occasion or one year after diagnosis conferred a significant survival advantage with a 25% reduction in mortality ($p = 0.01$).

The survival advantage of the ALS clinic group thus appears to reflect the increased mortality of the patients treated by general neurologists in the first 200–250 days; these patients are not well enough to attend the ALS clinic.

Inferior treatment by general neurologists is implied (for example, ''less attention was paid to early introduction of gastrostomy feeding''—for which no evidence was produced) and is suggested as the reason for the increased mortality.

We accept that a multidisciplinary clinic is valuable in the management of ALS, but this paper is not scientific evidence for this view. The paper would have been useful if the authors had matched ALS clinic and general neurology clinic patients, even retrospectively, for age at onset, mode of onset, disability, and duration of illness. Patients should have been deemed to have entered the ALS clinic cohort only from the date of first attendance at the ALS clinic and not from the date of diagnosis, which may have been up to one year previously. A treatment effect of the ALS clinic can only be possible from the date of first attendance. Censoring early deaths in the clearly more ill general neurology cohort should also have been considered. By avoiding these biases one might have a possible estimate of the effect of attendance at the ALS clinic.

M Hutchinson
St Vincent's University Hospital, Dublin 4, Republic of Ireland

R Galvin, B Sweeney
Cork University Hospital, Cork, Republic of Ireland

T Lynch
Mater Hospital, Dublin

R Murphy
Adelaide and Meath Hospital, Dublin

J Redmond
St James's Hospital, Dublin

Correspondence to: Prof M Hutchinson; mhutchin@iol.ie

References

1 **Traynor BJ**, Alexander M, Corr B, *et al*. Effect of a multidisciplinary amyotrophic lateral sclerosis (ALS) clinic on survival: a population based study, 1996–2000. *J Neurol Neurosurg Psychiatry* 2003;**74**:1258–61.
2 **Pocock SJ**, Clayton TC, Altman DG. Survival plots of time-to-event outcomes in clinical trials: good practice and pitfalls. *Lancet* 2002;**359**:1686–9.

Author's reply

We welcome the opportunity to reply to the points raised by Hutchinson and his colleagues concerning our recent paper and to provide further scientific evidence that patients attending a multidisciplinary ALS clinic have improved survival compared with patients attending a general neurology clinic.

The key criticism is that the survival benefit derived from attending the ALS clinic is a result of referral centre bias. Hutchinson *et al* maintain that the multidisciplinary ALS clinic selects for patients with milder disease, as only these patients live long enough to be referred to the ALS clinic. While we acknowledge that it is challenging to avoid referral bias when one is quantifying the effect of a referral centre, referral bias is not a prominent factor in our study, for the following reasons. First, survival analysis of patients diagnosed exclusively in the ALS clinic (that is, not referred from other neurologists) reveals a similar beneficial effect on mortality compared with the previously published data (median survival, 644 and 448 days for the ALS clinic ($n = 44$) and general neurology cohorts, respectively; log-rank test, $p = 0.02$); Second, ALS patients who live more than a year from the time of diagnosis (and therefore have ample opportunity for referral) continue to experience a survival advantage from attending the ALS clinic.

Hutchinson *et al* suggest that that the parallel nature of the survival curves (that is, the similar rate of decline of both cohorts) stems from the overrepresentation in the general neurology clinic of more disabled patients who die in the first 250 days and ''are not well enough to attend the ALS clinic.'' Consequently, the perceived difference in mortality is artefactual. In reality, the parallel nature of the survival curves provides the strongest proof of a robust improvement in survival along ALS patients attending the ALS clinic: survival curves would converge rather than remain parallel, if the improved survival observed in the ALS cohort reflected the early loss of sicker patients in the general neurology clinic cohort. Kaplan–Meier survival analysis demands that the death of each individual be an independent event. Therefore, the prognosis of an individual who dies two years after diagnosis is unrelated to that of all other ALS patients who die within the first 250 days of diagnosis. The vast majority of positive intervention studies in both ALS patients and transgenic ALS mouse models show a parallel pattern of survival curves, as is seen in our paper. This common finding is thought to reflect the ability of an intervention to slow down, but not reverse, the progression of motor neurone degeneration that underlies ALS.

A single visit to the ALS clinic is associated with an improved survival of the ALS patient. The term ''ALS clinic'' is a misnomer. In fact, it represents a system of care that ''services the Irish ALS population by combining the existing infrastructure of community services and the services of a voluntary organisation with a hospital based system.''[1] The primary advantage of all ''multidisciplinary clinics'' is the coordination of a network of hospital and community based ancillary services (including respiratory medicine, nursing, occupational and physical therapy, speech and swallowing, nutrition, home help, counselling, and so on) that facilitate symptomatic interventions for each ALS patient, both in a hospital setting and in their home.[2] Therefore, any patient who attends the clinic on a single occasion is enrolled in this system and is assiduously followed up. When a patient becomes too ill to travel to the clinic, home visits are undertaken by a specialist ALS nurse who coordinates and integrates community based, hospital based, and, in the latter stages, hospice based care. The improved survival observed in patients who attend the clinic on one occasion is thus a testimony to the ''ALS clinic'' system and contradicts the assertion that the observed difference in survival arises from the exclusion of ALS patients who are not fit enough to travel.

In our opinion, the criticism of the use of Kaplan–Meier survival curves rather than tables to present survival data is not valid. The vast majority of modern peer reviewed journals, including *JNNP*, do not publish survival tables, as the graphic representation of survival curves provides a greater wealth of data.

Similarly, if the baseline characteristics of patients attending the multidisciplinary clinic are solely responsible for our findings, attendance at the ALS clinic would not be independently predictive of survival in the Cox proportional hazards model. The Cox proportional hazards model is a popular mathematical model that allows estimation of hazard ratios and survival curves, *even though the baseline hazard is not specified*. Furthermore, it has been established that the site of onset, age, sex, and delay in diagnosis are surrogate markers of ALS disability.

The purpose of our study was to determine the optimum method of providing care to ALS patients. We agree that a randomly assigned study in which age, sex, site of onset, and disability are matched for each cohort would be ideal to demonstrate a difference between two different clinic types. However, this could only be accomplished in the setting of a formal randomised clinical trial, which would be both logistically difficult and ethically questionable.

B J Traynor
Massachusetts General Hospital-East, Charlestown, MA, USA

O Hardiman
Beaumont Hospital, Dublin

References

1 **Traynor BJ**, Alexander M, Corr B, *et al*. Effect of a multidisciplinary amyotrophic lateral sclerosis (ALS) clinic on ALS survival: a population based study, 1996–2000. *J Neurol Neurosurg Psychiatry* 2003;**74**:1258–61.
2 **Leigh PN**, Abrahams S, Al-Chalabi A, *et al*. The management of motor neurone disease. *J Neurol Neurosurg Psychiatry* 2003;**74**(suppl IV): iv32–47.

Outcome of contemporary surgery for chronic subdural haematoma: evidence based review

We read with interest the report by Weigel *et al*[1] on the outcome of contemporary surgery for chronic subdural haematoma, and commend the authors for attempting to review such an extensive and diverse range of publications. The paper ably demonstrates the lack of quality evidence for the management of this common condition. However, we are concerned about the description of the paper as ''evidence based''. Exclusion criteria were broad, and fewer than 5% of papers found in the Medline literature search were included in the final analysis. Correspondence with the original authors for further data or clarification is an acceptable and expected part of evidence based analysis, and would have increased paper and patient numbers significantly.[2 3] The data examined do not appear to have been paired, as age and comorbidity will have dramatic effects on outcome, irrespective of surgical technique. In this context, unpaired univariate statistical analysis is unable to produce meaningful significance. Further detracting factors include limited search procedures, absent

quality assessment and weightings of individual papers, exclusion of premorbid status in deciding success rates, and a burr hole diameter defined as up to 3 cm—classified by many neurosurgeons as a craniotomy. We are concerned that, on a less careful reading, this paper could serve as a reference in the realm of ''evidence based medicine'', when it fails to adhere to most criteria of good evidence based medicine.

A Brodbelt, P Warnke
The Walton Centre for Neurology and Neurosurgery, Liverpool L9 7LJ, UK

Correspondence to: A Brodbelt; abrodbelt@doctors.org.uk

REFERENCES

1 **Weigel R**, Schmiedek P, Krauss JK. Outcome of contemporary surgery for chronic subdural haematoma: evidence based review. *J Neurol Neurosurg Psychiatry* 2003;**74**:937–43.
2 **Moher D**, Cook DJ, Eastwood S, *et al*. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of reporting of meta-analyses. *Lancet* 1999;**354**:1896–900.
3 **Greenhalgh T**. *How to read a paper*, 2nd ed. London: BMJ Books, 2001.

Author's reply

We appreciate the comments by Brodbelt and Warnke on our recent evidence based review on the outcome of contemporary surgery for chronic subdural haematoma. We completely agree with them that one of the surprising findings of our review was that there is indeed a paucity of methodological good studies on the surgical management of one of the most common entities seen in neurosurgical clinical routine. As most studies we reviewed were retrospective and some relied solely on expert opinions, it was not possible to achieve our initial goal of carrying out a meta-analysis of the data. Nevertheless, it was possible to scrutinise the available data with the armamentarium of evidence based methodology. It is obvious, however, that the conclusions to be drawn depend on the primary data. The proposals of the quorum conference cited are concerned primarily with improving the quality of meta-analysis of randomised clinical trials.

Good clinical practice is not necessarily good evidence based medicine. There are many problems in the methodology of evidence based medicine itself, and the validity of its recommendations are increasingly being questioned. Finally, the key to understanding an article or a review is always the critical appraisal of reader themselves. This is no less important for meta-analyses or evidence based reviews. Even to the ''less careful reading'' it should be clear that our review provides an inventory of the current situation but that a critical analysis of the data does not allow one to go further and specify guidelines. We hope that our review will stimulate our colleagues to provide high quality evidence in the future. There are many questions to be answered.

R Weigel, J K Krauss
Department of Neurosurgery, University Hospital, Klinikum Mannheim, Germany

Correspondence to: J K Krauss; joachim.krauss@nch.ma.uni-heidelberg.de

Mesodiencephalic targeting of stimulating electrodes in patients with tremor caused by multiple sclerosis

The review of deep brain stimulation (DBS) for tremor in patients with multiple sclerosis by Wishart and colleagues[1] was a good summary of the current literature, its shortcomings, and the problems associated with this type of surgery. We have recently published a report on the difficulties invloved[2] and would like to add a comment about targeting the site of DBS implantation in the mesodiencephalon in this patient group.

An earlier review of stereotactic ablative and DBS surgery showed that a range of different thalamic subnuclei and mesodiencephalic areas has been targeted, with variable success.[3] Although a target in the thalamic nucleus ventrointermedius (Vim) is often cited, we have found—like Aziz's group[4 5]—that a more anterior and ventral electrode placement was most likely to reduce the tremor. In the 12 patients implanted in our series,[6] the median coordinates of the site of optimal intraoperative tremor suppression were 13.5 mm lateral to the midline, 2 mm behind the AC–PC (anterior commissural–posterior commissural) midpoint, and 2.5 mm deep to the AC–PC plane. These coordinates suggest a subthalamic–zona incerta target, which would interrupt the dentato–Vim projections. The deepest of the quadripolar electrodes was inserted at this site, suggesting that the remaining rostral electrodes straddle the Vim or nucleus ventro-oralis posterior, which lies anterior to the Vim.

Although our targets are not dissimilar to those reported by Aziz's group,[4 5] we have not done intraoperative microelectrode recordings or postoperative magnetic resonance imaging to confirm our intraoperative targeting. Furthermore, most patients with tremor caused by multiple sclerosis have major brain distortions because of demyelination, plaque formation, and ex vacuo hydrocephalus when they come to stereotactic surgery. It is difficult, therefore, to know how their mesodiencephalic anatomy conforms to a stereotactic atlas. This may explain why, in our experience, targeting in patients with multiple sclerosis is considerably more demanding than in patients with either Parkinson's disease or essential tremor.

I R Whittle, Y H Yau, J Hooper
Department of Clinical Neurosciences, Western General Hospital, Crewe Rd, Edinburgh EH4 2XU, UK

Correspondence to: Professor I R Whittle; irw@skull.dcn.ed.ac.uk

References

1 **Wishart HA**, Roberts DW, Roth RM, *et al*. Chronic deep brain stimulation for the treatment of tremor of multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2003;**74**:1392–7.
2 **Hooper J**, Whittle IR. Costs of thalamic deep brain stimulation for movement disorders in patients with multiple sclerosis. *Br J Neurosurg* 2003;**17**:40–5.
3 **Haddow LJ**, Mumford C, Whittle IR. Stereotactic treatment of tremor due to multiple sclerosis. *Neurosurg Q* 1997;**7**:23–34.
4 **Alusi SH**, Aziz TZ, Glickman S, *et al*. Stereotactic lesional surgery for the treatment of tremor in multiple sclerosis—a prospective case–controlled study. *Brain* 2001;**124**:1576–89.
5 **Nandi D**, Chir M, Liu X, *et al*. Electrophysiological confirmation of the zona incerta as a target for surgical treatment of disabling involuntary arm movements in multiple sclerosis: use of local field potentials. *J Clin Neurosci* 2002;**9**:64–8.
6 **Hooper J**, Taylor R, Pentland B, *et al*. A prospective study of thalamic deep brain stimulation for the treatment of movement disorders in multiple sclerosis. *Br J Neurosurg* 2002;**16**:102–9.

Assessing tremor reduction and quality of life following thalamic deep brain stimulation for the treatment of tremor in multiple sclerosis

We read with interest the paper by Wishart *et al*.[1] on chronic deep brain stimulation (DBS) for the treatment of tremor in multiple sclerosis. We would like to highlight two important points.

First, reduction in tremor should not be the ultimate goal of this surgery. It is a means to an end. The most important outcome for the patient must be improved function. Surgery that reduces tremor but does not improve limb function (for example, residual ataxia) is of questionable benefit for the patient, although surgeons may mistake it as ''successful'' if they only assess tremor. The authors' review of the literature outlined many papers that focused on tremor but made no mention of function. In the authors' own series of four patients, improvements in tremor ''translated into improvements in aspects of daily functioning'' but no details were provided on how this was measured. We addressed this point in a recent paper dealing with thalamic DBS for 12 patients with multiple sclerosis and tremor but unfortunately this was not included in the authors' review.[2]

Second, the option of unilateral thalamic DBS in a patient with bilateral upper limb tremor should be discussed. We have found that, following DBS control of their dominant hand, some patients decide they do not need (or want) the other side done. If they have significant head tremor, however, bilateral surgery is required.[3]

C Berk, J Carr, M Sinden, J Martzke, C R Honey
Surgical Centre for Movement Disorders, Division of Neurosurgery, University of British Columbia, Vancouver, BC, Canada

Correspondence to: Dr C Berk; caglarberk@hotmail.com

References

1 **Wishart HA**, Roberts DW, Roth RM, *et al*. Chronic deep brain stimulation for the treatment of tremor in multiple sclerosis: review and case reports. *J Neurol Neurosurg Psychiatry* 2003;**74**:1392–7.
2 **Berk C**, Carr J, Sinden M, *et al*. Thalamic deep brain stimulation for the treatment of tremor due to multiple sclerosis: a prospective study of tremor and quality of life. *J Neurosurg* 2002;**97**:815–20.
3 **Berk C**, Honey CR. Bilateral thalamic deep brain stimulation for the treatment of head tremor: report of two cases. *J Neurosurg* 2002;**96**:615–18.

Author's reply

We value Dr Berk and colleagues' commentary and their input on the relevance of assessing limb function and its implications for quality of life. Our manuscript was written before their important contribution[1] appeared in our literature search, and we