. Rates vary largely worldwide, being lowest in Africa and Asia and highest in Europe, North America, and Australasia. In the United Kingdom the lifetime incidence of colorectal cancer in people at average risk is 5% and the age standardised incidence rate is 44.3 per 100,000 population.3

How does colorectal cancer develop?
In most cases colorectal cancers arise from dysplastic adenomatous polyps. A multistep process involves the inactivation of a variety of genes that suppress tumours and repair DNA and the simultaneous activation of oncogenes. This confers a selective growth advantage to the colonic epithelial cell and drives the transformation from normal epithelium to adenomatous polyp to invasive colorectal cancer.4 Germline (hereditary) mutations underlie the well described inherited colon cancer syndromes whereas sporadic cancers arise from a stepwise accumulation of somatic genetic mutations. A single germline mutation in the APC tumour suppressor gene is responsible for the dominantly inherited syndrome, familial adenomatous polyposis coli. It is characterised by the development of hundreds to thousands of adenomatous polyps in the colon and development of colorectal cancer and other cancers in the third and fourth decade of life. Clinical expression of the disease is seen when the inherited mutation of one APC allele is followed by a “second hit” mutation or deletion of the second allele.

Who is at greatest risk of colorectal cancer?
Increasing age is the greatest risk factor for sporadic colorectal cancer: 99% of cases occur in people aged more than 40 and 85% in those aged more than 60 (fig 1). In Europe the incidence of colorectal cancer is gradually increasing, in part due to the ageing of the population but also due to an increase in the age specific incidence, suggesting that lifestyle or environmental factors, or both, contribute. The much higher incidence of colorectal cancer in more affluent countries compared with less developed countries is also thought to be related to lifestyle factors such as obesity and consumption of processed meat, and an inverse relation with physical activity and consumption of fruit and vegetables.

Next to age, family history is the most common risk factor for colorectal cancer. Familial adenomatous polyposis and hereditary non-polyposis colorectal cancer are the most common of the familial cancer syndromes, but together these two syndromes account for fewer than 5% of cases. About 10-20% of patients describe a family history of colorectal cancer, but the pattern of inheritance and clinical features are not consistent with one of these well characterised syndromes (table 1).5

What are the symptoms of colorectal cancer?
Abdominal pain, change in bowel habit, and rectal bleeding or anaemia are the commonest presenting symptoms of colorectal cancer but these symptoms also commonly occur in other gastrointestinal conditions. A change in bowel habit is a more common presenting symptom for left sided cancers caused by a progressive narrowing of the bowel lumen, with diarrhoea, a change in stool form, and eventually intestinal obstruction. About 10% of patients with iron deficiency anaemia have colorectal cancer, most commonly on the right side, and thus iron deficiency in men, and women who are not menstruating, is an indication for urgent referral and investigation.7,8

In 2005 the National Institute for Health and Clinical Excellence issued updated UK based guidelines that outlined signs and symptoms warranting
urgent referral (within two weeks) for further specialist review or investigation of suspected colorectal cancer (table 2).

**How should suspected colorectal cancer be investigated?**

**Colon imaging**

Table 3 summarises the advantages and disadvantages of the various investigations of the colon. All methods for examining the whole colon require full preparation of the bowel with oral laxatives, and the diagnostic yield of the examination depends on adequate preparation. Computed tomographic colonography (virtual colonoscopy) provides an endoluminal view of the colon similar to that of traditional colonoscopy. Technical improvements with this method (intravenous contrast material and oral faecal tagging agents) may allow stool and polyps to be differentiated and thus obviate the need for prior bowel preparation. The probability of colorectal cancer is low in patients with symptoms that suggest a lesion in the left colon (change in bowel habit or fresh rectal bleeding) but who do not have polyps or cancer visible at flexible sigmoidoscopy. Thus this may be an appropriate investigation in low risk patients—for example, fresh rectal bleeding only in patients aged less than 50 years—but otherwise the entire colon should be examined when colorectal cancer is suspected clinically.

Patient choice is an important factor in deciding on type of investigation. Prospective studies of patients who underwent two, or in some cases three, consecutive imaging tests showed that computed tomographic colonography and standard colonoscopy were equally acceptable, and both were preferable to double contrast barium enema. Plain computed tomography of the abdomen is a useful investigation in patients with a large palpable abdominal mass of unclear colonic origin.

**Frail and elderly patients**

Conventional colon imaging tests may be difficult to carry out in elderly or frail patients because of immobility and poor tolerance to bowel preparation. Prospective studies with clinical outcome at 12-30 months have shown that in patients with symptoms plain computed tomography of the abdomen with oral contrast (but without bowel preparation) has a sensitivity for detection of colon cancer of 88-94%. Equivocal tests may need further investigation.

**Other tests**

Testing for faecal occult blood and measurement of serum tumour markers such as carcinoembryonic antigen are not useful in the investigation of suspected colorectal cancer. Faecal occult blood testing is an effective means of population screening in asymptomatic people but it is too insensitive to guide the investigation of patients with colonic symptoms. Similarly, tumour markers lack sensitivity and specificity but may be useful in the follow-up of treated patients. Wireless capsule endoscopy for imaging the colon is currently under development.

**How is colorectal cancer managed?**

Staging of the disease and complete visualisation of the colon are required once colorectal cancer is diagnosed, other than in the emergency setting. Liver and chest imaging, usually with computed tomography, is necessary to detect metastases, and a complete colonic assessment can detect synchronous cancers, present in 3-5% of patients. Endorectal ultrasonography or magnetic resonance imaging is also necessary to stage rectal cancer. Surgical resection for localised colorectal cancer offers the only curative possibility. Postoperative chemotherapy offers a survival benefit for patients after

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**Table 1 | Lifetime risk of dying from colorectal cancer according to family history, and recommendations for colonic screening in United Kingdom**

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Lifetime risk of colorectal cancer</th>
<th>Refer for colonic screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk in general population</td>
<td>1:50</td>
<td>No</td>
</tr>
<tr>
<td>One first degree relative affected (any age)</td>
<td>2-3-fold increased</td>
<td>No</td>
</tr>
<tr>
<td>One first degree relative affected (age 65 years)</td>
<td>3-4-fold increased</td>
<td>Yes</td>
</tr>
<tr>
<td>Two first degree relatives affected (any age)</td>
<td>3-4-fold increased</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Initial colonoscopy is recommended between the ages of 35 and 40 years, or 10 years before the age of cancer diagnosis in the family member if this is earlier. American guidelines use a cut-off value of ≥60 years.

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**Table 2 | Referral guidelines from the National Institute for Health and Clinical Excellence for suspected colorectal cancer, 2005**

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>Age threshold (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal bleeding with change in bowel habit to looser stools or increased frequency of defecation, or both, persistent for six weeks</td>
<td>≥40</td>
</tr>
<tr>
<td>Definite palpable right sided lower abdominal mass consistent with involvement of large bowel</td>
<td>All</td>
</tr>
<tr>
<td>Definite palpable rectal (not pelvic) mass</td>
<td>All</td>
</tr>
<tr>
<td>Rectal bleeding persistently without anal symptoms*</td>
<td>≥26†</td>
</tr>
<tr>
<td>Change of bowel habit to looser stools or increased frequency of defecation, or both, without rectal bleeding, persistent for six weeks</td>
<td>≥60†</td>
</tr>
<tr>
<td>Iron deficiency anaemia without obvious causes (haemoglobin level &lt;110 g/l in men or &lt;100 g/l in women who are not menstruating)</td>
<td>Any</td>
</tr>
</tbody>
</table>

*Include soreness, discomfort, itching, lumps, prolapse, and pain.
†60 years is considered maximum age threshold. Local cancer networks may elect to set lower thresholds (for example, 55 or 50 years).
‡British Society of Gastroenterology recommends urgent referral and investigation for any level of iron deficiency anaemia."
resection of stage II disease and selected patients with stage III disease. Preoperative chemoradiotherapy improves survival compared with surgery alone for rectal cancer. Palliative chemotherapy can alleviate symptoms, improve quality of life, and improve survival in patients with metastatic colorectal cancer.18 In some cases survival is improved by resection of liver and lung metastases.

**What is the prognosis of colorectal cancer?**

The outcome of colorectal cancer depends on the stage at diagnosis; about half of patients presenting with symptoms are at Duke’s stage C or D (table 4).20 21 Five year survival rates are lower in the United Kingdom, Denmark, and eastern European countries compared with the European average of about 50%.22 Analysis of the EUROCARE data (European cancer registries study) suggests that lower survival in the United Kingdom results from later stage at presentation and diagnosis rather than inferior treatment for a similar stage.23

**Who should enter a screening programme?**

Healthy asymptomatic people with a family history of colorectal cancer should be considered for screening (table 1).16 Conventional colonoscopy remains the ideal investigation but computed tomographic colonography is used to examine the remaining colon when colonoscopy is incomplete—for example, as a result of technical difficulties preventing passage of the scope. The aim of colonic surveillance is to identify and remove adenomatous polyps thus preventing subsequent development into invasive cancer.

**Inflammatory bowel disease**

Patients with longstanding total ulcerative colitis and Crohn’s colitis are also at risk for colorectal cancer. National guidelines recommend that colonoscopic surveillance should begin after 8-10 years for pancolitis and 15-20 years for left sided disease. A recent Cochrane review did not find conclusive evidence that surveillance colonoscopy prolongs survival in these patients. Cancers are, however, likely to be detected at an earlier stage, with an associated better prognosis, and indirect evidence suggests that surveillance reduces death from colorectal cancer associated with irritable bowel disease.24

**What are the methods for screening populations for colorectal cancer?**

Population screening for colorectal cancer has been the subject of several recent high quality controlled clinical trials. The most widely investigated screening modality has been faecal occult blood testing based on the knowledge that cancer and polyps may bleed. A positive result is followed by imaging of the whole colon, usually with colonoscopy. Cancers detected by such screening are at an earlier stage (mostly Duke’s A and B) than

---

**Table 3 | Comparison of current methods for examining the colon**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Seda-</th>
<th>Perfora-</th>
<th>Biopsy or</th>
<th>Sensitivity for detection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic:</td>
<td>tion</td>
<td>tion (diagnostic)</td>
<td>polypectomy, or both</td>
<td>Cancer</td>
</tr>
<tr>
<td>Standard (optical) colonoscopy</td>
<td>Usually</td>
<td>2:1000*</td>
<td>Yes</td>
<td>98</td>
</tr>
<tr>
<td>Flexible sigmoidoscopy</td>
<td>Rarely</td>
<td>1:10 000*</td>
<td>Yes</td>
<td>Examine left colon only</td>
</tr>
<tr>
<td>Radiological:</td>
<td></td>
<td></td>
<td></td>
<td>Examine left colon only</td>
</tr>
<tr>
<td>Double contrast barium enema</td>
<td>No</td>
<td>1:10 000</td>
<td>No</td>
<td>48</td>
</tr>
<tr>
<td>Computed tomographic (virtual)</td>
<td>No</td>
<td>5:10 000</td>
<td>No</td>
<td>59-85</td>
</tr>
</tbody>
</table>

*Highly operator dependent. Many expert endoscopists have lower rates than in quoted published series.

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**Table 4 | Approximate frequency and five year relative survival by Duke’s stage**

<table>
<thead>
<tr>
<th>Duke’s stage modified (equivalent TNM stage)</th>
<th>Description</th>
<th>5 yearly survival rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (stage I)</td>
<td>Localised to mucosa and submucosa</td>
<td>93</td>
</tr>
<tr>
<td>B (stage IIA and IIB)</td>
<td>Extending into or through muscle layer without lymph node involvement</td>
<td>72-85</td>
</tr>
<tr>
<td>C (stage IIA-C)</td>
<td>Lymph node involvement</td>
<td>44-83</td>
</tr>
<tr>
<td>D (stage IV)</td>
<td>Distant metastases</td>
<td>8</td>
</tr>
</tbody>
</table>

TNM=tumour, node, metastasis staging system.
symptomatic cancers (table 4). 20 Meta-analysis of four randomised controlled trials has shown that screening using faecal occult blood testing reduced the risk of death from colorectal cancer by 25% of those screened. It is estimated that screening using faecal occult blood testing will avoid about 1 in 6 of deaths from colorectal cancer. 21 Ongoing studies should prove if removal of polyps reduces the subsequent development of colorectal cancer. The National Health Service bowel cancer screening programme began in 2006 and will be phased in gradually over three years. Home testing kits for faecal occult blood testing are sent to people aged 60-69 years every two years and on request to those aged 70 or more. Patients with positive results are invited to undergo colonoscopy at their local designated screening centre (fig 2). Other screening strategies include flexible sigmoidoscopy every five years with or without faecal occult blood testing, double contrast barium enema, or colonoscopy every 10 years. All of these methods, used in people from age 50 years, reduce mortality from colorectal cancer compared with no screening and the cost per life saved compares favourably with mammography for women aged more than 50 and treatment of moderate hypertension. No single strategy has, however, proved to be the most effective or cost effective for screening.22 American guidelines recommend that people at average risk should be offered one of these screening strategies from age 50 and thus at a younger age than in the United Kingdom but at a higher cost per life saved.23

**SUMMARY POINTS**

The lifetime risk of developing colorectal cancer is about 5%

Increasing age and a family history of colorectal cancer are the greatest risk factors for the disease

Patients presenting with suspicious symptoms and signs should be referred and investigated urgently in a specialised unit

Colonoscopy and computed tomographic colonography are of equal sensitivity for detection of colorectal cancer

Colonoscopy allows biopsy of suspicious lesions and removal of polyps

Population screening by testing for faecal occult blood has begun in the United Kingdom

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**Contributors:** ABB and CA participated in the literature search and writing of the article. ABB is the guarantor.

**Competing interests:** None declared.

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

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**Additional educational resources**

National Institute for Health and Clinical Excellence (www.nice.org.uk/guidance/ —Department of Health document for improving outcomes in colorectal cancer

British Society of Gastroenterology (www.bsg.org.uk)—Clinical practice guidelines for a variety of gastrointestinal conditions

Cochrane Library (www.cochrane.org)—Independent systematic reviews of healthcare interventions to guide clinical decision making

**Information for patients**

NHS cancer screening programmes (www.cancerscreening.nhs.uk/bowel/index.html) —Contains information leaflets about the NHS bowel cancer screening programme

BBC (www.bbc.co.uk/health/conditions/cancer/typescancer_bowel.shtml)—Information about bowel cancer, with a section on lifestyles that are associated with a reduced risk, and details of organisations that can provide medical and emotional help and support

Cancer Research UK (http://info.cancerresearchuk.org)—Colorectal cancer and other cancers covered in detail


GUIDELINES

Assessment, investigation, and early management of head injury: summary of NICE guidance

David Yates,1 Rifna Akhtar,2 Jennifer Hill2 on behalf of the Guideline Development Group

Why read this?
Head injury is a major public health problem both logistically and clinically. Many patients seek healthcare advice for this, although relatively few will need care in a neuroscience centre. Most will make a good recovery, but the incidence of ensuing disability even after apparently “minor” injury is surprisingly high.

This article summarises the most recent guidance update from the National Institute for Health and Clinical Excellence (NICE) on the appropriate investigation and early care of patients with head injury, where there has been a significant shift from “admit and observe” to “diagnose and decide.”

Recommendations
NICE recommendations are based on systematic reviews of best available evidence. When minimal evidence is available, a range of consensus techniques is used to develop recommendations. In this summary, recommendations derived primarily from consensus techniques are indicated with an asterisk (*).

CT imaging of the head in adults
Request computed tomography (CT) brain scan immediately for adult patients with any of the following risk factors:
• Glasgow coma score <13 on initial assessment in the emergency department
• Glasgow coma score <15 two hours after the injury on assessment in the emergency department
• Suspected open or depressed skull fracture
• Any sign of basal skull fracture
• Post-traumatic seizure
• Focal neurological deficit
• One or more episodes of vomiting
• Amnesia for events more than 30 minutes before impact.

CT imaging of the head in children
Request computed tomography of the brain immediately for children with any one of the following risk factors:
• Age over 1 year: Glasgow coma score <14 on assessment in the emergency department
• Age under 1 year: Glasgow coma score paediatric <15 on assessment in the emergency department
• Age under 1 year and presence of bruise, swelling, or laceration (>5 cm) on the head
• Dangerous mechanism of injury
• Clinical suspicion of non-accidental injury
• Loss of consciousness lasting more than five minutes (witnessed)
• Post-traumatic seizure but no history of epilepsy
• Abnormal drowsiness
• Suspected open or depressed skull injury, or tense fontanelle
• Any sign of basal skull fracture
• Focal neurological deficit
• Three or more discrete episodes of vomiting
• Amnesia (antegrade or retrograde) lasting more than five minutes.

Imaging of the cervical spine
The initial investigation of choice for the detection of injuries to the cervical spine remains the plain radiograph, but in the following circumstances computed tomography is now preferred.

In adults and children 10 years or older
Request computed tomography of the cervical spine immediately for patients with the following risk factors:
• Glasgow coma score <13 on initial assessment
• Intubated patients
• Technically inadequate plain film series
• Continued clinical suspicion of injury despite a normal x ray
• Patient is being scanned for multi-region trauma.

In children under 10 years
Because of increased risks associated with irradiation in young children, particularly to the thyroid gland, computed tomography of the cervical spine should only be requested when:
• A child has a severe head injury (Glasgow coma score ≤8),
• A strong clinical suspicion of injury exists despite normal plain films, or
• Plain films are technically inadequate.

Transport
All patients who have sustained a head injury should...
be transported directly to a facility with the necessary resources to resuscitate, investigate, and initially manage multiple injuries. It is expected that all acute hospitals and all neuroscience units accepting patients directly from the incident will have these resources, and that these resources will be appropriate for the patient’s age.*

Local guidelines on the interhospital transfer of patients with head injuries should be drawn up between the referring hospital trusts, the neuroscience unit, and the local ambulance service. These should recognise the merit of transferring all patients with serious head injuries (GCS ≤8), irrespective of their need for neurosurgery. However, if transfer of those who do not require neurosurgery is not possible, ongoing liaison with the neuroscience unit regarding clinical management is essential.*

Advice on long term problems and support
Advise all patients and their carers of the possibility of long term symptoms and disabilities after head injury. Information should be provided on support services that they could contact if they experience long term problems.

Overcoming barriers
Although implementation of these guidelines is clearly intended to improve patient care, the sheer number of

patients with head injury means that any change in policy may have important effects on the ambulance service, neuroscience centres, and the other work of emergency, intensive care, and radiology departments. Reassuringly, though, the major change advocated in the first NICE head injury guideline—from a policy of admission (with plain skull radiographs being used as a triage tool), to diagnosis through computed tomography—was not as disruptive as many had anticipated and led to improvements with safe early discharge, evidence of a reduction in the numbers of admitted patients and cost savings in some centres.* The modest increase in the use of computed tomography for imaging of the cervical spine recommended in this update should be even less disruptive.

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


RATIONAL IMAGING

Uterine artery embolisation to treat uterine fibroids

A Watkinson,1 A Nicholson2

Women may now have another effective, safe, and minimally invasive treatment option for treating fibroids

The patient
A 34 year old woman presented to her gynaecologist with menorrhagia associated with dysmenorrhoea and urinary frequency. She was nulliparous but had been trying to become pregnant for several years.

What is the next investigation?
Transabdominal or transvaginal ultrasound is the most commonly performed imaging test for investigating menorrhagia with dysmenorrhoea or pressure related symptoms. If the results suggest uterine fibroids and uterine artery embolisation is a treatment option, we recommend magnetic resonance imaging with gadolinium (dimeglumine gadopentetate) enhancement (fig 1) because it has advantages before and after treatment (table).1,2

Outcome
Imaging confirmed the presence of an enlarged multiloculated fibroid uterus—the largest fibroid was intramural and measured 14.2 cm. Treatment options included:

- Medical treatment (tranexemic acid with or without gonadotrophin analogue)
- Mirena coil
- Endometrial ablation techniques
- Myomectomy
- Hysterectomy
- Uterine artery embolisation
- Magnetic resonance guided focused ultrasound surgery

Medical management had been tried unsuccessfully and endometrial ablative techniques were not considered appropriate because the fibroids were intramural. Magnetic resonance guided focused ultrasound surgery shows promise,1 but it is still a research tool with limited availability. The referring gynaecologist thought that the morphology of the fibroids made them unsuitable for myomectomy, and the patient was keen to avoid hysterectomy as she wanted to conceive in the future. Although current advice is that embolisation should be offered only to women who have completed their families,3 successful pregnancies have been reported after this procedure.2 The patient’s concentrations of follicle stimulating hormone were at the upper limit of normal (7.5 IU/l).

After discussing all options with her gynaecologist and an interventional radiologist, the patient chose to
The risk of premature hysterectomy can approach 25% in women aged 1-2% in most series but 2.9% at 12 months for complications is around 10% at one year for treatment failure is around 10% at one year.8 Quality adjusted life year scores increase with the desire for pregnancy and the age of the patient, and older patients are less likely to need reintervention.

Benefits
Around 80-90% of patients will be asymptomatic or have significantly improved symptoms at one year, with an associated 40-75% reduction in fibroid volume. Recent studies support good outcomes at five years. However, 20-25% of patients will need further treatment, including repeat embolisation or surgery (myomectomy or hysterectomy) within five years.8 10

Patients usually have a shorter stay in hospital (24 hours), faster recovery and return to work (seven to 10 days), and lower rate of major morbidity (such as damage to the bowel or bladder) than those who have a hysterectomy or myomectomy; minor complication rates are similar.8 10 In addition, patients who want to conceive in the future or who have no other conservative treatment option can retain their uterus.

Economic modelling indicates that uterine artery embolisation is a cost effective treatment with significant savings over open surgery at one year.8 Quality adjusted life year scores increase with the desire for pregnancy and the age of the patient, and older patients are less likely to need reintervention.2

Adverse effects
Most patients have pain of varying severity, which can usually be controlled by analgesia. Postembolisation syndrome occurs in up to 52% of patients.8 This constitutes a general malaise, with mild pyrexia and flu-like symptoms, which is self limiting and usually lasts for seven to 10 days.

A persistent non-offensive discharge (negative on bacterial culture) occurs in 7-14% of cases. It may be more common with submucosal fibroids.5 6 8 10

The risk of hysterectomy and or repeat uterine artery embolisation for treatment failure is around 10% at one year.8 10

Comparison of pelvic ultrasound and magnetic resonance imaging (MRI) for uterine pathology

<table>
<thead>
<tr>
<th>Factor</th>
<th>Ultrasound</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>Relatively cheap</td>
<td>More expensive</td>
</tr>
<tr>
<td>Availability</td>
<td>Widely available</td>
<td>Limited resource</td>
</tr>
<tr>
<td>First line investigation</td>
<td>Yes1</td>
<td>Problem solving1</td>
</tr>
<tr>
<td>Uses ionising radiation</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Sensitivity for all uterine pathologies</td>
<td>48-100%1</td>
<td>—</td>
</tr>
<tr>
<td>Specificity for all uterine pathologies</td>
<td>12-100%1</td>
<td>—</td>
</tr>
<tr>
<td>Diagnosis of pelvic pathologies other than fibroids</td>
<td>89% sensitivity and specificity1</td>
<td>89% sensitivity and specificity1</td>
</tr>
<tr>
<td>Fibroid size, position, and vascularity as a predictor of success</td>
<td>Poor1</td>
<td>Excellent1</td>
</tr>
<tr>
<td>For assessing complications (such as abscess or sloughed fibroid within endometrial cavity)</td>
<td>Poor1 2 3</td>
<td>Excellent1 2 3</td>
</tr>
</tbody>
</table>

LEARNING POINTS
- Uterine artery embolisation is a safe and effective minimally invasive technique for treating symptomatic uterine fibroids
- Recent NICE guidelines support its use as an alternative to myomectomy or hysterectomy in women with symptomatic fibroids larger than 3 cm who wish to preserve fertility
- The risk of hysterectomy or repeat uterine artery embolisation for treatment failure is around 10% at one year and 20-25% within five years
- The risk of hysterectomy for complications is 2.9% at 12 months
- The risk of premature ovarian failure is around 1-2% in most series but increases with age; it can approach 25% in women over 45

![Fig 1 | Gadolinium enhanced axial T1 weighted magnetic resonance imaging of the pelvis before embolisation. The uterus is enlarged, mainly as a result of a 14.2 cm intramural vascular fibroid, which shows pronounced enhancement](image-url)
year and rises to 20-25% within five years. There is also a 2.9% risk of hysterectomy within 12 months as a result of uterine sepsis or uncontrollable pain.

The risk of premature ovarian failure is around 1-2% in most series. However, this risk increases with age, and it can be as high as 23% in women over 45. If the patient becomes pregnant, there is a theoretical risk of uterine rupture or intrauterine growth retardation. The miscarriage rate is also 40-70% higher than in an age matched population. Late expulsion of a fibroid can also occur in 2.2-7.7% of cases.

Indications and contraindications for uterine artery embolisation

Accepted indications (strong evidence base)
- Menorrhagia
- Dysmenorrhoea
- Pressure symptoms including abdominal bloating, frequency, nocturia, and constipation

Controversial indications (weak evidence base)
- Asymptomatic patients
- Failure to conceive and all other treatments for fibroids have failed or are not indicated
- Adenomyosis

Contraindications
- Subserosal and submucosal fibroids on a narrow stalk are a relative contraindication because they could detach after infarction and lie free in the retroperitoneum or uterine cavity, where they might become infected. Although no evidence exists to support this hypothesis, it seems sensible to avoid the procedure for such fibroids
- The desire to avoid hysterectomy under any circumstances is an absolute contraindication as there is a small risk of hysterectomy as a result of uterine sepsis or uncontrollable pain after the procedure (2.9% at 12 months).

The risk related to radiation is small. Operators are encouraged to use pulsed fluoroscopy and minimise angiographic runs to keep the dose of radiation low. Studies have shown that skin injuries are unlikely, ovarian doses are below the threshold for permanent or temporary sterility, and that the stochastic risk for radiation induced cancer and genetic injury to future children is not substantial.

Questions for further research

Despite the successful pregnancy in this case, it is unclear what advice to give patients about future pregnancy. Many successful pregnancies have been reported, but rates of miscarriage, caesarean section, and preterm delivery are higher than in age matched women without fibroids. A randomised trial comparing uterine artery embolisation and myomectomy with pregnancy outcome as the primary endpoint would be valuable, as would more research into the effect of uterine artery embolisation on ovarian function and long term fertility.

Many technical problems are yet to be resolved, including the ideal embolic agent, the efficacy of single dose antibiotics, and patient selection as an indicator of success. In addition, NICE has called for further research into the psychosexual impact of uterine artery embolisation and myomectomy, the effect of uterine artery embolisation on uterine blood flow, and how uterine artery embolisation reduces heavy menstrual bleeding.

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Competing interests: AW is a clinical adviser to Biocompatibles Ltd.

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Fig 2: Left: pre-embolisation angiography performed from the right groin via a selective catheter in the left uterine artery shows the typical vascular appearances of the hypertrophied arteries supplying the uterine fibroid (arrows). Right: angiography after embolisation with polyvinyl alcohol shows contrast stasis, with no distal flow to the fibroid.

Fig 3: Gadolinium enhanced axial T1 weighted magnetic resonance imaging of the pelvis two months after the procedure. The fibroid is greatly reduced in size and is not contrast enhanced, as it is avascular.
Fluoride: a whiter than white reputation?

PERSONAL VIEW Rod Griffiths

In 1964, when I was a medical student, Birmingham City Council decided to fluoridate its water supply. Over the weekend that the fluoride was supposed to be added, the Sunday Mirror carried many letters from people who could taste the difference and felt a variety of symptoms. On Monday the Medical Office of Health announced that a technical hitch meant that the fluoride would not in fact be added for another month. There were no further protests.

Thirty years later I was regional director of public health for the West Midlands (which includes Birmingham). From time to time the issue of fluoridation was raised, most often as some sort of scare about cancer, bone fractures, dental fluorosis, or allergies. A little over half of the region was fluoridated, and we knew in some detail which areas had fluoridated water and which did not. We examined every claim made against fluoride, and like most of the international public health agencies we were never able to find any evidence of the various allegations of harm. We even found that the incidence of some cancers seemed to be less in fluoridated areas, although such results may be due to chance.

We looked at most cancers and a range of other conditions, particularly in bones. We found it impossible to get any of this work into major journals; we were told that such studies were old hat. I remember being attacked for wasting time at the conference of the International Association of Cancer Registries. “Everyone knows about fluoride,” I was told. “We know that it does no harm. The reasons why people protest about it have nothing to do with health.”

Media interest has fluctuated over the years. I was once invited to defend our fluoridation policy on BBC Radio 4’s You and Yours consumer affairs programme in a debate with John Yiamouyiannis, a famous US campaigner against fluoridation. I described our studies, and Dr Yiamouyiannis replied that there was no point in doing such studies in England because the English drank a lot of tea, which has so much fluoride in it that it would mask any differences that might occur from putting fluoride in the drinking water. I said I was sure that listeners would be pleased to know that fluoride in the water was no more dangerous than drinking tea. You and Yours cut that section; I don’t know why.

Too much fluoride can lead to fluorosis: mottling of the teeth. Is this a problem? Dentists say that they can detect it in a proportion of patients in fluoridated areas, but I’ve never heard anyone complain about it outside fluoridation debates. Birmingham has had fluoride for 40 years; if fluorosis was a major problem I ought to have heard jokes about Brummies and their funny teeth by now.

Another issue that has caused some confusion over the years is natural fluoride in water. For geological reasons rivers and ground water in some areas have more fluoride; in fact it was the good dental health of people in those areas that first led to the idea of artificial fluoridation of water supplies. It is irrational to behave as though natural fluoride is somehow fine while artificial fluoridation is not. In our urbanised world there is really no such thing as natural water supplies in much of the country. Birmingham, Manchester, and Liverpool get their water from Wales—is that “natural”?

The important question is whether fluoridation does any good. On balance, it seems that it does. Dental health in the fluoridated areas of the West Midlands is among the best in the country, even though we are far from best on other indicators, such as obesity, heart disease, and life expectancy. Is it really possible that the West Midlands has a diet that gives it the best teeth in the country and also a high prevalence of obesity among women?

Clearly, it would be better if there was evidence that met modern standards, but how many trials conducted between 1930 and 1960 would meet those standards? It may be true that there could be hazards from fluoride at levels that we cannot detect, and for academic researchers this may well matter. But the key question I was asked as regional director of public health was whether we should take the fluoride out of Birmingham’s water. My answer has always been no, because I could not detect any harm with the tools that were available to me. I always made it clear that if evidence of harm were to emerge then we would stop the fluoridation.

If we stopped fluoridation the population of Birmingham would end up with worse dental health, as has happened in the places where fluoridation schemes have been stopped. Furthermore the burden would tend to fall unequally: poorer children would get more dental problems than rich children.

Of course, the issue must be debated. Any large scale public health measure involves judgment about the balance of probabilities, and it would be exceptional for a population based measure to have no possible risk of harm to anyone. The ethical debate over fluoridation happens precisely because it is a population measure; if it were a drug then individuals could make decisions about their own compliance.

What remains surprising and under-researched is the vehemence of some people’s opinions on the matter. The general public do not know much about fluoridation; for instance, surveys have shown that many people believe that their water is fluoridated when it is not. Why do some people become so passionate about fluoride, when other regulations about harmful chemicals to which we are all exposed through agriculture and industry attract so much less attention?

Rod Griffiths is a retired doctor
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Power to the people

The fan of the overhead projector whizzed as the lights dimmed. The acetates were first dropped, then placed either upside down or back to front, or written on by the shaking hand of the quivering voiced junior doctor. Senior doctors had access to the medical illustration department and so had “professional slides”; they marched confidently up the steps with a carousel of slides, only to be crushed as these were duly dropped or placed upside down or, most commonly, got stuck, often at a cringe-making “funny” slide that filled the lecture theatre with strangled laughter. The lecture based undergraduate curriculum involved skipping as many lectures as possible and dozing through the hypnotic dullness of the rest.

But in the darkness of a postgraduate lecture in the summer of 1995 the earth shook and I awoke from my hypnagogia. Whirling text, typewriter effect, chequerboard changes, animation, a galaxy of graphs—a meteorite called PowerPoint had smashed into planet Presentation. Overnight the dinosaurs that once terrorised doctors—the overhead and slide projectors—died out. When their remains are stumbled across in some dusty hospital store cupboard, young doctors attempt to piece together what they might have been used for—some funky psychedelic 1970s lamps, perhaps?

I have no memory of the content of this lecture for I was possessed by the special effects. Entranced, I experimented recreationally, changing fonts then twirling, zooming, and screeching them to a halt. Clapping, maniacal laughter—and words walked on screen and bowed. It was like university again, when crowds had gathered to watch me play the “Rolling Thunder” arcade game—I was an expert. I developed a range of five-minute PowerPoint presentations on common topics like contraception that automatically rolled to my disembodied voiceover. Imaginatively I called them “PowerConsults.” Patients seemed amused, but mainly they were bemused.

My change of heart began when lectures became increasingly complex and bloated—50 flaming slides all regrettably available to download off the web. My toes curled at homogenous and ubiquitous clip art—and the “funny” slide unfortunately never got stuck. Worse still, dreadful and weak material was concealed by the whizz-bang of presentation special effects. PowerPoint our saviour was in reality a tyranny of tedium, mere style over substance. The great art of presentation lost.

Now freed from the PowerPoint spell I stand in the glare of the lights with only a flip chart, eyeballing my audience. Some performances are good, some bad, and some great, but above all there is real communication. So down with PowerPoint—let the “power” be the passion that shines in your eyes—the “point” those three themes that constitute any argument that you will defend to the last.

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

Dear Ofcare . . .

. . . I was pleased to hear that you’re going to start levying fines on naughty NHS organisations that don’t keep up standards. I’ve always been a believer that the punishment should fit the crime, so I herewith enclose some suggestions.

Firstly, I’d like you to pop into Seddle ward in St Fritters’ Hospital (take the lift to the top floor, end of the corridor, first right) and set about that sloppy sister with the red hair. She wouldn’t know a care protocol from the 263 bus timetable. And according to the woman I met in surgical outpatients, she’s got a fancy man from Supplies whom she meets in the sluice while the student nurses are doing the drugs round. I’d respectfully suggest a two-year compulsory secondment to that nunnery at the top of the hill.

While you’re at St Fritters, you should pay a visit to Catering. When my next-door neighbour was in having her gallbladder out, they kept sending up those cook-chill dinners (cooked on the outside, chilled on the inside, according to Gloria). And she found a human hair in the casserole. Personally, I’d make the head chef go on one of those Jamie Oliver courses and put up “five a day” posters in every ward at his own expense.

I don’t really want to complain about the little cottage hospital as it’s so convenient for my hip physio, but I’ll do my duty. My nephew went to the A&E with a rugby injury (somewhere near the groin—I didn’t like to ask). Apparently, the doctor’s tie dragged right across the lad’s pubes when he was examining him. Five minutes later, he was bending over a cot and the kiddly grabbed his tie and stuffed it in its mouth. It’s a difficult one this, because I think they’re all as bad as each other, so I recommend all the male doctors in that hospital should wear bow-ties for 12 months.

One final tip-off. The GP surgery on the corner of the High St has got a receptionist with a loose tongue. I was in the queue behind her in Asda the other day and she was spilling the beans about Mrs Connors’ biopsy. What she needs in my view is for her smutty little diary to be scanned in and put on the practice website so the rest of us can poke our noses into her private business.

I do hope these suggestions help. Good luck with the new regulator.

Mildred Trotterby
Trisha Greenhalgh is professor of primary health care, University College London p.greenhalgh@pcps.ucl.ac.uk

Trisha Greenhalgh
Des Spence

FROM THE FRONTLINE

Des Spence

OUTSIDE THE BOX

Trisha Greenhalgh

VIEWS & REVIEWS
A burning question

Great works of literature have meanings beyond the most obvious, and judged by this standard Max Frisch’s play The Fire Raisers is a great work. Frisch was a Swiss who worked for a number of years as an architect before turning full time to writing. No doubt unfairly, we do not normally associate the Swiss with literature: whoever uses the phrase “Swiss literature,” for example? Nor do we expect the best societies always to produce the best literature; for what is good for people is not necessarily good for writing.

In The Fire Raisers, an entire town is subject to a rash of arson attacks, so that everyone is terrified by the prospect of further attacks. The action of the play takes place in the home of Herr Biedermann, a rich bourgeois who makes his money from the manufacture and sale of fake hair restorative. Two dubious characters, Schmitz and Eisenring, take up residence in Herr Biedermann’s attic. He does not want them there, but is too cowardly and pusillanimous to evict them.

Gradually, they make it clear to Herr Biedermann that they are the arsonists of whom the town is afraid. They move drums of petrol into the attic; they ask Herr Biedermann for help with the fuse with which they are going to light the fire; they even ask him, successfully, for the matches with which to start it. After dinner, they burn the house down, and the final scene takes place in Hell, where Herr Biedermann and his wife protest their innocence.

Frisch, of course, lived through the Nazi takeover of Germany, but saw it from the German-speaking fringe. It doesn’t take much historical knowledge to understand that he is writing about the Nazi era, but not just about the Nazi era: his play is about the perpetual human temptation not to see, and then to compromise with evil.

Eisenring tells Herr Biedermann the secret of his success (but still Herr Biedermann disguises the truth from himself): “Joking is the third best method of hoodwinking people. The second best is sentimentality. The kind of stuff [Schmitz] goes on for—an orphanage, and so on. But the best and safest method—in my opinion—is to tell the plain unvarnished truth. Oddly enough. No one believes it.”

And Hitler, as we know, did not do anything that he did not say he was going to do in Mein Kampf.

What has all this to do with us, you ask. Well, a friend of mine was recently told by a manager of no clinical experience said that, by a set date, a set number of patients should have been on a set drug for a set period of time. If not, funding would decline.

A manager of no clinical experience said that, by a set date, a set number of patients should have been on a set drug for a set period of time. If not, funding would decline stuffed with chestnuts (before accepting the invitation, Eisenring makes sure there is to be red cabbage also), and though the two are complete ruffians, they insist that the best silver, including finger bowls, be laid on a damask tablecloth. After dinner, they burn the house down, and the final scene takes place in Hell, where Herr Biedermann and his wife protest their innocence.

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And Hitler, as we know, did not do anything that he did not say he was going to do in Mein Kampf.

What has all this to do with us, you ask. Well, a friend of mine was recently told by a manager of no clinical experience whatever that, by a set date, a set number of patients should have been on a set drug for a set period of time. If not, funding would decline.

Sometimes I wonder whether we in the medical profession have been, in our own small way, a pack of Herr Biedermanns.

Theodore Dalrymple is a writer and retired doctor.

BETWEEN THE LINES

Theodore Dalrymple

A manager of no clinical experience said that, by a set date, a set number of patients should have been on a set drug for a set period of time. If not, funding would decline.

MEDICAL CLASSICS

A Journal of the Plague Year
By Daniel Defoe
First published 1722

A Journal of the Plague Year is a work of fiction masquerading as a work of fact. It reads as if it were an unembellished account of the personal experiences of someone who survived the epidemic of bubonic plague that struck London in the summer of 1665. But, although its author, Daniel Defoe, probably did do exactly that, he can only have been about five years old at the time of the epidemic and his childish recollections would surely have been too distant and too unreliable to allow him to write about it more than 50 years later. No, like any modern novelist, he must have researched it and imagined it before he wrote it.

I doubt if Defoe would score high marks on a contemporary course of creative writing. There’s no plot—just a straightforward linear narrative. There’s no attempt at characterisation; indeed, the only character in the book is the narrator and the reader learns little about him except that he’s an acute observer with a sceptical turn of mind. And there’s no fancy writing—no imaginative description, no dramatic crises, no surprises. Instead, he gives us a worm’s eye view of how the texture of everyday life is turned upside down in a city hit by a disaster that its inhabitants could neither understand nor mitigate.

As the epidemic takes hold in the outer parishes of London, the rich, including the royal court, close their houses and flee. Merchants try to find sanctuary on their ships moored on the Thames. The poor have nowhere to go. Astrology and superstition thrive. Some see an opportunity to make a fast buck by taking advantage of a ready market for useless prophylactics and quick cures. Magistrates are forced to take emergency measures to curb the spread of the disease. They direct that households containing an infected person should be shut up and a watchman appointed to ensure that no one escapes; that graves be dug at least six feet deep (a practice that has persisted ever since in England); that extra people are employed to carry away and bury the dead. Even so, mortality continues to increase.

Towards the end of the book, its narrator reflects on how much has been destroyed: lives, livelihoods, and much of the trade on which the economic success of the city depended. But he finds something positive in the way the disaster brought about the reconciliation of people with different religious views: “... a close conversing with death, or with diseases that threaten death, would scum off the gall from our tempers, remove the animosities among us and bring us to see with differing eyes than those which we looked on things before.”

Mark Twain’s definition of a classic as a book that people praise and don’t read is surely correct. Perhaps it’s worth making an exception for this particular classic and actually turning its pages. After all, things might not be so different today if terrorists successfully detonated a dirty bomb in the centre of an over-populated capital city or if a virulent strain of influenza emerged.

Christopher Martyn, associate editor, BMJ christophermartyn@bmj.com
**Keeping up appearances**

What will cosmetic surgery mean to humanity if we all end up trying to look the same?

**Richard Hurley** is impressed by a prophetic play that explores this nightmarish idea.

“You can’t sell anything with that face.” Lette’s sudden awareness of his own unattractiveness is how this short play begins. *The Ugly One* is sharp, simply written, and surreally funny. It raises fundamental questions about what happens to self image and wider identity when facial appearance can be changed at will.

Lette assumes he is to give a sales presentation on the connector that he has invented and patented. But Scheffler, his boss at the electronic components factory, forbids him on the grounds of his looks. Instead Scheffler wants to send the better looking junior, Karlmann.

“You’re a very beautiful human being,” Lette’s wife, Fanny, consoles him. She’s learnt to overcome her initial repugnance at looking at his face by concentrating on his left eye alone.

The four actors play seven parts in their own clothes without leaving the stage or changing their name, voice, or appearance. And there is no differentiation between scenes, which merge in a dream-like sequence.

Scheffler is also the name of the plastic surgeon who relishes the challenge of remodelling Lette’s face to help him advance his career. “Will my wife recognise me afterwards?” “Let’s hope not!” quips the surgeon. When Lette’s bandages are removed Scheffler beams at his masterpiece: “You look neat as a pin.” But Fanny asks, “Is that him?” And Lette notices that she looks at him and kisses him differently—greedily.

Mass media foists on us an ideal of beauty, often as part of efforts to sell us something. The celebrities who embody our current notions of sexual attractiveness and youthfulness often depend on cosmetic surgery for their looks. Thus are capitalism, cosmetic surgery, and celebrity culture interlinked. More disposable wealth, advances in surgical technology, and demand from consumers have encouraged cheap, widely available cosmetic surgery in the West. Once a luxury that only rich people could afford, cosmetic surgery is now a lifestyle choice available to all.

Now that Lette is considered supremely beautiful he has everything. Scheffler lets him give the presentation, and he becomes the face of the company. Sales rocket. Women queue to meet him. And Scheffler pays him to advertise his remarkably successful surgical technique. But Lette becomes hubristic, greedy, and difficult. He has affairs, and he stops doing research. “He presents his face, [but] he’s already forgotten what a connector is,” Karlmann sneers.

Magazines, newspapers, and television programmes—from dramas such as *Nip/Tuck* to reality shows that depict live operations—push the idea that success and happiness really are only skin deep, that looks are at least as important as talent or experience.

MTV’s show *I Want a Famous Face* takes these ideas to an extreme—it documents people who want to change their faces to look like celebrities. *The Ugly One* extrapolates our obsession with superficial beauty and celebrity to a disturbing conclusion.

Karlmann wants some of Lette’s success and opts for Scheffler’s surgery. And he gets the same face. Soon Fanny starts to notice Lette lookalikes everywhere, and she starts an affair with one. “Are you doing this for revenge?” Karlmann asks. “No, I just like your face.” From here the confusion grows.

The subplot of Lette’s work mirrors the main storyline. He owns the patent of the individual connector that he has invented. And he demonstrates intricate familiarity with this component, but so, later in the play, does Karlmann. From a unique, owned template, the connector is remade and sold many times—just like Lette’s face. Ownership and experience don’t guarantee him any rights—over who sells his connector at presentations or over who can sport his face.

Looks aren’t enough, if everyone’s beautiful: Lette is fired because of his deteriorating attitude, and there are cheaper lookalikes who can do his job. “But the others aren’t the real thing,” he protests. “Neither are you.”

Before an unpredictably funny ending, Fanny reassures him: “You’re taking this all terribly seriously. It’s not like you’re the only one having this problem.”

In an era in which cosmetic surgery is readily available, combined with intense fascination with celebrity, *The Ugly One* asks what control we have over how our facial appearance is used by other people. It’s also slick, tightly performed, and hugely entertaining.

**The Ugly One**

Written by Marius von Mayenburg

Royal Court Theatre, London, until 13 October

Rating: ****

**Once a luxury that only rich people could afford, cosmetic surgery is now a lifestyle choice available to all**

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Lette (Michael Gould, left) finds that a new face does not give him everything he expected.
For the full versions of articles in this section see bmj.com

James Hill (“Hamish”) Barber
Former professor of general practice University of Glasgow (b 1933; q Edinburgh 1957; MD, FRCP, FRCR), d 26 August 2007.

After five years in the Royal Air Force, James Hill Barber (“Hamish”) obtained his MD while working as a general practitioner in Callendar. He was the first general practitioner appointed to the Livingston project, involving joint hospital and general practice appointments. In 1972 he was appointed senior lecturer at Glasgow University, writing The Textbook of General Practice Medicine and becoming the first professor of general practice. His innovations over two decades included computer assisted learning, a module based MSc in general practice, and healthvisitor-led preventive programmes. An expert yachtsman and model boat builder, Hamish had 10 fishing boats on permanent display at the Scottish Fisheries Museum, Anstruther. He leaves a wife, Marion; four children from his first marriage; and 11 grandchildren.

Graham Watt
John Howie

Francis Oughterson Brown
Former consultant radiologist Stirling Royal Infirmary (b 1921; q Cambridge/Glasgow 1945; FRFPS, FRCP, FRCR), died from dermatomyositis on 16 May 2007.

After qualifying, Francis Oughterson Brown was posted to the Canal Zone, Palestine, and Cyprus with the Royal Army Medical Corps. In the post-war confusion he enjoyed working around regulations—for example, converting sick parade into individual appointments and presenting the sick report in verse. He was appointed to Stirling Royal Infirmary as consultant in 1959, retiring in 1983. He enjoyed providing a general diagnostic service, and invasive investigations before digital imaging took over. He also trained foreign radiologists in Stirling and Sierra Leone, and served on the hospital and Forth Valley Health Boards. He leaves a wife, Betty; two children; and four grandchildren.

Colin Brown

Adrian Michael Easty
Former general practitioner Swinton, Manchester (b 1931; q Manchester 1956; DRCOG, MRCGP), died from myeloid leukaemia on 13 August 2007.

Adrian Michael Easty worked as a family practitioner for 33 years. Latterly his special interest was hill and long distance walking. He was happy in his last years to have completed the 930 miles walking along the Way of St James, from Le Puy in France to Santiago de Compostella, at the end of the Spanish Camino. He leaves a wife, Mary, and three children.

A M Easty

June Mary Fletcher
Former general practitioner Chippenham (b 1927; q Bristol 1946), died from recurrent cancer on 15 November 2006.

June Mary Fletcher (née Smith) held posts as registrar in obstetrics and gynaecology and in paediatrics in Bristol. In 1953 she settled in general practice in Chippenham, where she specialised in obstetrics in the local maternity hospital. She was also the medical officer to a local 30-bed former isolation hospital, and provided inpatient care for general and elderly patients in the two other community hospitals. She was for many years the chair of the governors of two comprehensive schools, and active in local literary groups. Predeceased by her husband, Wallace, she leaves three stepchildren.

N D Whyatt

Lesley Baker

Dorothea Koffman (née Herrmann)
Former specialist in community medicine (child health) Leicestershire Area Health Authority (b 1916; q Berne, Switzerland, 1949; DPH, FFPHM, FRCPCH), died after an intracerebral haemorrhage on 20 July 2007.

Dorothea Koffman grew up in Berlin between the world wars but was unable to attend a German university because her mother was Jewish. She began her studies in Prague in 1935, transferring to Switzerland when the political situation worsened. Unable to return to Germany, she visited her childhood sweetheart, Jurij, in England, acquiring his Soviet citizenship when they married; later they were both naturalised British. After qualification, Dorothea began work in otorhinolaryngology in England, after which she gravitated to public health. She combined community child health services in Leicester, Leicestershire, and Rutland, retiring in 1978. Following Jurij’s death in 1989, Dorothea became an expert on the life and work of Charles Darwin.

Andrew Koffman

Rita Statham
Former medical officer in family planning Nottingham (b 1932; q Manchester 1956; MRCOG, MFFP), died from breast cancer and Clostridium difficile on 8 March 2007.

Rita Statham trained as an obstetrician and gynaecologist at the Jessop Hospital for Women. She married Roy Statham and moved to Nottingham in the 1960s. Rita worked in the Nottingham Family Planning Association, training doctors and nurses and running family planning clinics. She was also clinical assistant in obstetrics in the Firs Maternity and City Hospitals, Nottingham, for over 20 years. She retired in 1995. She leaves Roy, three daughters, and three grandsons.

Lesley Baker

Edward Hamilton Wood
Former consultant surgeon Royal Alexandria Hospital, Rhyd (b 1937; q Birmingham 1961; FRCSEd), died from a heart attack on 26 August 2006.

Ed Wood trained as a general and vascular surgeon at the Glasgow Royal Infirmary, having completed his house jobs in Hereford and post-registration appointments in obstetrics and accident and emergency medicine in Birmingham. He was appointed consultant surgeon in 1974 but retired on grounds of ill health in 1989. He was in great demand as a quiz master. He leaves his former wife, Jane; partner, Jed; three children; and three grandchildren.

Campbell Mackenzie
House cats may serve as sensitive sentinels in assessing human exposure and adverse health outcomes related to low level but chronic PBDEs (polybrominated diphenyl ethers) found in flame retardants, which end up as household dust. The risks in young animals, through even brief exposure in cat food, include mild learning impairments and reduced concentrations of circulating thyroxine. The risks are unknown in humans, but parents may be advised to vacuum frequently (Science News Online 15 September 2007).

People with fatty livers tend to develop insulin resistance and raised glucose concentrations, but Japanese researchers now think that whether diabetes develops depends on the type of fatty acids in the liver. They created a strain of mice lacking an enzyme that increases the length of the carbon chain of fatty acids, and these mutant mice developed fatty livers which were predominantly made up of shorter fatty acids. When fed on high fat diets, these mice developed fatty livers but not insulin resistance or high glucose levels (Nature Medicine 30 September 2007).

Bed rails are often put in place to prevent people falling out of bed, and they’re used for other reasons too. They can help patients manoeuvre themselves in bed or can be used as an aid to transferring in and out of bed. But because of a belief among the public that bed rails should and ought to stop falls, in a substantial number of negligence claims the failure to apply them is specifically mentioned (Clinical Risk 2007;13:173-8).

In line with some doctors Minerva knows, an addiction psychiatrist paraphrases the saying misattributed to Göring: “Whenever I hear the words ‘evidence based’ I reach for my gun” (SCANbites 2007;4(Autumn):2). He says the existing literature fails to adequately reflect his practice, because his core intervention of “boundary setting” is completely ignored by researchers. Every team treats every individual patient differently to find boundaries that work.

What can be done about MRSA (methicillin resistant Staphylococcus aureus), apart from the obvious hand washing? The Annals of the Royal College of Surgeons of England (2007;89:661-4; 665-7; 668-71) carries three papers with suggestions. One says that surgical marker pens should be disposable; another, that case notes might be carriers of infection between healthcare workers. The third paper points the finger at hospital bed control handsets as a possible culprit.

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To see if an electronic anaesthetic information management system could be linked with a drug dispensing system in a large US hospital, more than 11 000 cases were reviewed. The investigation compared records of drugs recorded as given to patients, with the records of drugs recorded as removed from the dispensing system. Discrepancies occurred in 15% of cases; three quarters of these resulted from an error either in the amount of drug waste documented or in documenting the drug given (Anesthesia and Analgesia 2007;105:1061-5).

The relation between a high total cholesterol level and the risk of a stroke is not as obvious as you might think. In a Danish study of 652 unselected patients with ischaemic stroke who arrived at hospital within 24 hours of the onset of the stroke, the severity of the strokes was measured with the Scandinavian stroke scale and mortality within 10 years of the stroke was established. A survival analysis showed an inverse linear relation between serum cholesterol and mortality, favouring the hypothesis that high cholesterol levels favour the development of minor, rather than major, strokes (Stroke 2007;38:2646).

A curious observation in Blood (2007;110:2231-4) describes how cells from allogeneic blood and marrow transplants can contribute to the formation of non-haematopoietic tissues. Using a technique known as short random repeat analysis, researchers found that, two or more years after transplantation, fingernail clippings from nine out of 21 stem cell recipients contained up to 73% of donor DNA.

Do people who cope well with stress have something special going on? A paper in Psychosomatic Medicine (2007;69:614-20) suggests the answer may lie in our serotonin transporter (5-HTT) genotypes. A longitudinal study in 1993 assessed coping strategies, and 10 years later researchers determined genotypes for 5-HTT promoter polymorphism from genomic DNA obtained from 127 participants. The long and the short of it is that the short variant of the 5-HTT promoter gene was associated with the use of fewer problem solving strategies.

Evidence from several types of studies of varying quality shows that garlic protects against colorectal cancer (Journal of Nutrition 2007;137:2264-9). Though measures of garlic intake vary in human epidemiological studies, even stronger evidence comes from animal studies, which consistently find a protective effect.