the differences between them in fully evaluating migraine studies. And because of differences in the design and execution of such studies, it remains hazardous to draw comparative conclusions from independent studies, as Goadsby states.

I also suggest caution in the use of the concepts of "therapeutic penalty," and the "number needed to harm," as discussed by Goadsby. Such approaches treat all adverse events as equally important. However, the frequent occurrence of relatively trivial events such as mild dry mouth is of far less consequence than the infrequent occurrence of, say, myocardial ischaemia. It would not be appropriate to give them the same weight, as is done with both of these approaches.

For truly meaningful comparisons of both efficacy and safety, head to head comparative trials remain the definitive approach. Hopefully, such trials will be forthcoming to allow for truly valid comparisons among the triptans.

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Goadsby replies:

I thank van der Kuy and Lohman for their interest in the editorial¹ and agree that treatment choice is difficult. We have all struggled with a construct that would absorb both the benefit and payment for headache relief and considered a gain/penalty ratio as suggested, being mindful of the issues of measurement that surround the end points currently employed in clinical studies. I have tried to do something similar for number needed to treat and found, as the correspondents show, that it is not very sensitive, and there are issues with the confidence intervals. This is, in part, an indictment of the problems with current end points as they are translated into clinical practice. Perhaps we will only be able to sort these compounds out when more direct head to head comparisons are made. In the meantime the trial data must be mixed with clinical experience. My experience has been that whereas the differences between the triptans are not huge there are differences that matter in practice, and fitting the drug to the clinical problem can be very rewarding in terms of satisfying a patient's unmet therapeutic needs. Since the editorial a further compound has been approved in Europe, rizatriptan at a dose of 10 mg orally, bringing to four (including sumatriptan, naratriptan, and zolmitriptan), the choices we have for non-ergotamine based specific antimigraine treatments. The data² indicate that rizatriptan will

also have an important place in the treatment of acute migraine attacks.

In regard to the numbers that have been used. Unfortunately, the summary data, indeed the field, represent a moving target. The data quoted in the text were from a single large study,³ whereas those used in the figure were from a meta-analysis that included many more patients and perhaps is likely to be a more accurate representation of the differences (Tfelt-Hansen, personal communication). The problem is that the meta-analysis covers studies that are older and the newer study was more or less contemporaneous with the newer drug developments. One could argue for either data set and we all await with interest the new comparative study between sumatriptan and zolmitriptan that has been completed but not yet formally reported.

In regard to Meijer's comments, I would agree that the placebo provides an assessment of various things including the therapeutic effect, which I am not sure is different from the therapeutic gain, given that in some settings the treatment may be worse than the natural history of the disorder. In any event the therapeutic gain is merely the reciprocal of the number needed to treat analysis which is a well developed concept.⁴ Certainly in the editorial the point was made that direct comparative studies are lacking; however, by standard criteria the triptan developments are reasonably suited to this methodology.⁵

Klein makes some very interesting points from the perspective of an ex-member of the pharmaceutical industry team that developed zolmitriptan.⁶ He starts by identifying the caveats in the editorial and suggests that I ignored them. I simply presented one way of looking at the trial data having identified potential weaknesses, I am not sure that this equates to ignoring those caveats. Others have found that taking account of placebo responses is useful across a range of clinical disciplines, including neuropathic pain,⁷ epilepsy,⁸ and myocardial infarction,⁹ although not without criticism.

The example of the zolmitriptan development programme, of which Klein was directly involved, is curious. The very large placebo response quoted, in a study that has never been published (Diener, H-C et al, 3rd European Headache Federation Meeting Sardinia, 1996), may have resulted from a very skewed randomisation in favour of active treatments, so that there were very few patients entered in the placebo arm which was then a noisy data point with wide confidence intervals that contributed little to the meta-analysis. This outcome really makes the point for me that such overall analyses can be very useful when individual studies are problematic to interpret. In regard to making hazardous conclusions, I would suggest that ignoring the placebo effects offers a tool by which efficacy outcomes can be inflated for rather obvious purposes somewhat more hazardous than those employed in the editorial. Concerning side effects, similar comments may be applied. Calculating therapeutic penalty is nothing more than making an overall tolerability index. It does not consider safety and was never suggested by myself to do so. No clinician would weigh myocardial infarction equal with dry mouth and to suggest that this has been done is simply incorrect. Safety is a completely different issue and is considered by practitioners on another level. If there is any confusion about safety and tolerability it is in the mind of industry, not on the clinical

side. I would agree that more head to head comparisons are necessary and stated this before commenting on the available triptans.

In addition, I would like to correct the naratriptan logD_{pH7.4} which is -0.2 not -0.02, a typographical error pointed out to me by an alert neurological colleague (Professor Allan Purdy, Halifax, Canada) to whom I am grateful. Triptans seem to have come of age in that we can have a mature, data driven debate about their use and misuse in clinical practice. Headache as a subspeciality is better for this, as is neurology in general. Patient care is well served by such discussions as we seek to do the best job for this very common clinical problem.

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- 1 Goadsby PJ. A Triptan too far. *J Neurol Neurosurg Psychiatry* 1998;**64**:143-7.
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Line bisection in hemianopia

Barton and Black indicated in a recent report that hemianopic subjects without unilateral neglect may demonstrate a horizontal line bisection bias towards the scotomatous field.¹ Their study was prompted by their impression that the influence of visual field defects on spatial tasks has been little studied. The authors unfortunately seem not to have been aware of studies by Kerkhoff et al²⁻⁴ that not only replicated Barton and Black's findings but indicate that such findings have been recorded as long ago as 1894. It would be useful if Barton and Black could indicate whether any aspects of their study are distinguished from the preceding reports.

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- 1 Barton JJS, Black SE. Line bisection in hemianopia. *J Neurol Neurosurg Psychiatry* 1998;**64**:660-2.
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The authors reply:

Mark is right in noting that Kerkhoff *et al* have mentioned this phenomenon of contralateral bisection bias in hemianopia. We will first examine the data provided by Kerkhoff *et al*, then peruse the literature he quotes, to answer Mark's question.

Firstly, two of the three papers quoted by Mark do not provide data on hemianopic bisection bias. In one,¹ the phenomenon is mentioned in a single sentence in the methods section; in the other,² a German review contrasting hemianopia and hemineglect published last year, there is a short discussion about bisection without experimental data. The third paper studied bisection of vertical or horizontal lines in a series of six patients³: however, all had bilateral cerebral damage and complex bilateral field defects, not hemianopia. Extrapolating from such unusual patients to those with more common unilateral hemianopia is not always appropriate.

Kerkhoff *et al* state that others have made this observation before.¹⁻³ He quotes two works from the English literature. One is the paper by Schenkenberg *et al*.⁴ This report analysed by side of brain damage without respect to hemianopia. Furthermore, hemianopic bias cannot be deduced from their tabulated data: there is bisection data for only six patients with hemifield defects without neglect, five with left hemispheric lesions, and the type of field defect is not stated. An informal *t* test on the small sample of five patients with left hemispheric lesions shows no difference from the controls.

Another citation is a monograph by Teuber *et al*.⁵ This was also puzzling, because line bisection did not seem to be reported in the methods or results. We believe that Kerkhoff *et al* may have been referring to patients with lateral or vertical shift of fixation ("pseudo-fovea", p 79). It does not necessarily follow that a shift of fixation leads to a shift in bisection judgments, though. Teuber *et al* do state that this might occur (p 82), and refer to another work of theirs,⁶ a case study of a man with a right occipital wound and left hemianopia. However, his bisection errors were biased rightward, as with neglect, rather than leftward, as we find with hemianopia.

Kerkhoff *et al* are more accurate in noting precedents in the older German literature. We became aware of these when we had a German monograph of Werth translated recently.⁷ Axenfeld⁸ does seem to be the first to make this finding, in his report of a man with left hemianopia and leftward bisection errors. Apart from precedence, though, few conclusions are permitted from a single case study without controls.

The most important work we discovered is that by Liepmann and Kalmus.⁹ These authors documented contralateral bisection bias in 10 patients with homonymous hemianopia and one with bitemporal hemianopia. Interestingly, they noted that this bias was not present with very small or very large lines. They dismissed Axenfeld's hypothesis that the error was related to a coexistent gaze palsy,⁸ but speculated that it was related to increased numbers of saccades and fixations into the blind hemifield, an explanation which resembles the idea that the bias may be secondary to an adaptive shift of attention. (Note, though, that we and others have provided evidence that the spatial representation within normal hemifields can itself generate this type of bias.^{7,10})

We appreciate the opportunity to publicise the prior observations of Axenfeld⁸ and Liep-

mann and Kalmus,⁹ and the prescience of the latter's speculations. Among our colleagues, "hemianopic bisection error" does not seem to be well known. We would also suggest that its scientific foundation in the German literature could be improved. We have provided better evidence for both the existence of the bias and the conclusion that it is caused by hemianopia, with the use of statistical analysis, normal controls, and non-hemianopic brain-damaged controls, none of which were used in the older German work. We hope that our brief initial report and this correspondence increase awareness of "hemianopic bisection error".

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- 1 Kerkhoff G, Münßinger U, Meier EK. Neurovisual rehabilitation in cerebral blindness. *Arch Neurol* 1994;51:474-81.
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Myoclonus of peripheral origin

We read with interest the recently published article by Assal *et al* on "Post-traumatic stimulus suppressible myoclonus of peripheral origin".¹ They presented a patient with painless "myoclonus" of the first dorsal interosseous muscle of the foot that was abolished by local anaesthetic block. Electromyography showed bursts of rhythmic spontaneous grouping of motor units of 200 to 400 ms duration occurring at 1.6 Hz frequency. We take issue with the usage of the term "myoclonus" for the abnormal movements described. Myoclonus is a brief, shock-like, involuntary movement with EMG activity usually lasting less than 200 ms (often even 50 ms or less).² Myoclonic discharges are usually arrhythmic and irregular, with the exception of segmental (brainstem or spinal) myoclonus which presents with rhythmic, long EMG bursts (>100 ms) involving several spinal or body segments. Descriptions of the electrophysiology of peripheral myoclonus are scarce. In our experience, the EMG bursts in peripheral myoclonus can be >100 ms in duration (rarely more than 200 ms), but are not truly sinusoidal, are irregular in frequency and duration, and have a very variable interburst interval. By contrast, in the case presented by Assal *et al*, the EMG bursts appear sinusoidal, regular in frequency, and

come in trains of EMG activity that are interrupted by periods of silence. Furthermore, even in rhythmic myoclonus with long EMG bursts, the movements still appear brief and shock-like. In contrast, the description by Assal *et al* of the "myoclonus" in their case was continuous and rhythmic. It also seems unlikely that EMG discharges of 400 ms duration will appear brief or shock-like. We agree that the EMG bursts resemble that of the painful legs and moving toes (PLMT) syndrome, which is often associated with peripheral nerve or nerve root lesions.³ A variant of PLMT, however, can have no associated pain and is referred to as the painless legs and moving toes syndrome.⁴ The EMG findings presented by Assal *et al* may very well represent myokymia. Myokymic discharges fire rhythmically at 1-20 Hz and in trains that last a few seconds followed by a short period of silence.⁵ Myokymia is often seen in peripheral nerve disorders, is abolished by local nerve blocks, and is thought to represent ectopically generated potentials in demyelinated nerve fibres. A myokymic EMG pattern has also been described in PLMT due to hypertrophic mononeuritis.⁶

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The authors reply:

We thank Evidente and Caviness for their interest in our paper. Their comments on the descriptive term we used to describe the abnormal movements of the second toe of our patient are well taken. We already partially considered this issue in our discussion.¹

We do not agree that "myokymia" would adequately describe these movements for the following reasons. Clinically, there were no quivering nor undulating movements of the skin overlying the muscle, and, although myokymia may sometimes lead to a movement of the fingers or toes, this movement is of very limited magnitude, in our experience not nearly as gross as that seen in our patient.^{2,3} Electrophysiologically, EMG myokymic discharges concern single motor units⁴ whereas many motor units fired synchronously in our patient. In some conditions myokymia may be related to the discharge of numerous single or grouped fasciculation potentials,⁵ but this activity does not manifest gross rhythmic muscle contractions either.² Moreover, when myokymia have a peripheral origin, the ectopic activity originates from the motor nerve supplying the contracting muscle^{2,3,6} whereas we showed that this was not the case in our patient.¹

The particular condition in our patient was that the abnormal impulse generator seemed to be located on a sensory nerve (branch of