

Fast track admission for children with sickle cell crises

Should morphine or pethidine be given?

EDITOR—Davies and Oni's review of the management of sickle cell disease¹ was published in the same issue of the *BMJ* as the evaluation by Fertleman et al of a fast track admission policy for children with sickle cell crises.² The review is based on the practice at the Central Middlesex Hospital, where pethidine has been associated with fits, and morphine is the preferred analgesic.¹ At the North Middlesex Hospital, only a few miles away, pethidine is evidently preferred in children.² Was this difference of approach noted by the editorial staff? Which group is right?

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- 1 Davies SC, Oni L. Management of patients with sickle cell disease. *BMJ* 1997;315:656-60. (13 September.)
- 2 Fertleman CR, Gallagher A, Rossiter MA. Evaluation of fast track admission policy for children with sickle cell crises: questionnaire survey of parents' preferences. *BMJ* 1997;315:650. (13 September.)

Advice to authors

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When deciding which letters to publish we favour originality, assertions supported by data or by citation, and a clear prose style. Letters should have fewer than 400 words (please give a word count) and no more than five references (including one to the *BMJ* article to which they relate); references should be in the Vancouver style. We welcome pictures.

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Letters will be edited and may be shortened.

Opiates other than pethidine are better

EDITOR—We applaud the fast track admission policy for children with sickle cell crises that has been set up by Fertleman et al at the North Middlesex Hospital.¹ We fully agree that early delivery of adequate analgesia by specialised staff should be the objective of all units managing acute sickle crises.

However, we disagree with the choice of pethidine. While being an effective analgesic, pethidine is a well documented cause of unpredictable neurotoxicity, usually in the form of fits, in both adults² and children.³ Indeed, this point was made by Davies and Oni in their review of the management of patients with sickle cell disease in the same issue of the *BMJ*.⁴

To switch from pethidine to other opiates is difficult for patients, their carers, and staff, but we urge paediatricians to adhere to the recommendations highlighted elsewhere⁵ and promote a uniform approach to the pharmacological management of acute sickle crises. Deviation from these standards can lead to enormous difficulties in managing painful crises in adulthood.

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Jamaican sickle cell clinics offer an alternative to admission

EDITOR—The rationale behind initiating and appraising a fast track treatment policy for children with sickle cell crises as described by Fertleman et al is laudable.¹ I do not agree, however, with their underlying assumption that the patients' demand for immediate and effective pain relief is best supplied by hospital admission.

Some families of children with sickle cell disease prefer to manage painful crises at home.^{2,3} In the United States, patients with sickle cell disease attending comprehensive sickle cell centres have fewer visits to accident

and emergency units and fewer hospital admissions than those managed elsewhere. This has resulted in considerable savings to the healthcare sector.⁴ In Jamaica, sickle cell clinics provide daycare facilities where rapid assessment of ill patients by a medical attendant experienced in sickle cell disease results in appropriate treatment and admission if necessary. This approach allows immediate and effective analgesia and reassurance about the painful crisis in comforting surroundings without routine hospital admission.

The provision of dedicated sickle cell units with daycare facilities in the United Kingdom should provide a more rational use of resources currently allocated to inpatient care. Such centres would provide rapid pain relief as part of a holistic approach to managing sickle cell disease. Experience in Jamaica suggests that this is welcomed by both patients and their caregivers.

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Authors' reply

EDITOR—Daggett and D'Sa and Parker comment on the use of pethidine rather than morphine in our study. This is because most patients with uncomplicated painful sickle cell crises prefer pethidine to morphine when opiate analgesia is needed. They believe that pethidine has less unpleasant side effects than morphine as it does not cause dysphoria and it causes less itch and nausea than morphine. At the North Middlesex Hospital we acknowledge the known dose related neurotoxicity of pethidine in adults. Our adult patients are treated with no more than 100 mg every 2 hours up to a total of 1 g a day. This dose (14-20 mg/kg/day) is much lower than that reported to cause neurotoxicity (30 mg/kg/day).¹ Diamorphine or morphine is used in patients with established renal failure, those who have had convulsions from any cause, and those who have had any complications or problems associated with the use of pethidine.

We give even smaller doses to children. They receive a maximum of 12 mg/kg/day, and potential neurotoxicity is highlighted in the paediatric protocol. Since the introduction of analgesia pumps that are controlled by patients in 1996 we have been switching patients over to morphine.

Ware suggests that we set up day care facilities for sickle cell patients. With the fast track admission system parents had 24 hour telephone access to experienced nurses who knew their children well. Sometimes the parents gave oral analgesia for crises at home and avoided hospital admission. At other times parents wanted the child to be assessed as they were not sure whether admission was needed. The North Middlesex paediatric department is committed to keeping children out of hospital when possible and to shorter inpatient stays. A recent audit of fast track admission showed a reduction in length of stay. In addition, we have established a children's day assessment unit.² Our haematology department has sought funding for a project entitled supported home management for uncomplicated sickle cell pain crises from the Department of Health under its ethnic minority health improvement scheme. Supported home management will be achieved by recruiting an additional two H grade nurses to the community based symptom care team. If successful, it will be extended to include children.

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Management of sickle cell disease

Non-addictive analgesics can be as effective as morphine and pethidine

EDITOR—I am concerned at the increasing use of pethidine and morphine analgesia in young African and Afro-Caribbean children with sickle cell anaemia, as described by Fertleman et al and by Davies and Oni.^{1,2} I am astonished that a vulnerable section of the community is being given addictive drugs when non-addictive analgesics would be just as effective, particularly in a society where drug addiction among young people is recognised as a problem.

I have nursed patients with sickle cell disease in Trinidad and in Ghana, where the numbers of sufferers are much larger than those found in the United Kingdom. Education of parents and children by public health nurses in schools and in the community about their condition, regular follow up by clinicians, and admission when in crisis, with paracetamol being given alone or in combination with codeine when something stronger is required, went a long way to ensuring a normal existence for such

children. I remember only one occasion when pethidine was used, and that was given in a small dose to a patient in labour. More recently pethidine has been used in small doses in the Caribbean, but never morphine—for obvious reasons. I am baffled why children here should need it.

The claim that parents and children are demanding opiates for pain control shows a lack of education and knowledge about the illness and the long term effect of such drugs on their part. I have come across several young addicts in hospitals across London, and I wonder how long it will be before they end up in a criminal situation.

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Management would improve if doctors listened more to patients

EDITOR—As a 51 year old patient with heterozygous sickle cell anaemia and a national campaigner for improved services in hospitals since 1974, I note that pethidine has been discounted for morphine infusions in the review article by Davies and Oni.¹ In my experience, however, the reason pethidine has a bad name is that it is wrongly prescribed—that is, at too high a dose (200 mg) and too frequently (every two hours)—as happened in the case of the patient with homozygous sickle cell anaemia who died in a London teaching hospital after two days of "continuous intravenous infusion of pethidine at a dosage of 100-150 mg an hour."² From morphine we have progressed to diamorphine—that is, heroin—which is now being increasingly used as the first line of treatment.

I know that these heavy narcotics are lovely to have when you are in acute pain, but as I grow older I am more and more convinced that their dangers greatly outweigh their benefits. I travel around the country teaching and lecturing to patients and their relatives on how to maintain good health and keep themselves out of hospital. What I miss most when I am unfortunate enough to end up at an accident and emergency department with a sickle cell crisis are doctors who will listen to me, for I know more about my condition than any of them. To have a protocol thrust down my throat by the attending doctors without them listening to what I know about how I should or should not be managed is sad indeed. Every adult patient knows something that the doctors do not know, and they should be listened to more often if the management of sickle cell crisis is to be improved.

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Hearing loss may occur after sickle cell crises, especially in children

EDITOR—Davies and Oni's clinical review of the management of patients with sickle cell disease omits to mention audiovestibular dysfunction—that is, hearing loss and vestibular disease.¹ Large series report a prevalence of hearing loss of 11-41% in sickle cell disease.² The cochlear microvasculature in young children may be particularly susceptible to occlusion,³ and children should have audiometry after sickle cell crises to exclude a readily manageable cause of educational handicap and preventable disability.

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Contraception with medroxyprogesterone may be beneficial

EDITOR—The comprehensive and helpful review by Davies and Oni on the management of patients with sickle cell disease did not include an important aspect of care relating to contraceptive requirements.¹ Some patients with homozygous sickle cell disease have fewer crises while using three monthly injections of medroxyprogesterone acetate 150 mg (Depo-Provera).² Work published in 1971 suggests that medroxyprogesterone acetate may exert its beneficial action through stabilising the red cell membrane in sickle cell disease.³ Therefore this method of contraception is of particular value for women with sickle cell disease.

However, women who are considering medroxyprogesterone acetate as a method of contraception must be informed that the vaginal bleeding pattern after the injections will be completely unpredictable and that they must be willing to accept this. During 1996-7 this method of contraception was used by over 1000 women attending our centre, mainly those aged 20-24 years. We believe that its advantages of high efficacy, ease of compliance, and lack of serious adverse cardiovascular effects despite extensive use indicate that it probably should be more widely used for contraception as a positive choice. It has additional benefits for women who have sickle cell disease.

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Acute chest syndrome is common in children before puberty

EDITOR—In their comprehensive review of sickle cell disease Davies and Oni report that the acute chest syndrome is uncommon before puberty,¹ but it is in fact one of the commonest causes of admission in children with sickle cell disease. In the cooperative study of sickle cell disease in the United States the incidence of the acute chest syndrome was greatest before the age of 10 years and declined thereafter.² Over half of children with homozygous sickle cell anaemia had at least one episode of the syndrome in the first 10 years of life in the United States³ and Jamaica (unpublished data). The syndrome is an important cause of immediate death at all ages after 2 years,^{4,5} and those who have an episode before 2 years of age are less likely to survive to the age of 40 years.²

The acute chest syndrome is defined by the appearance of a new infiltrate on chest radiography. Features commonly include fever; respiratory symptoms such as cough, dyspnoea, and chest pain; and respiratory signs of crepitations and tachypnoea. The underlying mechanisms include infection, pulmonary fat embolism, and pulmonary sequestration, and clinical distinction is usually impossible. Infections may be more important in young children, and acute chest syndrome of infectious aetiology may be more severe than pneumonia caused by the same organisms in children without sickle cell disease.⁴ Caregivers must be aware of the frequency and potentially serious nature of this syndrome in children.

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Authors' reply

EDITOR—These letters are a microcosm of the debate between professionals and patients about the management of painful sickle crises, reflecting in part the paucity of evidence.

Pain is subjective, and a person's response to it is defined by cultural, demographic, and socioeconomic factors, as well as their anticipation of a response. Patients may underplay their pain as a coping strategy if good analgesia is unavailable, for whatever reason. So whereas physicians in the United Kingdom, the United States, and France generally recognise the necessity for opiates to be available for

patients presenting to hospital, physicians in the Caribbean may not because Caribbean patients suffer less pain. Alternatively, the early death rate related to sickle cell disease is far higher in underdeveloped countries¹ than in developed countries,² so those patients who die early might have become the patients whom we in developed countries recognise as severely affected by pain. We have seen no patients develop opiate addiction after appropriate inpatient treatment, but we advise against opiate use in the community because of these risks.

Debate ranges over the use of pethidine, yet Pryle et al have shown that many patients have toxic concentrations of norpethadine acid while receiving optimal analgesia (which may result from the abnormal absorption of pethidine in sickle cell disease).³ This is supported by frequent anecdotes (from at least six of the major London sickle units) of patients having fits while taking pethidine, although the risks may be lowest in childhood as the youngest patient of whom we are aware was aged 12 years. Our local policies have been informed by advice from our patients, pain and palliative care specialists, and clinical pharmacologists, but they do not obviate the central role of the doctor to listen to and communicate with the patient.

Our review was limited for reasons of space, but we agree with Savundra that audiovestibular dysfunction occurs as a consequence of sickling. In our experience, however, almost all cases are reversible, so we arrange audiometry only when an apparently severe or chronic problem is reported by the family or school.

We agree with Kirkman and Elstein, but as the frequency of the V Leiden gene is so low in the population affected by sickle cell disease⁴ we also include consideration of low dose combined contraceptives when counselling patients.

As for the acute chest syndrome, unlike some practitioners we distinguish and exclude infective pneumonias, which are common in childhood, from other sickle related pulmonary complications.

We recognise the benefits of a comprehensive care programme but any community services must be linked, with easy access, to specialist hospital services.

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Management of aseptic meningitis secondary to intravenous immunoglobulin

EDITOR—Picton and Chisholm describe a case of aseptic meningitis related to high dose intravenous immunoglobulin diagnosed on the basis of eosinophils in the cerebrospinal fluid.¹ This adverse effect varies in presentation from a transient headache after the infusion to vomiting, photophobia, neck stiffness, and severe headache. The timing of symptoms may be delayed by up to seven days, though most occur within 48 hours after the treatment.² The symptoms are not always recurrent, particularly with the milder forms. The mechanism is not understood, and any interventions are empirical.

Several measures are helpful in managing those patients who have an ongoing requirement for high dose intravenous immunoglobulin. When starting treatment we use a slow rate and a dilute solution of immunoglobulin. The first dose (of 2 g/kg total) is given over five days at a 3% solution—that is, 0.4 g/kg/day not faster than 6 g per hour. This approximates more closely the infusion rate and dilution usually given as replacement for hypogammaglobulinaemia, where complications such as aseptic meningitis are much less frequent. When the initial treatment has been uncomplicated the next infusion of 2 g/kg can be given over three days and if successful then reduced to a two day administration time. The concentration may also be increased to 12%, reducing nursing time to change the bottles. The patient needs to be encouraged to maintain a good fluid intake.

If symptoms occur over the first 48 hours of treatment with high dose intravenous immunoglobulin it is possible to use paracetamol alone or with codeine as premedication and to tailor the rate of subsequent infusions. In addition, prehydration and the use of an antihistamine—for example, cetirizine, which may influence eosinophil migration in addition to blocking H₁ receptors—has been helpful in some patients.

Recognition of aseptic meningitis as an adverse reaction of high dose intravenous immunoglobulin is important as it may be treated effectively in many patients, allowing the continuation of treatment. Computed tomography and lumbar puncture may be avoided, particularly when high dose intravenous immunoglobulin is used for one of its many unlicensed indications (accounting for 60% of its use) in a setting of limited experience with this form of treatment.

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Coordinated neonatal screening programme for haemoglobin disorders is needed

EDITOR—Modell et al's audit of prenatal diagnosis for haemoglobin disorders shows the lack of a public health approach to the issue in the United Kingdom.¹

Firstly, numbers of affected births for sickle cell disease in the United Kingdom are not reported and, in fact, are not known. This reflects the lack of a coordinated neonatal screening programme (despite good evidence of the effectiveness of neonatal screening in reducing mortality) and of adequate data collection.² As a result, inconsistent local antenatal and neonatal screening programmes are developing and their effectiveness remains uncertain.³ This is in contrast to programmes for phenylketonuria and congenital hypothyroidism, for which national registers have been established for many years. Without details of the methods used or validation against observed numbers in a large population, the estimates of birth prevalence reported should be treated with caution.

Secondly, table 4 in the paper should report the proportion of all parents identified who attend for prenatal diagnosis. It does not include those parents who are identified as being at risk but do not come forward for prenatal diagnosis: having been counselled previously, some parents opt not to have prenatal diagnosis in subsequent pregnancies.

Thirdly, the success of an antenatal screening programme depends crucially on effective education of professionals and communities. Professionals can then advise appropriately and couples can make informed reproductive choices. The authors' failure to mention these points in their discussion of utilisation of prenatal diagnosis suggests a lack of a population approach. This is despite evidence of the gaps in knowledge among both professionals and the relevant communities.^{4,5}

Screening programmes should not be treated as a technical matter in isolation from the populations to which they relate. The failure of the United Kingdom to develop a coordinated neonatal screening programme is mirrored by the continuing lack of coordinated community education and professional training. A coherent national policy and services are needed for both antenatal and neonatal screening, linked to culturally appropriate community education programmes involving the relevant communities and support to ensure adequate data collection. This is emphasised by the estimates for Greater London that the total of 9000 affected individuals in 1996 will rise to 12 500 by 2011.³

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Future of preschool vision screening

Conclusions for or against services are invalid without appropriate research evidence

EDITOR—Rahi and Dezateux highlighted the current dilemma about preschool vision screening.¹ A systematic review has detailed the lack of published evidence on whether the target conditions (amblyopia, non-obvious squint, and refractive error) are disabling and whether detection at preschool age results in better treatment outcomes than detection at school age.²

The review concludes that published hard evidence is lacking on preschool vision screening but then recommends that providers consider discontinuing current programmes. Without appropriate high quality research evidence, conclusions either in favour of or against these services are equally invalid. Ongoing research into this subject has occurred within a multidisciplinary birth cohort study of 14 000 children born in Avon between April 1991 and December 1992.³ A randomised controlled trial of screening methods for ocular defects in children under 3 years of age has collected data on whether any disability in social, physical, or cognitive function is associated with the target defects at the age of 4½ years.^{4,5} The birth cohort study aims to complete a detailed, multidisciplinary assessment of all 14 000 children at the age of 7 years, half of whom will have had preschool vision screening while the other half will have not. This will provide high quality data on whether the target defects are associated with suboptimal performance in other areas of life at this age and, if so, whether preschool screening resulted in a better outcome (visual, educational, or developmental) than screening at school age. As stated in the review,² these data are necessary to decide whether to support preschool vision screening.

The review's recommendations lack objectivity and suggest that the authors believe that preschool vision screening is not worth while, despite the lack of adequate data on which to base such a conclusion. The removal of existing services on the basis of this review would be unfortunate if subsequent research showed beyond doubt that

preschool vision screening was beneficial. Given the substantial indirect (animal) and retrospective (clinical) evidence already suggesting that the target conditions are both disabling and better treated as early as possible, policymakers might be better advised not to act on the review's recommendations until the results of the birth cohort study and other relevant work become available. This would allow time to complete the collection and presentation of the much needed data and would avoid the possibility of a beneficial intervention being inappropriately withdrawn.

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Cost effectiveness of screening for amblyopia is a public health issue

EDITOR—Rahi and Dezateux discussed the detection and management of squint and amblyopia¹ and the results of a systematic review.² The cost effectiveness of such screening programmes for amblyopia is a public health issue that deserves wide debate. We wish to raise three points.

Firstly, in the everyday experience of those working with amblyopic children, patching the non-amblyopic eye is effective in substantially improving the visual acuity of the amblyopic eye. A recent audit at Moorfields showed that 85% of children who underwent patching for amblyopia achieved a visual acuity of 6/9 or better in their amblyopic eye. Against this background we do not believe it would be ethical to conduct any trial in which children were randomly allocated to a non-treatment group. We are not particularly surprised that there are no such trials in the literature. A Medline search failed to find any randomised trials of appendicectomy in the treatment of acute appendicitis. In general the more effective a treatment the less likely it is to have been subjected to controlled trials.

Secondly, in the year between April 1990 and March 1991, 101 people were registered as blind or partially sighted because of amblyopia.³ In assessing the impact of loss

of vision in the good eye on people with amblyopia, however, it is important to include not only those with dense amblyopia who become registered as blind or partially sighted but also those with milder amblyopia. To be left with one eye that has an acuity of 6/12 or below will probably result in the loss of a patient's driving licence and quite possibly his or her job as well. It is mainly for this reason that we aim to improve the acuity of an amblyopic eye to 6/9 or better.

Finally, we regularly see children who present with untreated amblyopia at age 7 or older whose condition is essentially untreatable. Parents usually express regret that the problem had not been found earlier, and such feelings are likely to have an impact on family life for years to come. Not patching the eyes of children may reduce family stress in the short term, but possible long term effects have to be set against this.

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Review article did not separate review and implementation processes

EDITOR—The editorial by Rahi and Dezaux¹ started a dialogue on preschool vision screening in response to a recent systematic review by Snowdon and Stewart-Brown² which highlights how little we know about the clinical course and treatment of amblyopia. Unfortunately however, the review is not set within the context of prevailing scientific and clinical opinion. Nobel Prize winners Hubel and Wiesel and other researchers showed that amblyopia should be identified and treated as early as possible. The worldwide wave of enthusiasm that this research generated was enormous and led to the establishment of national preschool vision screening in the United Kingdom. So, it is no surprise that no rigorous treatment trials were identified³: they would have been precluded on ethical grounds. It is pity that other levels of evidence³ used to guide clinical practice⁴ were ignored by the reviewers.

Snowdon and Stewart-Brown should have stayed within their objective: "To provide evidence on which decisions about the future provision of this service can be made." Unfortunately they did not, and they recommended that "purchasers and providers should be appraised of the results of this review and advised not to implement new screening programmes. Providers currently offering screening programmes should consider discontinuing them." From two researchers in isolation such firm recommendations are extraordinary and contrast

starkly with the approach for developing clinical practice.^{3,4}

This review fails to separate the review and implementation processes. Review is a research task, but effective implementation requires wide consultation with every section of the community so that vision screening can be prioritised within the context of the health of the nation.⁵ Failure to wait for this open debate indicates a lack of confidence and an implicit recognition that their recommendations could not withstand this crucial process.

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- 1 Rahi JS, Dezaux C. The future of preschool vision screening services in Britain. *BMJ* 1997;315:1247-8. (15 November.)
- 2 Snowdon SK, Stewart-Brown SL. *Pre-school vision screening: results of a systematic review*. York: NHS Centre for Reviews and Dissemination, 1997. (CRD report 9.)
- 3 Scottish Intercollegiate Guidelines Network. *Clinical guidelines: criteria for appraisal for national use*. London: BMA, 1996.
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The existence of a service is not evidence of its value

EDITOR—In their editorial on the recently published systematic review on preschool vision screening Rahi and Dezaux do not grasp the nettle of evidence based medicine.^{1,2} They warn: "In the current climate there is a danger that existing, but incompletely researched, services may be discontinued prematurely." Far from being a danger, this is one of the advantages of moving towards evidence based medicine. The funds released can then be used to support services for which there is solid evidence of efficacy but insufficient resources—for example, screening for diabetic retinopathy. It should not be presumed that the existence of a service is in itself evidence of its value.

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- 1 Rahi JS, Dezaux C. The future of preschool vision screening services in Britain. *BMJ* 1997;315:1247-8. (15 November.)
- 2 Snowdon SK, Stewart-Brown SL. *Pre-school vision screening: results of a systematic review*. York: NHS Centre for Reviews and Dissemination, 1997. (CRD report 9.)

Authors' reply

EDITOR—The findings of the systematic review of preschool vision screening¹ should be discussed widely, and we are encouraged by this debate in the letters pages. The broader issue of levels of evidence required for policy decisions have also been debated at a recent national meeting.²

We welcome this opportunity to reiterate our concerns about policy decisions being based on incomplete research evidence. Preschool vision screening is not an isolated event. It occurs within a complex continuum of surveillance and screening for visual defects in childhood, including the current examination at school entry, the effectiveness of which has been increasingly questioned.^{3,4}

As vision screening at school entry has not been similarly reviewed, it seems premature to make policy recommendations about preschool services in isolation.

We agree with Aylward that "it should not be presumed that the existence of a service is in itself evidence of its value." Equally, no evidence of the benefit of a service is not evidence of no benefit.⁵

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- 1 Snowdon SK, Stewart-Brown SL. *Pre-school vision screening: results of a systematic review*. York: NHS Centre for Reviews and Dissemination, 1997. (CRD report 9.)
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Doctors are not pressured into giving prescriptions

EDITOR—From their study of general practices in Australia, Cockburn and Pit suggested that patients who expect a prescription are more likely to be given one by their doctor.¹ We found similar results in an unpublished study that looked at all consultations in five Oxford general practices over one week in 1994. Questionnaires were given to patients before consultation to ascertain age, sex, and whether a prescription was expected. Patients were excluded from the study if they were attending for special clinics, receiving repeat prescriptions, or less than 18 years old. For each eligible patient (n=371) the doctors received a complementary questionnaire asking whether they prescribed a drug and, if they did, to indicate their confidence in its pharmacological efficacy on a visual analogue scale (0-100%). Doctors were blinded to the patients' responses.

We found that 184 (50%) patients received a prescription—the same proportion as that in Cockburn and Pit's study (169 (50%))—although a higher proportion of the Oxford patients expected one (239 (64%) v 160 (48%)). Patients who expected a prescription were more than twice as likely to receive one (relative risk = 2.12; 95% confidence interval 1.39 to 2.83). The doctors' confidence in the pharmacological efficacy of their prescription was not affected by whether a patient expected a prescription or not, with mean figures recorded on the visual analogue scale of 81% and 82% respectively. This implies that doctors are not pressured into giving prescriptions that they do not believe to be of benefit. Patients aged over 65 were significantly more likely than younger patients to expect a prescription (52/61 (85%) v 187/310 (60%), $\chi^2=13.8$, df=1, $P<0.001$). This greater expectation was not reflected in a higher rate of prescribing.

Younger patients may more clearly express their expectation of receiving a prescription or have a clearer idea of when a prescription is required.

An understanding of the dynamics of prescribing helps to promote rational prescribing and is an important aspect of most medical consultations.

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I Cockburn J, Pit S. Prescribing behaviour in clinical practice: patients' expectations and doctors' perceptions of patients' expectations—a questionnaire study. *BMJ* 1997; 315:520-3. (30 August.)

Article showed how not to read economic evaluations

EDITOR—Although parts of Greenhalgh's paper on economic analyses were helpful to our non-economist colleagues, many parts showed a poor understanding of the subject and the paper is likely to be of little help in assessing the value of studies.¹ Much of the paper was devoted to cost-utility analysis (where this was occasionally confused with cost-benefit analysis and Greenhalgh showed an ignorance of the methods of utility estimation). The short description of cost-consequences analysis seemed to confuse it with cost-effectiveness analysis. There were also important errors in some of the paragraphs explaining "Ten questions to ask about an economic analysis."

Question 2, on the perspective of economic evaluations. This paragraph missed the point, referring to interest groups and funding rather than objective viewpoints, which should be stated in the paper (for example, the NHS, patient, or society).

Question 3, on the clinical effectiveness of the interventions. The "gold standard" economic evaluation is conducted alongside a randomised controlled trial. In these circumstances the relative effectiveness of the interventions is unknown at the outset. Moreover, a less effective intervention may still be tried first if it is substantially less costly than other interventions.

Question 5, on method of analyses. Cost-utility analysis and cost-benefit analysis are both multidimensional. Cost-utility analysis is appropriate if the outcomes have both quality of life and quantity of life dimensions and can be valued as health states; cost-benefit analysis is appropriate if the outcomes can be valued in monetary terms.

In addition to the above errors there were important omissions. For example, Greenhalgh did not mention that readers should be aware of the methods used for the estimation of resources. They should also be aware of the importance of varying the outcomes (for example, within confidence intervals) as well as the costs in the sensitivity analysis.

The guidelines for authors and peer reviewers of economic submissions to the *BMJ* form a more accurate and informative guide for non-experts and experts alike.²

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- Greenhalgh T. Papers that tell you what things cost (economic analyses). *BMJ* 1997;315:596-9. (6 September.)
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Use of lasers can cause visual impairment

EDITOR—Marshall discussed potential loss of vision as a result of being exposed to laser beams used as weapons in modern warfare.¹ It is dreadful to imagine people being rendered blind by laser weapons, be they military personnel or not and regardless of whether the intention was to blind or not. Even where laser beams do not cause overt loss of vision, however, they may impair visual function, particularly blue-green colour vision.²

Until recently many ophthalmologists inadvertently damaged their colour vision by using medical lasers.³ Care must be taken to ensure that military personnel, for whom the ability to discriminate colours accurately may be critical, do not do likewise.

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- Marshall J. Blinding laser weapons. *BMJ* 1997;315:1392. (29 November.)
- Harwerth RS, Sperling HG. Prolonged color blindness induced by intense spectral lights in rhesus monkeys. *Science* 1971;174:520-3.
- Hardy KJ, Lipton J, Foster DH, Scarpello JHB. Laser safety and ophthalmologists. *Lancet* 1991;338:1338.

Separate R&D budget is needed for monitoring effects of new drugs

EDITOR—The pharmaceutical industry exists to make medicines and to make money from these medicines. Specialists like to use promising medicines as soon as possible, and patients and pressure groups have agitated for easier access to new medicines. These lobbies form a powerful force. With existing checks and safeguards—licensing authorities, formulary committees—many drugs are introduced, some of which are no more effective than older ones or turn out to be harmful. Even if the systems are improved and extended it is probably not possible to resist introducing drugs that have promise but for which the evidence of added benefit falls short of proof. Furthermore, there is often "creep" of use: a drug may enter use as a third line "add on" drug, but its use is soon extended.

Once a considerable number of patients are taking a drug and it is thought to be useful, the prospects for undertaking further randomised trials diminish rapidly. We are left unsure of the frequency of side effects and whether the drug is tolerated as well in practice as in the trials. A centrally coordinated NHS system is required to address this type of question. For certain expensive drugs it should be possible to link funding to an obligation to collect information. For example, a drug that causes neutropenia might be funded for five years initially, during which time patients would have a full blood count performed regularly. Provided the sample was big enough, we would soon know the incidence of neutropenia when the drug is used in every day practice outside a trial. For other drugs the issues might relate to duration of stay in hospital or some other clinically relevant end point.

For such a system to work, mechanisms for data collection would need to be straightforward, and a small number of clear objectives would have to be identified for a limited number of drugs. Here the NHS research and development directorate could have a role. A separate drugs budget for research and development (say 1-2% of the total drugs budget) could be used to facilitate the introduction of certain expensive new drugs in a way that ensured that useful data are collected. Specialists would be able to continue to use expensive new drugs of potential value, patients would get access to such medicines, and the NHS would have a mechanism to stop funding if use in practice does not match up to expectations.

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Resource allocation to health authorities

Expenditure on private health care must be taken into account

EDITOR—Diderichsen et al make a common mistake in their article comparing resource allocation in Britain and Sweden.¹ The use of the word "Britain" is misleading because the resource allocation formula described in the article is not the British but the English formula. Some of the articles referenced include "English" in their titles but are represented by Diderichsen et al as referring to Britain.¹

Wales and Scotland do not use the English formula; they have different methods for allocating resources.^{2,3} These methods may have their problems but at least the countries did not use the revision that was applied in England during 1991-5. Wales considered reducing the weighting applied to the standardised mortality ratio, in line with England, but rejected the proposal. Since 1991 the proxy for morbidity used in the Welsh formula is the standardised mortality ratio for those aged under 75, with

a weighting of 1. There is now some recognition in Wales that the 1996 English formula is probably a better measure of need, but so far there is only a proposal to test it in Wales rather than to use it.

The task of identifying relations between resources and use of services is complicated by the lack of detailed data on use of private health care in Britain. It is not clear from the article whether Sweden also has this information gap, but I assume that data on the use of private health care were not included in the analysis. Interestingly, the 1990 Welsh review of the formula raised an issue being considered by the new British government²: the desire to take account of expenditure on private health care.⁴ But without detailed information it is difficult to see how this could be done. At the very least, providers of private health care should be obliged to submit basic demographic and treatment summaries at the level of postcode to the health authorities where patients were resident. This would assist the difficult process of setting population weighted budgets for general practitioner fundholders and for total purchasing.⁵ Variations in the level of expenditure on private health care are particularly important in budget setting for small populations and for elective services.

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- 1 Diderichsen F, Varde E, Whitehead M. Resource allocation to health authorities: the quest for an equitable formula in Britain and Sweden. *BMJ* 1997;315:875-8. (4 October.)
- 2 Welsh Office NHS Directorate. *Implementing the white paper: options for a weighted capitation revenue resource allocation formula*. Cardiff: Welsh Office, 1990.
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- 4 Timmins N. Private care may affect allocation of NHS money. *Financial Times* 1997 Sept 12.
- 5 Mays N, Goodwin N, Bevan N, Wyke S. What is total purchasing? *BMJ* 1997;315:652-5. (15 September.)

Lessons learnt many years ago have been forgotten

EDITOR—In their article on comparing resource allocation in England and Sweden, Diderichsen et al comment on the political nature of the process and the consequence for services of large shifts in the formula.¹ The original Resource Allocation Working Party in England, of which I was a member, considered both these aspects. Because the incidence of illness is higher in deprived people living in poor housing, the remedy is to do something about these conditions (the underlying cause) rather than just treat a symptom (use of health services). Funding health services is cheaper than providing remedies for deprivation.

Thus if authorities are given the chance they will fund the cheap option. Because of that, the original working party avoided using any non-health indicator, in order not to provide excuses for not remedying the cause. The way in which different administrations used different social indicators in allocating the rate support grant—for example, the proportion of single households or ethnic minority groups—also led us to avoid any model requiring complex mathematical modelling or assignment of weights to indi-

vidual variables. Thus the model used was relatively simple and transparent and could be checked easily.

Furthermore, the use of indices of both illness and social factors involves double counting: poor people have more illnesses. A resource allocation formula has to be robust and not subject to large annual swings; the data have to be reliable, up to date, and available each year; and the formula has to be credible and not subject to “fiddling.”

It is unfortunate that the lessons we learnt have been forgotten and that the current English and Swedish formulas are used to apply sticking plasters rather than tackle the fundamental issues of ill health.

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- 1 Diderichsen F, Varde E, Whitehead M. Resource allocation to health authorities: the quest for an equitable formula in Britain and Sweden. *BMJ* 1997;315:875-8. (4 October.)

New biomolecular assays must be tested by direct study in the developing world

EDITOR—Garner et al's editorial on appropriate diagnostics in developing countries is welcome to those who develop novel diagnostic systems for tuberculosis, which remains the most important infectious disease globally.¹ Conventional diagnosis is difficult, and most developments have centred on molecular amplification techniques, often using the polymerase chain reaction, which are expensive and less sensitive than culture.^{2,3} Ethical issues arise if precious samples such as cerebrospinal fluid are repeatedly subdivided for research.

Per capita healthcare spending in the developed world is low, and the validity of any test for an infectious disease such as tuberculosis will depend on whether it is being used as a clinical diagnostic or public health surveillance tool. For such a test to be useful clinically, effective treatment regimens must be available; in the case of tuberculosis, better diagnosis coupled with an inability to treat cases successfully will increase treatment failure and encourage the development of drug resistance.

We recently described a rapid mycobacteriophage method for diagnosing drug resistant *Mycobacterium tuberculosis*, which was developed with developing countries in mind.⁴ It is inexpensive, uses equipment found in many laboratories, and becomes safer over time as the virus kills the bacterium.

Samples arriving for a rapid molecular diagnosis (Fastrack, which is a national service based on the polymerase chain reaction provided by our laboratory in Britain) were also analysed by the rapid mycobacteriophage method for both diagnosis and the detection of rifampicin resistance. The specificity of the method for “precious” samples is encouraging. For example, a bronchoalveolar lavage sample that was positive for acid fast bacilli on microscopy and culture was positive both with the

polymerase chain reaction and by the rapid mycobacteriophage method. Susceptibility to rifampicin was shown by the rapid mycobacteriophage method within 72 hours and confirmed by conventional culture four weeks later. A sample of cerebrospinal fluid that was negative on microscopy and culture was positive by both the polymerase chain reaction and the rapid mycobacteriophage method, and biochemical and clinical signs were consistent with tubercular meningitis. The patient responded to quadruple chemotherapy. A systematic prospective study is under way to confirm the utility of this method for diagnosis.

The robustness of new biomolecular assays can be tested only by direct study in the developing world, a process that the scientific community must actively encourage. Laboratories in the developed world need to produce innovative solutions applicable to the developing world, in addition to addressing the diagnostic needs of their own healthcare systems.

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- 1 Garner P, Kiani A, Supachutikul A. Diagnostics in developing countries. *BMJ* 1997;315:760-1. (27 September.)
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BMA cannot bring proceedings arising out of incidents in other countries

EDITOR—In his letter Khan asks a hypothetical question of the BMA's legal department¹: how would it respond to complaints of racism in the NHS by a non-white doctor from another country in the European Union? The answer is straightforward. The regional and legal services of the BMA would investigate the matter, give advice, and, if appropriate, assist the member in taking action. What we are unable to do is bring proceedings arising out of incidents in other countries; in Khan's case this would have meant in German courts or tribunals under German law. It is for this reason that Khan was advised to seek the help of the Marburger Bund, which we knew from correspondence was trying to assist him.

Members of the BMA who are resident overseas (such as Khan) are charged a substantially reduced subscription for the very reason that they are unable to benefit from the full range of the BMA's services.

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- 1 Khan HH. Racism continues among doctors in Europe. *BMJ* 1998;316:390. (31 January.)