Reviewer's report

Title: The Multiple Sclerosis Risk Sharing Scheme Monitoring Study - early results and lessons for the future

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Reviewer: Jock Murray

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General comments

This is a very interesting story with unique ramifications for social, academic and industry relationships and responsibilities. It is unfortunate that it is not told in a more interesting manner.

Those who have not followed the story of NICE, especially outside the UK, will pass over the title and the abstract without recognizing the importance and implications of this story. And the text doesn’t bring it alive either. I believe this is an introduction to an important but controversial concept that brings physicians, researchers, statisticians, health economists, government and industry representatives to the same table to assess the implications of spending large amounts of money to provide better health outcomes for patients suffering from a serious and debilitating life long illness. It needs to clarify the process better as it outlines the early stages of data collection.

The risk sharing concept should be explained further, both the current arrangement and the future arrangements determined by the cost-effectiveness results.

In the Background (page 4) there is a strong second sentence that reads like a truism, and which underlies the concept of this study, but is unreferenced. It would be interesting to know from where this axiom comes. “Where such interventions have been shown to be effective, and randomized controlled trials (RCTs) are no longer acceptable, careful use of finite resources demands that health services should pay in proportion to benefit.” Is that an accepted principle nailed to a door somewhere or the opinion of the authors?

Aside from the question of whether this kind of study can really determine cost-effectiveness in a convincing way, given the expected drop-out and switching rate, the changing population of people accessing the drugs in coming years compared to the group in this study, the diminishing numbers who will stay in for ten years, and the effect of newer drugs on the scene, (among many other difficulties), there are problems evident in the data collection system revealed here. The argument of the paper is that such data collection is possible. I am not confident of this when 12% of assessments at year one either not done or not reported. And it is 21.5% at year two and 28.2% at year three. It would seem to me that there are serious deficiencies in the data collection, to the point that it is
unlikely there will be convincing conclusions with the passing years.

The paper could have made the argument that data collection in this way is possible if they had made more effort to get reports in and clean up the data before moving to publication. The assessments and information on the patients are straightforward, uncomplicated and standard, and the information should be transmitted electronically shortly after the visit, so why is there such data loss?

There are two major issues involved with this publication: 1. the risk sharing scheme, and 2. the monitoring methodology. This paper deals with the second. However I would like to comment of the first as well. The distribution of EDSS scores of the patients entered extend into levels where we would not expect much benefit from therapy (as we have learned in recent years) Thus showing cost effectiveness with a large number of patients in the EDSS 4.5 to 6 range will mask a lot of the benefit of the drug in early mild cases. But in the future, when the initial population of patients have been treated, will mostly be early mild cases, who will get even greater benefit than the pivotal trials showed. It would be unfortunate if the conclusions of this study involving a lot of long standing MS patients with extensive disability, suggested minimal benefit for the drugs, when in the future they will mostly be used in early, mild cases who will get a lot more benefit.

It would be more revealing to separate out those patients who were put on the drug at onset of their disease, to see the cost-effectiveness of the drugs in the future.

1. Is the question posed by the authors well defined?
The publication argues that monitoring of a risk sharing scheme can be effectively done, and the incompleteness of the data-collection argues against that.

2. Are the methods appropriate and well described?
The method and policing of complete and timely transmission of data is not explained, and what will be done about the missing data.

3. Are the data sound?
The rate of increasing missing data year by year suggests the results of the study will not be convincing after the ten years planned for the data collection.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition.
Although not clear, the ethics submission and the ownership by the MS Trust makes this likely. The tantalizing but unexplained reference to conflicts over the data access and publication rights raises questions but I assume the authors were applying the standards.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The authors argue that the difficulties in establishing the Risk Sharing Scheme can be overcome and the scientific challenges addressed but this reviewer is not convinced on either count.

6. Are the limitations of the work clearly stated?
I think there are many limitations beyond those discussed, both in the scheme and in the monitoring to date.

The authors rightly indicate that some studies are now showing a natural history that is milder than previously reported (British Columbia; Iceland) so further thought needs to be given to the comparison with one natural history cohort, as there are now many such natural history cohorts and they do show differing results.

7. Do the authors acknowledge other contributions to this area?
Yes

8. Do the title and abstract accurately convey what has been found?
The title adds that there are lessons for the future, but there is little on lessons for the future.

Discretionary revisions

Define “postcode prescribing” (page 4)
Give some explanation of ScHARR

I would have liked to see the ABN criteria added in an appendix or table, as that determined who was entered into the Risk Sharing System.

Explain further why the data here may not be the same as that in future publications.

Major Compulsory Revisions

None