

EDITORIAL

Not such a bright idea: the UK risk-sharing scheme for beta interferon and glatiramer acetate in multiple sclerosis

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UK neurologists have been slow to prescribe beta interferon and other potentially disease-modifying drugs for multiple sclerosis (MS). We have been constrained by our notorious conservatism, which is in part based on our demand for good evidence before changing practice, particularly when it comes to very expensive therapeutic interventions such as beta interferon. But there has been another constraint – the UK National Health Service (NHS) has a centralized command and control system (which I personally rather approve of) that would not sanction the prescription of beta interferon because of its very high cost. After all, to prescribe even just to those patients conforming to the Association of British Neurologists (ABN) guidelines would cost roughly £120 million per annum, enough to fund about 1200 new consultant neurologists (which would quadruple our present number), or 4000 physiotherapists, or 8000 medical secretaries. It is all very well for individual neurologists to stamp their feet in protest at lack of funding, but these huge financial decisions cannot be easy for the Department of Health. Moreover, the decisions have been made even more difficult by extreme pressure from MS patients and their organizations, many of whom had come to believe they were being denied a treatment that might restore them to normal. And of course the pharmaceutical industry wished to sell their licensed products and – not unreasonably – pursued all avenues to do so.

Fortunately for the Minister of Health, he had the option of referring beta interferon and glatiramer to the National Institute for Clinical Excellence (NICE), a body set up to provide in-

dependent (of government) advice on the cost-effectiveness of new therapeutic interventions. After a rather lengthy process, including several appeals against the original 'no' decision, NICE finally advised that these treatments were not cost-effective and could not be recommended for use in the NHS. Even if the 2–3-year treatment effect reported in the trials could be maintained for 20 years, and the economic model NICE used turns out to be sufficiently robust, the cost would still be far too high at about £50 000–£100 000 per QALY. Curiously, on the very same day that 'independent' NICE announced their final decision, the Department of Health brought forth a rabbit from the hat. Beta interferon could after all – and should – be prescribed for patients conforming to ABN guidelines, they told us, but at the same time the prognosis of all treated patients should be monitored for 10 years and compared with what we know of the natural history without disease-modifying treatment (basically a well studied cohort from Ontario). If their prognosis turns out to be as good as predicted from the treatment trials, and the cost per QALY is kept below about £40 000 per annum, the companies could continue to charge the present rate for the drug. If the prognosis turns out to be not so good, the charge would have to be reduced. At a stroke, the Minister of Health was provided with a convenient fig leaf to protect him against the wrath of MS patients, and any financial risk was apparently shared between the government and the companies. Sounds too good to be true, and it is – both practically and scientifically.

In the UK we have less than 400 consultant neurologists, about 1 per 180 000 population, and each of us on average might look after about 200 MS patients. Suddenly, we are expected to review all the MS patients who *might* be eligible for treatment, treat those that are, follow them up for 10 years and measure their outcome in terms of the Expanded Disability Status Scale (EDSS). And of course it will also take a huge amount of time to explain to those who are not eligible for treatment why they will not get what they may (mistakenly) regard as a cure. Even deciding treatment eligibility is not easy and is often open to debate – after all, what is the difference between a minor relapse and having a bad day, in retrospect? The cost of providing more neurologists, more MS nurses, and the resources tenaciously to follow up all the patients will be enormous – and the huge drug costs are supposed to come from budgets that were set before NICE made its final decision and the scheme was announced. The risk-sharing scheme is certainly not for the faint hearted. It will be the biggest (about 10 000 patients) and longest (about 10 years) cohort study in MS ever attempted, and certainly the biggest and longest cohort study of any neurological disorder worldwide. Quite a challenge!

The scientific problem is obvious. Just how can one compare the prognosis of a highly variable disease between a group of patients openly given beta interferon or glatiramer and a historical control group in another country, using a poor outcome measure that has been widely criticised? Patients may drop in and out of treatment as well as switch between the different forms of beta interferon and glatiramer, both patients and the observers measuring their outcome will know which treatment they are taking, and some will be lost to follow-up. It will be all but impossible to adjust for case mix, which after all is why we do randomised trials in the first place

– case mix at baseline is equalized by the process of randomization, and no amount of clever statistical adjustment can do the same.

There is no shared risk at all in all this – if the treatment appears as good as the companies say it is (and the biases inherent in the scheme make this rather likely), the government will go on paying for the drug. If not, the government will still go on paying as the scientific, political, financial and even legal battles rage on over the decades ahead.

This is a defeat for evidence-based medicine, but I am not sure who the victors are. Certainly not the patients, who are fed up with our genuinely held uncertainties about just what these treatments can achieve, and our inability to conduct the randomised trials to resolve these uncertainties. Perhaps the pharmaceutical companies are the victors – after all, they stand to make billions at no risk at all. Or maybe the politicians, who have given the public what they want, but who will have moved on by the time the risk sharing scheme is exposed as a lot of nonsense.

What we really need is more randomised evidence, preferably collected independently of industry, on which to base treatment decisions. Of course that will be difficult, but not impossible. Keeping patients on long-term treatment, particularly if the outcomes are too subjective to allow open rather than placebo control, will require a lot of energy and commitment from patients and investigators. It is extraordinarily unfortunate that a recently proposed UK trial in first episode patients is unlikely to be funded; ironically the existence of the risk sharing scheme was quite incorrectly thought to make the trial design in some way invalid.

As in all adversity, there is a silver lining. The beta interferon saga, which some day must be told in full, has certainly focused the minds of politicians, health care planners, managers and neurologists on the unmet needs of MS patients – and about time too. More resources are flowing to MS patients, but one wonders who is getting less. And the risk sharing scheme will eventually provide an amazingly useful cohort of MS patients if the organisers can stay alive and keep it going for 10 years – so good luck to them! The scheme may even provide the infrastructure for the randomised trials that really need to be done. If I am wrong, and the risk sharing scheme really is a great new idea, it is curious that it is not being taken up for other interventions. Maybe the government realizes that similar schemes would be just a bit too risky, for them.