Reviewer’s report

Title: Impact on healthcare resource utilization of multiple sclerosis in Spain

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Reviewer: Marcello Moccia

Reviewer's report:

Sicras-Mainar and colleagues reported on healthcare resource utilisation in a Spanish population of multiple sclerosis patients. The paper is clear and well written. The longitudinal dataset allows interesting analyses. However, I have two major concerns I would like the authors to address.

Inclusion criteria deserve to be fully clarified. First of all, it is not clear whether the population was selected from existing records for general medical purposes, or from specific multiple sclerosis datasets. Indeed, on the one hand authors use quite general diagnostic criteria (e.g. in the ICD-9 clinically isolated syndrome is considered as multiple sclerosis). On the other hand, authors included rather specific clinical features, such as EDSS and the diagnosis of CIS (which is then not analysed). In addition, what is a long-term prescription program? Does it specifically involve disease modifying treatments? If so, authors likely only included relapsing remitting multiple sclerosis. Otherwise, I would assume authors were treating progressive multiple sclerosis (what eligibility criteria does the local regulatory body apply?). Also, the inclusion of the treated population might depict a non-representative multiple sclerosis population. Accordingly, prevalence they found is relatively low.

Overall, statistics need a revision. Analyses are based on the classification EDSS 0-3.5 or >4.0, which is not completely reliable, as the 2 groups differ in size (150 vs 70) and do not depict specifically different multiple sclerosis populations. I would suggest authors to use regression models to assess associations between EDSS (as a continuous variable) and different costs/variables of healthcare resource utilization. Also, models should be adjusted for a subset of covariates such as age, gender, disease duration, EDSS, disease course.

Some minor points:

For the EDSS, can you please provide median and range?

Results of regression models have to be completed by reporting 95% confidence intervals.

Associations not including costs (e.g. between EDSS and age, time since diagnosis, relapses etc) are out of the objectives of this paper and can be removed.
Among limitations, authors should consider the use of standard cost for sick leave, rather than the specific costs depending on patients' income.

In the abstract, the ANCOVA is mentioned as main statistical analysis. However, results from regression models are reported. Please, consider revising with more complete statistical methods.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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