Letters

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Prognosis of symptoms that are medically unexplained

Every neurology service should have access to specialist liaison psychiatry

EDITOR—Crimlisk et al's report on the outcome of motor symptoms that were medically unexplained in a cohort first identified at the National Hospital for Nervous Diseases is welcomed by those interested in the psychiatry of physical illness.[1] Slater's work, based on cohorts recruited in the 1950s, overestimated the likelihood of misdiagnosis in modern neurology,[2] and his conclusions have dissuaded psychiatrists from becoming involved in the management of hysteria.

O'Brien's editorial on Crimlisk et al's study could have sounded two cautionary notes.[3] Firstly, the study was not based on a true inception cohort, and it was recruited from a highly specialised centre. Usually, these factors lead to the finding of a worse prognosis than if only incident cases were included and the sample was less prone to recruitment bias. In this case, however, the bias may have been in the other direction. Patients seen at the National Hospital are likely to have been more exhaustively investigated and observed for longer (either in this episode or before referral) than they would be in most hospitals, so that the chances of misdiagnosis are reduced. We should not generalise the study findings to hospitals where initial assessment may be undertaken with little or no access to specialist neurological opinion or investigations.

Secondly, the negative message—that high rates of undetected neurological disease are not seen at follow up—has been allowed to obscure the important positive findings of the study. Even years later, the patients had disabling physical symptoms and substantial psychiatric problems. As in Slater's original study, preventable deaths occurred from suicide and the complications of immobility. Many people were apparently not referred for psychiatric help either at the time of the initial presentation or subsequently.

The important conclusion of Crimlisk et al's study must be that every neurology service should have easy access to referral to specialist liaison psychiatry.[4] This group of patients, who are difficult to treat, are often resistant to treatment, and have a poor prognosis, may then have a reasonable chance of obtaining appropriate treatment for their primary disorder.

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1 Crimlisk HL, Bhatia K, Cope H, David A, Marsden CD, Ron MA. Slater revisited: 6 year follow up study of patients with medically unexplained motor symptoms. *BMJ* 1998; 316:582-6. (21 February.)
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Clinical guidelines are needed

EDITOR—Crimlisk et al's study of the prognosis of unexplained motor symptoms[1] repeats that of Slater 30 years ago.[2] In an editorial O'Brien requests that other groups with unexplained symptoms be compared,[3] but he takes no account of the findings of the only previous follow up study from the National Hospital for Neurology and Neurosurgery comparable in size to Slater's study.[4] That follow up study looked at the clinical history of patients presenting between 1978 and 1980 with unexplained seizures and sensory deficits as well as motor symptoms, in similar proportions to those in Slater's study. All of the patients had been referred for a psychiatric opinion, unlike either Slater's or Crimlisk et al's patients. Forty one per cent of our patients (10 year follow up) failed to improve compared with 52% of patients in Crimlisk et al's study (six year follow up), with two of our patients going into remission after between six and 10 years. This percentage was maintained across the sample (n = 73), which included large subgroups of patients with motor symptoms (n = 31) and pseudoseizures (n = 27).

The examination of predictive factors evident on initial examination showed associations between persistence of symptoms and length of history. Psychiatric diagnoses of affective and personality disorders, confirmed by Crimlisk et al for their patients with motor symptoms, could be made irrespective of index symptom. Only three of our patients, belonging to the subgroup of patients with motor symptoms, developed neurological disease that accounted for the initial symptom; organic disease had not been suspected at presentation. The initial diagnosis was probably complicated by the presence of other unexplained symptoms in two of these patients and by a temporary response to behaviour therapy in the third.

Crimlisk et al's study is methodologically rigorous. Future studies, however, should clarify the concept of organicity that they used in selecting patients and in assessing outcome. A reliance on consensus will restrict the generalisability of findings. Several additional factors that were evident at assessment and that were likely to influence judgments of organicity were independently associated with clinical outcome in the earlier study.[4] These factors included the number of neurological signs (irrespective of type), the prescription of non-psychotropic drugs, a provisional neurological diagnosis for a symptom, and a recorded history of psychiatric help.

Future studies of patients with unexplained symptoms need to collect initial clinical data on individual findings and signs. The validity of clinical data as indicators of organicity can then be established in the light of outcome. If reliable and objective clinical guidelines can then be produced this would benefit all assessors of patients with unexplained symptoms.

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1 Crimlisk H, Bhatia K, Cope H, David A, Marsden CD, Ron MA. Slater revisited: 6 year follow up study of patients with medically unexplained motor symptoms. *BMJ* 1998; 316:582-6. (21 February.)

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Psychological aspects of investigations must be addressed early

EDITOR—In his editorial on neurological symptoms that are medically unexplained O'Brien mentions the dangers of inappropriate investigations and the unprofitability of repeat investigations for the same complaint.[1] He fails to point out, however, that such investigations perpetuate an organic view of the origin of the symptoms and make it harder to tell patients later that there may be a psychological component to the aetiology of their symptoms. Investigations aimed at reassuring the patient may have the opposite effect unless psychological aspects are addressed early.[2]

Of greater concern, however, is O'Brien's interchangeable use of the terms non-organic symptoms and hysteria. It is inappropriate to label all non-organic symptoms as psychiatric in origin as they are not all associated with clearly discernible psychiatric morbidity.[3 4] When an association does exist between non-organic symptoms and psychiatric morbidity this is a medical explanation for the symptoms. To say otherwise artificially separates the practice of psychiatry from the rest of the medical specialties.

Practitioners should ask for psychiatric advice if investigations are inconclusive, but diagnosis by exclusion and looking for psychiatric morbidity only at this late stage can be problematic. A facility for re-evaluation should primarily be reserved for those patients whose symptoms either progress or are truly medically unexplained.

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Follow up study needs to be continued for longer

EDITOR—Crimlisk et al's attempt to "revisit Slater" does not quite live up to its title.[1] Slater's seminal study described a 10 year follow up of 85 patients referred to the National Hospital for Nervous Disease, of whom about a third developed an established organic illness within 7-11 years.[2 3] Crimlisk et al have followed up their subjects after only six years, and it is premature to conclude that "the emergence of a subsequent organic explanation for these [motor] symptoms is rare."

Although the authors emphasise that good follow up data were obtained on nine tenths of their patients, only three quarters were re-examined clinically. As 55 patients underwent full interview and examination but 59 patients were assessed with the scale of affective disorders and schizophrenia, four patients assessed with the scale must have been interviewed by telephone. A telephone interview and the examination of medical records are inadequate for establishing diagnoses such as personality disorder or somatisation disorder.

These criticisms are balanced against the clarity of sampling from a well circumscribed group of patients with unexplained motor symptoms and the pursuit of prognostic indicators. Crimlisk et al's findings, however, are the result of a short term to medium term follow up study with a relatively high attrition rate. If more definitive results are available from the same sample in five years' time the sobriquet "Slater revisited" might truly be deserved.

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Applying results of randomised trials to patients

N of 1 trials are needed

EDITOR—Guyatt et al's proposal for analysing randomised trials[1] is misguided, flies in the face of elementary statistical theory, and should be resisted. There are three obvious sources of variability in clinical trials. Firstly, pure differences occur between patients: some are more seriously ill than others. Secondly, there is variability within patients: even given the same treatment they, or their measurements, may vary from time to time. Thirdly, some patients may react more favourably to a given treatment than other patients. The parallel group trial does not and cannot distinguish between the three types of variability unless we can find meaningful ways of classifying subgroups.[2–3] The standard crossover trial will distinguish between the first type of variability and the other two but not easily between the second and third,[4] and certainly not in the form of analysis suggested by Guyatt et al.

Guyatt et al have implicitly assumed that which of two treatments is better for a patient can be determined by comparing one period of treatment on each. This is at complete variance to advice Guyatt and coworkers have given elsewhere.[5] They have previously suggested that to establish efficacy for individual patients the patients should be randomised to repeated periods of treatment and control: the so called "n of l" method.

Nothing from the two clinical trials presented by Guyatt et al is inconsistent with the theory that all patients benefitted equally. If we wish to establish what proportion of patients benefit from treatments, rather than merely being satisfied with average effects, then we need random effect models and sequences of n of 1 trials.[3] Since the method which they propose does not correctly partition the sources of random variability, it will simply produce random results.

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Authors' reply

EDITOR—Contrary to Senn's interpretation, we do not propose deciding on which individual patients in the trial benefit but rather the overall proportion who obtained a particular magnitude of benefit. Senn identifies three sources of variation in individual patient's responses—differences between patients, differences within patients due to random variation, and differences due to a systematic treatment by patient interaction. To that we may add a fourth—the overall main effect of treatment.

Senn's logic fails when he argues that nothing from the two clinical trials is inconsistent with the theory that all patients benefitted equally. Quite the contrary, the key is that randomising patients to treatment and control and aggregating results across patients permits independent estimates of the main effect of treatment and the other three sources of variance. The sources of variance are confounded in a parallel group design; patient variance is separable in a crossover design; but all are separable from the overall treatment effect by virtue of the use of a sample of patients and random allocation.

In our previous work on n of 1 clinical trials we recommend multiple periods of treatment and control in order to establish the efficacy for individual patients.[1] The principle is the same—multiple observations, whether from a single patient or multiple patients, permit separate estimation of the main treatment effect and other sources of variation. Rather than "flying in the face of elementary statistical theory" this experimental approach follows directly from such theory.

Our paper showed how we can make the results of trials examining quality of life more easily interpretable by estimating the proportion of patients who benefit from a treatment. Senn's letter highlights a question

clinicians may legitimately ask: "Ah, but which patients?" N of 1 randomised trials will still be required to address this question.

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Relation of rates of self referral to A&E departments to deprivation

Robust markers are needed of variations in case mix among practices

EDITOR—Carlisle et al report an association between markers of social deprivation derived from the 1991 census and out of hours contacts with both general practice services and accident and emergency departments.[1]

We undertook a related study in east London, based on 63 000 attendances by adults at accident and emergency departments.[2] This showed that factors related to social deprivation accounted for 48% of the variation in total adult attendance rates between practices. This was so even in an area of consistently high deprivation where the practices' underprivileged area (Jarman) scores ranged from 30.4 to 62.1 (median value 42.5). In contrast to Carlisle et al, we included in the multivariate analysis explanatory variables relating to practice size and resources, since organisational factors are often cited as causes of high use of accident and emergency departments among inner city populations.[3] We found that practice characteristics (partnership size, female partner, practice manager, nurse, training status, and computer) did not predict rates of attendance, while markers of deprivation did. Distance from the hospital was negatively correlated with attendance rates in the univariate analysis but not in the multivariate analysis.

Carlisle et al's paper mentioned another intriguing finding: wide variation in out of hours use of both general practitioners and accident and emergency departments between practices serving populations from the same wards. We recently completed a study examining the outcomes of all attendances at an accident and emergency department by patients from two practices over seven months.[4] The practices were in Tower Hamlets, had similar underprivileged area scores, were in close proximity to each other, and were within 2 km of the nearest hospital.[4] While the attendance rates at accident and emergency departments from the two practices were significantly different, the outcomes, in terms of the proportions of patients admitted and referred on to outpatients, were similar (table). This suggests that case mix and severity vary between apparently similar practice populations.

Rates of attendance at accident and emergency (A & E) department and outcomes for two general practices in Tower Hamlets, London

	Practice 1	Practice 2
Underprivileged area score	52.0	51.2
Practice population:		
No of patients	7307	11 084
Proportion aged under 16 (%)	14.5	18.4
Annual rate of attendance at A&E* (per 1000 registered patients)	124.1	189.7
Rate of admission from A&E (%)	17.6	18.4
Rate of referral from A&E as outpatient (%)	8.3	10.0

*Assuming attendance rate is constant over time and multiplying figures for seven month study by 12/7.

If practice based budgets are to be based on an equitable allocation of scarce resources it is important to develop robust markers of variations in case mix among practices, which can contribute to the debate on resource allocation in primary care.

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Distance from department and deprivation are both important in explaining variations in rates

EDITOR—Carlisle et al's paper is an important contribution to the literature on accident and emergency workload and socioeconomic deprivation.[1] I have previously examined determinants of the use of services at the sole accident and emergency department in West Lothian district, Scotland (population 145 000).[2] I have reanalysed the data to examine, for all 26 local practices, the contributions of socioeconomic deprivation and proximity to the hospital to variations in annual rates of self referral to the department.

The straight line distance between the practice and the accident and emergency department was calculated with Pythagoras's theorem applied to the relevant grid references. The Carstairs deprivation score was allocated to practices by using the postcode sector for the practice address.[3] Spearman correlation coefficients were calculated between rates of attendance at the accident and emergency department, the deprivation measure for the practice, and the distance between the practice and the accident and emergency department. Stepwise linear regression analysis was used to examine further the relations between these variables.

The mean (SD) annual rate of self referral to the accident and emergency department for the 26 practices was 127.4 (45.5) attendances/1000 registered patients/year (median 132.7; range 30.0-212.2). There were significant correlations between rates of attendance at the department and the Carstairs deprivation score for the practice (Spearman $r=0.584$, $P<0.01$) and the distance between the practice and the department ($r=-0.486$, $P<0.05$). Distance to the department ($\beta=-0.5$, $r^2=23\%$) and the Carstairs deprivation score ($\beta=0.51$, $r^2=21\%$) accounted for 44% of the variation in attendance at the department between practices.

The recent steady rise in rates of attendance at accident and emergency departments requires explanation.[4] My previous study reported only distance as an independent predictor of rates of attendance at such departments after the accessibility of the general practitioner had been taken into consideration.[2] Carlisle et al studied out of hours activity; this work here relates to all attendances at an accident and emergency department by patients from practices in West Lothian. While Carlisle et al suggest that deprivation rather than proximity is the more important influence on attendance, the results presented here suggest that both distance and deprivation are of roughly equal importance in explaining variations between practices in self referral to an accident and emergency department. Studies of accident and emergency workload need to take account of proximity and deprivation as potentially important variables influencing utilisation of services.

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1 Carlisle R, Groom LM, Avery AJ, Boot D, Earwicker S. Relation of out of hours activity by general practice and accident and emergency services with deprivation in Nottingham: longitudinal survey. *BMJ* 1998;316:520-3. (14 February.)
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Bereavement in adult life

GPs should be accessible, not intrusive

EDITOR—Parkes summarises issues associated with bereavement in adulthood but risks medicalising a fundamental life experience.[1] The concept that grief is a process with discrete phases which must be passed through before final adjustment to the loss can take place has been challenged.[2] A more sociological model would suggest that rather than working their way through a range of emotions, bereaved people attempt to construct an accurate story about the life of the deceased which allows their memory of the

dead to become part of their lives. This biography is created by people who knew the individual, not by detached professionals.

Many general practitioners try to visit families at home shortly after a death has occurred; this may be, at least partially, related to the general practitioner's own needs since there is no compelling evidence that it is beneficial to the family. Indeed, it may be that a general practitioner's desire to do something to ease the pain of bereavement leads to more prescribing of benzodiazepines for those visited at an early stage.[3] Some commentators have suggested that general practitioners should visit bereaved relatives at intervals during the year after a death to ensure that the grieving process is progressing.[4] This suggestion ignores the trend away from time consuming home visits in primary care, the changes in society which make any unsolicited visit a potential threat or intrusion, and the lack of evidence for the benefits of such a paternalistic approach.

It is clear that a large number of bereaved people experience psychological disorders and ill health. The question is whether this gives doctors and others a mandate to step into an individual's grief and look for risk factors and evidence of progress through the grieving process. It is our responsibility to be accessible and approachable rather than intrusively proactive during this most fundamental of human experiences.

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1 Parkes CM. Coping with loss: bereavement in adult life. *BMJ* 1998;316:856-9. (14 March.)
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Psychotropic drugs may be appropriate treatment

Editor—Parkes's review of bereavement in adult life considers the psychosocial aspects of care but does not discuss psychotropic drugs.[1] Two questions commonly arise in clinical practice: whether hypnotic or anxiolytic drugs should be offered to recently bereaved people and, in the longer term, whether antidepressants are indicated for treating mood disorders after bereavement.

At one time, benzodiazepines were prescribed to bereaved relatives so freely that long term dependency could easily occur. This practice is now rightly discredited but perhaps the pendulum has swung too far. A woman recently contacted our unit in distress after asking her general practitioner for a one week supply of sleeping tablets after her husband's death; this request had been refused on the grounds that drugs would "block the grieving process." This attitude reflects the teaching encountered by medical students and junior doctors today—for example, through the widely attended advanced life support course; the manual for the course states that "a request for sedation for a relative should usually be gently refused. . . . The pain has to be experienced at some stage and delaying makes it worse."[2] In contrast, the *British National Formulary* sanctions short term prescribing of anxiolytic and hypnotic drugs "to alleviate acute conditions."[3] Though not all recently bereaved relatives want or need medication, some do find it helpful during this difficult experience.

As stated in Parkes's review, about a quarter of widows and widowers develop clinical depression or anxiety during the year following bereavement. Clinical depression may not be recognised in this context because its manifestations overlap with those of grief. Even when the condition is correctly diagnosed many doctors and patients consider drug treatment inappropriate. However, clinical experience and research evidence both support the view that antidepressant drugs are effective when the syndrome of major depression is present, whether or not there is an understandable cause such as bereavement or medical illness.[4]

Psychotropic drugs are sometimes dismissed as an inferior substitute for psychosocial care. In reality optimal management often combines both approaches.

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Author's reply

Editor—Although Mazza's warnings of the dangers of medicalising normal grief and of the inappropriate use of benzodiazepines are apt, the fact remains that a minority of bereaved people will develop psychiatric or psychosomatic disorders and may even die from heart disease or commit suicide if prompt and effective help is not given. They may be too depressed to ask for help or ignorant of the services that exist to help them. Doctors are often the only people in a position to assess risks from bereavement and to steer people in the right direction. For this reason alone I hope that Mazza will continue his practice of proactively visiting families after a bereavement. They will see this as an act of kindness rather than a form of medical imperialism.

I agree with Barraclough et al. Since anxiety and depression commonly coexist after bereavement and since some people are at risk of suicide it is wise to use an antidepressant drug that is anxiolytic and of low toxicity. For this reason, when indicated, I prescribe a selective serotonin reuptake inhibitor such as fluoxetine.

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Scottish data on intrapartum related deaths are in same direction as Welsh data

Editor—Stewart et al studied deaths related to intrapartum asphyxia in Wales and found that mortality was higher in babies born at night; during the holiday months of July and August; during February and August, when junior staff rotate to new posts; and towards the end of the week (although the latter two measures were not significant).[1] We have attempted to replicate their study, using records relating to births in Scotland during the same period (1993-5). Because of differences between Scottish and Welsh schools' academic terms, the peak holiday period in Scotland is a few weeks earlier than that in Wales. We therefore hypothesised that the effect of annual leave would arise in July alone.

Scotland does not use the confidential inquiry into stillbirths and deaths in infancy; instead, it uses a slightly different system, the Scottish stillbirth and infant death inquiry. This derives detailed information concerning all stillbirths and deaths of infants from the relevant healthcare establishments. This information is sufficient to define intrapartum related deaths, as in the confidential inquiry into stillbirths and deaths in infancy system. For the denominator we used the Scottish morbidity record (maternity) (known as SMR2). This system does not record the time of birth, but we were able to perform a record linkage using probability matching with birth registrations from the registrar general for Scotland, which allowed

Numbers of intrapartum related deaths in Scotland, 1993-5, by time of day, month, and day of week

Birth variables	No of births	No of deaths	Risk of death/ 1000 births
Time of day:			
Night (2100-0859)	80 948	69	0.85
Day (0900-2059)	96 931	62	0.63
Not known	6 427	1	0.15
Month:			
January	15 458	14	0.91
February	14 088	11	0.78
March	15 831	11	0.69
April	15 201	13	0.86
May	15 497	17	1.10
June	15 602	13	0.83
July	15 849	12	0.76
August	15 786	15	0.95
September	15 951	9	0.56
October	15 762	5	0.32
November	14 725	7	0.48
December	14 556	5	0.34
Day of week:			
Monday	26 436	26	0.98
Tuesday	27 715	22	0.79
Wednesday	28 213	16	0.57
Thursday	28 602	20	0.70
Friday	27 346	10	0.37
Saturday	23 871	20	0.84
Sunday	22 123	18	0.81

these data to be appended to each record. In all there were 132 intrapartum related deaths among 184 306 births. For 6427 birth records no time of birth was appended, usually because a matching record could not be found in the registrar general's birth registrations.

The table shows our findings. Altogether 125 deaths were of singleton infants and seven of a twin. Forty one deaths (22 at night) were associated with emergency caesarean section and 11 with elective caesarean section. There were 72 deaths during labour, 57 early neonatal deaths, and three late neonatal deaths. The relative risk of death at night compared with during the day was 1.33 (95% confidence interval 0.95 to 1.88); of death in July 1.06 (0.59 to 1.92); of death in February and August (change-over time) 1.27 (0.83 to 1.95); and of death at weekends (Saturday and Sunday) 1.22 (0.83 to 1.77).

Although these results are in the same broad direction as those of the Welsh study, none are as great and none are significant, despite the larger population. A more detailed comparison of data and of obstetric practices between these countries would be valuable.

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Children in the mountains

Advice given was too conservative

EDITOR—We agree with Pollard et al that infants and children below the age of 2 who are on treks should not sleep above 2000 m.[1] But we question their concluding remark that children aged 2-10 who are trekking should not sleep higher than 3000 m. In the absence of any firm data on acute mountain sickness in children, we believe that this advice is too conservative for children who can express themselves clearly—for instance, those aged 7 and older.

Firstly, in our experience the ability of the child to describe a problem clearly in words (so that, if necessary, descent can be planned promptly) is key in the decision whether children should accompany adults to high altitude. We believe that this was not emphasised enough in the editorial.

Secondly, most leaders of trekking groups in the Himalayas believe that dehydration is unhealthy at high altitude and that it may predispose to acute mountain sickness.[2] Monitoring children so that they drink plenty of fluids was not even mentioned, while drugs that may have a dubious role in children were discussed in some detail.

Thirdly, a leisurely itinerary when travelling with children to high altitude is of practical importance and needs to be emphasised.

We believe that the editorial will unnecessarily deter responsible parents from sharing the joys of trekking at high altitude (3000-5000 m in the Everest region) with their children aged over 7. There is no clear evidence of substantial risk, especially when the children are able to describe their symptoms properly, drink plenty of fluids, have proper high altitude trekking gear, and follow a graded rate of ascent.[3] The Himalayan Rescue Association's aid posts (which are staffed by doctors well versed in altitude sickness)—at Pheriche (4243 m) in the Everest region and Manang (3500 m) in the Annapurna region in Nepal—can attest to the safety of responsible and knowledgeable parents taking children up high. We agree that epidemiological data need to be collected to document this safety.

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Authors' reply

EDITOR—We do not believe that Basnyat et al's arguments can be sustained. They consider our suggestion that children aged 2-10 should not trek above 3000 m to be too conservative, at least for older children in this group. We recognise that this recommendation is conservative, but we think that it is justified, given the lack of information on children at high altitude. We doubt whether children aged under 5 can reliably communicate symptoms of acute mountain sickness to their guardians, and in our opinion it is unwise to expose young children to high altitude in a remote region when similar mountain holidays can be taken at low altitude. Our advice is directed at the general trekking public and their doctors rather than at informed high altitude experts, who may be in a better position to recognise signs of altitude illness in their own children.

We agree that adequate hydration should be maintained by those trekking at high altitude, but no data exist to support the suggestion that dehydration predisposes to acute mountain sickness. The reference cited by Basnyat et al is not a report of original research and actually concludes that there is no evidence that increased water intake prevents acute mountain sickness.[1] One attempt to investigate this issue directly found no increase in the incidence of acute mountain sickness in subjects purposely dehydrated.[2]

The authors' comment that drugs have a dubious role in the treatment of altitude illness is at variance with published studies in adults, which form the basis of standard practice. Drugs such as nifedipine and dexamethasone are widely used to treat serious altitude illness if descent is not possible or in conjunction with descent, although information on the use of these drugs in children is limited. We made no reference to the use of drugs to prevent acute mountain sickness in children, a practice we do not support.

The lack of information about altitude illness in young children trekking in Nepal is almost certainly due to the small numbers of lowland children who have been exposed to high altitude in this region. Among the few young children we have encountered trekking in the Everest region over several seasons, including when working with the Himalayan Rescue Association, we have treated several with acute mountain sickness and have noted the difficulty that parents sometimes have in interpreting changes in their child's behaviour. We remain convinced that high trekking holidays are inappropriate for young children who cannot communicate the onset of altitude illness.

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Further studies of value of spiral computed tomography are needed

EDITOR—An editorial by Hansell and Flower dealt with the challenge of adequately diagnosing pulmonary embolism with spiral computed tomography.[1] Although I am in favour of changing one's diagnostic algorithm in line with improvements in diagnostic modalities, I would like to take a closer look at the proof in support of this new technique.

As the editorial states, there is some evidence that large central emboli are easily visualised. The subsegmental vessels, however, remain a problem. Oser et al studied the anatomical distribution of pulmonary emboli by angiography and concluded that

spiral computed tomography would miss up to 30% of patients with angiographically proved pulmonary emboli.[2] This proportion corresponds well with findings of a study in patients with non-diagnostic results of lung scanning: pulmonary angiography showed emboli in subsegmental or smaller vessels in 15% of patients.[3]

In the first management study that used spiral computed tomography 164 patients with non-diagnostic results of lung scanning and a normal ultrasound scan of the deep leg veins remained untreated and were followed up for three months.[4] Spiral computed tomography gave normal results in 112 patients, and anticoagulant treatment was withheld. During follow up three patients developed deep vein thrombosis, two had non-fatal pulmonary embolism, and one died of proved pulmonary embolism (event rate 5.4% (95% confidence interval 1.9% to 11%) and mortality related to embolism 0.9% (95% confidence interval 0.02% to 5.0%)). These figures compare unfavourably with a management study that used lung scintigraphy in combination with repeat ultrasonography of the leg or pulmonary angiography.[5]

We would be ill advised to include spiral computed tomography in the routine clinical management of patients before further studies have been performed.

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Pressures in outpatient clinics

Putting up with overcrowded clinics disguises need for change

Editor—The pressure on outpatient clinics that Sellu highlights in his Personal View is commonplace and affects other aspects of hospital work, such as the planning of operating theatre schedules.[1] He is a victim of a system that exploits its employees while simultaneously making scapegoats of them in order to conceal inadequacies that the purchasers and the government are not honest enough to shoulder responsibility for. I fear that this self sacrifice by consultants who work for free on behalf of the trusts merely compounds the problem and compromises the quality of individual patient care.

Doctors have a duty of care to individual patients. It is not acceptable to covertly trim this care for the greater good. But when doctors accept an excessive caseload, albeit under pressure, and thus limit the time dedicated to each patient, quality of care is eroded. This is an ethical argument against the overcrowding of clinics and operating lists, particularly if clinicians fail to explain the situation to their patients.

Collusion with underfunding has other knock-on effects. For example, other staff are obliged to work long and often rushed hours with inadequate rest periods. Also, operating lists that overrun because they are overbooked delay emergency operations—to the detriment of patients and junior staff, who then work late into the night.

One of the few potential benefits that the purchaser-provider split offered was that it could pinpoint underprovision of resources. The purchasers used competition as a powerful tool to impose efficiency and cost savings. Despite this, waiting times have escalated. This system should have placed the responsibility for waiting lists firmly on the purchasers, who have it in their power to shorten them, given the money and will. The sacrificial approach by consultants is partly responsible for subverting this mechanism. This is part of the reason that provider trusts are still saddled with the responsibility for long waits even though these waits are largely beyond their control.

The only realistic way that underfunding will be corrected is to put purchasers and the government firmly on the spot. Unwilling cooperation in underhand rationing allows them to pretend that all is well and retards the impetus for change. Doctors should have none of it.

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1 Sellu D. Have we reached crisis management in outpatient clinics? *BMJ* 1998;316:635-6. (21 February.)

Increasing numbers of ward referrals are an additional pressure

Editor—Not only other surgeons but physicians too will have found Sellu's feelings about his outpatient clinics familiar.[1] A particular group of physicians on whom these pressures fall is consultant neurologists, who tend to be peripatetic and to have a limited number of sessions at district general hospitals, with little or no junior support.

As he points out, it is now impossible to achieve charter standards while trying to cater for the ever rising demand for outpatient services. Solutions lie either in reducing demand or in increasing supply, or both. He briefly refers to the problem of inappropriate referrals, which are just as likely with referrals marked urgent as with routine referrals, at least in my own practice. A simple solution based on increasing supply would do nothing to address this issue, and maybe, as he implies, an expansion of nurse led clinics would alleviate the load on the hospital service.

There is an additional workload that has also risen exponentially, to which Sellu did not refer: inpatient ward referrals, particularly in the case of neurologists at their district general hospital. For some years the number of ward referrals at my district general hospital that I saw personally was around 150. That number began to rise around 1995 and in 1997 was 292. In other words, in that short interval that particular element of my workload roughly doubled. Clearly if provision of service remains unaltered then the time available to see individual patients lessens, with the predictable consequences of a fall in quality of care and an increasing likelihood of misdiagnosis and mismanagement.

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1 Sellu D. Have we reached crisis management in outpatient clinics? *BMJ* 1998;316:635-6. (21 February.)

European register of patients with sickle cell disease treated with hydroxyurea is being set up

Editor—In 1995 Charache et al showed conclusively in the United States that hydroxyurea ameliorates the clinical consequences of sickle cell disease in most patients.[1] There is no biological reason to expect greatly different results in Britain. Moreover, there has not been any serious discussion at any meetings of European or North American experts that has been in support of repeating the study. Doing so is not warranted from either the research or cost perspectives.

We were therefore surprised to read the editorial by Olujohungbe et al on hydroxyurea treatment for sickle cell disease in Britain.[2] Many reasons are cited for low patient recruitment into trials which necessarily will be aggravated in patient groups who may already consider themselves misunderstood by society,[3] as is reported in sickle cell disease. In a pilot study of combination treatment with hydroxyurea and a short chain fatty acid, sodium valproate, we were able to recruit, albeit slowly, the 10 patients we needed. We believe that this was because there was a clear research question we were able to articulate to patients. Our patients have also expressed interest in joining national and multicentre trials.

The unsuccessful studies that Olujohungbe et al mentioned are not cited. If the object of these studies was to familiarise clinicians with hydroxyurea then the failure to recruit patients was predictable. Nor would such studies constitute research as supported by the NHS research and development levy.[4] The clinical research questions remaining for hydroxyurea and sickle cell disease need to be addressed by valid methodology and with appropriate sample sizes, which necessitates collaboration between hospitals or advanced laboratory facilities. Involvement of the nurse specialists and relevant community groups should improve patients' understanding, involvement, and therefore recruitment.

Both patients and clinicians remain concerned about the safety and toxicity of hydroxyurea. We are addressing this with the launch in the autumn of a European register of patients with sickle cell disease treated with hydroxyurea; this is on behalf of a European Union concerted action. Doctors will be able to submit data—demographic, clinical, laboratory, and outcome data (including details of toxicity) by post, fax, and email. Participating centres will receive regular reports. Our pilot study of 160 patients across Europe has reported four pregnancies, resulting in two normal babies, one termination, and one stillbirth; malignancies in two patients; and some minor problems, such as nail pigmentation, in eight. We shall be following up these patients and extending recruitment. Any clinicians interested in participating should fax their request for information to +44 (0)181 965 1115 after 15 October this year.

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1 Charache S, Terrin ML, Moore DR, Dover GJ, Barton FB, Eckert SV, et al. Hydroxyurea for treatment of severe sickle cell anaemia. *N Engl J Med* 1995;332:1317-22.
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Women's perception of risk of cancer

Editor—Figures recently published by the Cancer Research Campaign showed that cancer is now the leading cause of death in the United Kingdom.[1] This change seems to be due to a more rapid fall in mortality from heart disease than from cancer, although both are declining. For many years, women have believed cancer to be the greatest killer.[2 3]

Cancer education has aimed to reduce the related fear which could cause rejection of cancer screening and delay in seeking treatment.[4] Cancer education now needs to change to take account of the new statistics. It also needs to address risk reduction if a more rapid fall in mortality is to be achieved. In a small pilot survey, we have attempted to provide a new baseline of women's views on cancer with special reference to breast cancer, which is the commonest cause of death from cancer in UK women.[5]

The study was carried out in five Townswomen's Guild meetings in the north of England. A total of 37 women aged 45-75 participated (100% response). Participants completed a short anonymous questionnaire under the supervision of the researcher. Most of the questions were completed by ticking boxes.

Although 25 of the 37 women answered correctly that heart and circulatory diseases were the leading cause of death in men, only three considered it to be cancer. Twenty nine said that cancer caused the most deaths in women.

From a list of 12 types of cancer, 34 selected breast cancer as the commonest type among women in the United Kingdom. Thirty of the respondents said that women under the age of 55 were at greatest risk. The table shows the responses to a series of true and false statements relating to risk of breast cancer. Although this is only a small study, the findings point to the need to establish a new baseline of knowledge and beliefs on which education programmes to reduce risk of cancer, and breast cancer in particular, can be built.

We thank the Townswomen's Guilds for making this study possible and Dr David While for his advice.

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Participants' responses to statements relating to risk of breast cancer

Statement	No of respondents (n=37)	No (%) responding		Current scientific opinion
		True	False	
Breast feeding decreases the risk of breast cancer	34	28 (82)	6 (18)	Under evaluation
Women with a close relative with breast cancer are at a greater risk than women with no relatives with breast cancer	36	28 (78)	8 (22)	True
Not smoking reduces the risk of breast cancer	37	22 (59)	15 (41)	False
Taking the contraceptive pill increases the risk of breast cancer	37	20 (54)	17 (46)	Under evaluation
A low fat diet can decrease the risk of breast cancer	36	16 (44)	20 (56)	Under evaluation
Breast cancer can develop from bruising the breast	34	14 (41)	20 (59)	False
Women with children are less likely to get breast cancer than those without	35	10 (29)	25 (71)	True
There is a greater incidence of breast cancer among working class women	37	8 (22)	29 (78)	False

Magnesium sulphate in pre-eclampsia

Evidence supports its use

Editor—Gulmezoglu and Duley state that although magnesium sulphate is acknowledged as the preferred anticonvulsant for eclamptic women, there is little evidence to support or refute the use of anticonvulsants in pre-eclampsia.[1] However, a large placebo controlled randomised trial on the use of magnesium sulphate in severe pre-eclampsia has recently been published.[2]

Magnesium sulphate was found to be highly effective in severe pre-eclampsia (relative risk 0.09, 95% confidence interval 0.01 to 0.69).[2] The risk of seizures without magnesium sulphate was 3.2%, and the number of women with severe pre-eclampsia who needed to be treated with magnesium sulphate to prevent one case of eclampsia was 34. Previous studies have compared the efficacy of magnesium sulphate with that of phenytoin. Based on this evidence and using a framework for making therapeutic decisions,[3] obstetricians were willing to treat pre-eclamptic women with magnesium sulphate when the risk of seizures was above 2.5% and 1.75% in two UK studies (the corresponding numbers needed to treat were 57 and 77).[4 5]

Coetzee et al showed that the risk of seizures without magnesium sulphate was above this risk threshold (3.2%) and that the number needed to treat (34) was below the threshold for this criterion.[2] There should therefore be no uncertainty about the role and choice of magnesium sulphate as a prophylactic anticonvulsant in cases of severe pre-eclampsia that warrant delivery. Moreover, further trials of magnesium sulphate versus placebo in women with severe pre-eclampsia should be unnecessary.

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Still room for improvement

Editor—We welcome the increasing use of magnesium sulphate in the prevention of convulsions in pre-eclampsia.[1] We are, however, concerned that 23% of consultants would not use anticonvulsants in this clinical

circumstance and that, of those who do, only 52% would choose magnesium sulphate.

Current evidence supports the use of anticonvulsants in pre-eclampsia and magnesium sulphate as the drug of choice. Coetzee et al found a significant decrease in the incidence of eclampsia in women with severe pre-eclampsia treated with magnesium sulphate compared with those treated with placebo (0.3% *v* 3.2%).[2]

If we are to make substantial progress in reducing mortality from eclampsia in Britain we have to be able to prevent the first fit occurring. This conviction is supported by observations from two recent publications. In the British eclampsia survey by Douglas and Redman, 59% of 383 women with eclampsia had single fits,[3] and in the most recent confidential inquiry into maternal deaths, eight of the 11 women who died from eclampsia had single fits.[4]

To our knowledge, there is no evidence that the pathophysiology of the first fit is different from that of the second and subsequent fits, and thus the concept of the first versus recurrent fits is false. We must also take account of the suggested benefits to the fetus such as protection against cerebral palsy when magnesium sulphate is given to the mother.[5]

Use of magnesium sulphate should always be considered in pre-eclampsia until there is evidence to the contrary or the woman is entered into a study to evaluate the drug's efficacy. Uncertainty still exists about the threshold of severity of pre-eclampsia at which magnesium sulphate should be given.

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1 Gulmezoglu AM, Duley L. Use of anticonvulsants in eclampsia and pre-eclampsia: survey of obstetricians in the United Kingdom and Republic of Ireland. *BMJ* 1998; 316:975-6. (28 March.)
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Using email for abstracts submitted for conference was unexpectedly labour intensive

Editor—Recent speculation suggested a "utopian vision" for electronic scientific publishing.[1] Our experience in organising an international conference may be helpful in outlining the potential, but the current difficulties, of using electronic mail.

The annual scientific meeting of the Association of the University Departments of General Practice in Ireland, which attracted 458 delegates, was held in Dublin in July 1997. The closing day for the submission of abstracts was Friday 14 February, and submission by email was especially encouraged. A total of 334 abstracts was submitted, of which 241 were sent by email (table). The emails arrived in three forms: as a Word attachment (178), part of the email text (7), or an uuencoded document within the email (56). Altogether 49 of the 50 submissions received after the weekend of the closing date were sent by email. A total of 690 email messages relating to conference arrangements were also received.

Method of submission of abstracts for conference by date, 1997

Date submitted	Total No	No (%) sent by email
By Thursday 13 February	146	115 (78)
From Friday 14 February (closing date) to Monday morning 16 February	138	77 (56)
From Monday morning 16 February to Thursday 19 February	50	49 (98)
Total	334	241 (72)

The use of email was advantageous in two respects. Firstly, it was convenient for general conference inquiries, saving both time and expense on long distance telephone calls. Secondly, efficiency was increased because we did not have to type from a hard copy. There were several disadvantages, both expected and unexpected. As expected, we received a considerable proportion of submissions on or closely after the closing date by email. This caused a severe, short term, log jam. Translation of the uuencoded documents was labour intensive. An unexpected disadvantage was the failure of our virus checking program to remove a "concept virus." People still do not trust email, and we received a number of duplicates either by hard copy or by faxed copy. This resulted in a lot of work in matching abstracts. In addition, a lower proportion of referees than expected had email facilities. This resulted in the use of hard copy and surface mail for the assessment process and negated the potential efficiency of using email. Finally, there was no difference in the proportion of abstracts accepted that had been sent by email (61%) or by another method (76%).

In summary, we found email efficient for handling conference inquiries. Perhaps for a conference of this medium size, however, email should be restricted to those abstracts that have been selected for presentation.

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1 Bero L, Delmothe T, Dixon A, LaPorte RE, McLellan F, Newmark P, et al. What might an online scientific paper look like in five years' time? *BMJ* 1997;315:1692-7.

Human Fertilisation and Embryology Act 1990 discriminates against girls

Editor—We wish to respond to Deech's reply from the Human Fertilisation and Embryology Authority[1] to our letter expressing concern over the consent required from children before their gametes can be stored.[2] We believe that our views are far from "misguided"; they are reinforced by Deech's comments. Her reply relates only to prepubertal boys and makes no attempt to address the same issues for girls. Girls are born with their full complement of gametes (fulfilling the definition of the Human Fertilisation and Embryology Act) and, unlike boys, do not have an early immature state that puts them outside the act's criteria. Half of our patients are female, and their parents ask the same questions about the impact of chemotherapy on the future fertility of their child as the boys' parents do. If the girl is too young to understand these issues then it would not be possible to harvest her gametes and the act would discriminate against her future fertility.

With regard to male patients, it is not inconceivable that they may have reached Tanner stage 2 but still not have the depth of understanding to provide informed consent. Some 9% of boys aged under 11 will have reached stage 2 in their pubertal development, and these boys will be denied the possibility of gamete harvest because of the act.

We therefore reiterate our original statement that many of the obvious anomalies for children could be avoided if the Human Fertilisation and Embryology Authority accepted the principles guiding the clinical practice of all paediatricians in the United Kingdom: parents should be allowed to give consent to harvest and research, but future use of the stored gametes must have the consent of the patient.

The title of our previous letter still holds true: the Human Fertilisation and Embryology Act 1990 discriminates against children. It is now clear, however, that the act also contravenes the principles of sex discrimination.

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