Author's response to reviews

Title: Cost analysis of Multiple Sclerosis in Brazil: a cross-sectional multicenter study

Authors:

Nilceia Lopes da Silva (nilceia.lopes@novartis.com)
Maira L S Takemoto (maira.takemoto@anova.org.br)
Alfredo Damasceno (damascen@unicamp.br)
Yara D Fragoso (yara@bsnet.com.br)
Alessandro Finkelsztejn (alessandro.finkels@gmail.com)
Jefferson Becker (jeffersonbecker@hotmail.com)
Marcus V M Goncalves (marcusribeirao@yahoo.com.br)
Charles Tilbery (charlespt@einstein.br)
Enedina M L Oliveira (enedina.oliveira@unifesp.br)
Dagoberto Callegaro (dgcallegaro@yahoo.com)
Fernanda C Boulos (fernanda.boulos@novartis.com)

Version: 5 Date: 22 October 2015

Author's response to reviews: see over
Dear Editor,

Thank you for the new compliments and suggestions to our work. We have accepted almost all of the suggestions as described point-by-point, according with the reviewer, in the list below:

Reviewer 1: Amin Torabipour

#Title:

1. The title is not clear and concise. I recommend the following title: "Costs analysis of Multiple Sclerosis in Brazil: a cross-sectional multi center study"

R.: Modified as proposed.

#Abstract:

1-The method needs to be completed. The number of patients and time of study should be added in abstract.

R.: Modified as proposed.

2-this is a cross-sectional study (add type of study in methods section.)

R.: Modified as proposed.

#Main text:

- Methodology:

1-there is not sampling methods and sample size in methodology.

R.: Modified as proposed.

2-there is not a reference for "resource utilization" part in methodology.

R.: A published reference was not used to guide methods of resource utilization assessment. A statement clarifying that a specific study questionnaire was used was included in the paper.

3-Why authors have used from parametric and non-parametric tests (ANOVA and Kruskal-Wallis) Simultaneously? You have not answered this question in previous review.

R.: The respective test was performed by the variable distribution condition. If the variable was normally distributed, ANOVA one-way test was performed, otherwise, Kruskal-Wallis does. This is described on Statistical Analysis section. For the multivariate analysis, ANOVA with partial sum of squares test was employed.

4-why the t-test is not used for determination of difference between the means in two groups?

R.: Student's t-test is applied for comparison between two samples. When it is necessary to compare more than two samples if they have normal distributions, the most appropriate test to apply is the ANOVA (analysis of variance).
Results:

1-Did you calculate the travel expenses as unit costs? You have not answered this question.

R.: No. This information was not collected.

2- Please show the disease modifying drugs separately (in table 3). In methodology, you have stated that there was cost of DMTs separately.

R.: Costs were not calculated in accordance with each type of DMT separately. We only have this information as an aggregate measure.

3- in table1, type of medical insurance should be explained.

R.: As we have reported, the sample was obtained in study sites with different types of funding: 5 public, 1 private and 2 with mixed funding. For patients from mixed funding sites we do not have the information of type of medical insurance per patient. Thus, this information could not be added to table 1.

4-the statistical tests are not specified in figure1 and 2.

R.: Modified as proposed.

Discussion:

1-discuss more about the details of direct costs and compare these in other countries.

R.: Modified as proposed.

Conclusions:

1- conclusion is not relevant and concise. Particularly, first sentence of conclusion is not relevant to objectives of this study.

R.: Modified as proposed. The conclusion was rewritten.

Reviewer 2: Fernanda Queirós

#Reviewer's report:

The paper has significantly improved. However, there are still some issues to be addressed in order to have a sound manuscript. Please, when submitting the revised manuscript, include a point-by-point response to reviewers (indicating which changes you made, and where in the manuscript, to address the reviewer’s concern or explaining why you didn’t change what was asked) and a tracked-change copy.

R.: We would like to apologize for the absence of a tracked-change copy in our last submission. However, the cover letter including the point-by-point response to reviewers was uploaded in the specific space of the journal’s database.
# Major Compulsory Revisions

1. Your background section does not address "adverse impact on quality of life and significant economic burden for patients."

R.: The objectives were reviewed and some new information was added to the introduction.

2. Your primary objective is still confusing. What do you call "humanistic impact"? It needs a brief explanation because your background section, focused on the economic impact, does not clarify this humanistic aspect of your study. You may list the variables that represent "the humanistic and economic impacts of MS from the Brazilian household and healthcare system perspectives". Listing the variables may help to clarify what you investigated.

R.: The primary objective of the study was reviewed and stated to assess only the economic impact of the disease and the term “humanistic impact” was excluded. The study title was also revised as proposed by the other reviewer and stated as “Cost analysis of Multiple Sclerosis in Brazil: a cross-sectional multicenter study”.

3. Your background does not make it clear why you investigated the secondary objectives (the impact of fatigue on daily living of MS patients and to determine utility scores). Please, review this.

R.: Modified as proposed. Another paragraph was included in the background section.

4. You kept using the term "burden of disease" at the Discussion section, although you changed the term to "humanistic impact" at the introduction. Review again your objectives to help you define which term you will use throughout the entire paper. Again, as I already stated above, make sure your introduction offers a complete overview of all areas you covered in your objectives/results. It needs to be clear when reading your paper that your results are direct answers for your objectives.

R.: The terms “humanistic impact” “burden of disease” were excluded from the text.

5. At the Discussion you state "When the direct cost was stratified among disability levels, our findings corroborate results found by studies conducted worldwide which have shown that increasing on costs are directly proportional to increasing on disability level". However, at the Conclusion you say "When total costs were analyzed, the disease severity seemed not to influence." What you said in your Conclusion is also what one sees at your Table 3. You did not discuss why the overall costs with the disease do not vary by disability level. Review that because your Discussion section is, somehow, misleading the readers. Why would the costs vary at the 3 different Cost's category and not on the total cost? You need to answer this question at the Discussion.

R.: Both sections, discussion and conclusion, were reviewed and rewritten.

6. Conclusion is better than in the first draft. However, it is confusing and need to be reviewed for clarity, after you review your discussion section.

R.: Modified as proposed.
#Minor Essential Revisions

7. You need a transition from your second to third paragraph in the introduction. In the second you're talking about the costs associated with the disease worldwide and then, in the third, jump to describe the Brazilian health system. You may need to give some numbers from the articles "7, 26-28" to help transitioning to the Brazilian health system. 8. p. 4, line 134: measures of HRQL - spell HQLR (first time it appears in the text).

R.: Modified as proposed.

9. You did a good job clarifying the measure of utility. You can improve the writing, though, making clear why you used Health-related Quality of life to, later, transform its score in the utility score.

R.: This information was added in introduction and methods section.

10. "Once costs with DMTs influenced the interpretation of total costs among the severity groups and some of the assessed costs were funded by patients, data was stratified in three different categories: A, direct medical costs funded by the health system, excluding active drugs for MS; B, drugs for MS funded by the health system; and, C, direct medical and non-medical costs funded by patients (Table 3)." This explanation should come before the results described in the section "Costs".

R.: This information is described in methods section, “Costs” subtitle. However the order of paragraphs was modified as proposed.

11. Review the notes of your tables in order to make the format uniform. For instance, at Table 3, an asterisk (*) appears twice at the notes, but only once in the table. At this same table, why some of the values are in bold? You need to explain at the notes.

R.: Modified as proposed.

12. Figure 1 and 2: The labeling of the X axis is different across figures, although they are presenting the same categories. Review these. Use notes anytime you have abbreviations in graphs, figures or tables.

R.: Modified as proposed.