Reviewer's report

Title: The multiple sclerosis relapse experience: patient-reported outcomes from the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry

Version: 2 Date: 10 July 2013

Reviewer: Diane Cookfair

Reviewer's report:

General Comments:

This study addresses two issues of importance relating to the use of corticosteroids in the treatment of relapses in patients with multiple sclerosis (MS): 1) Patients’ perceptions of recovery in terms of symptom improvement or resolution; and 2) Patients’ perceptions of the effect of treatment on facilitating/improving recovery. Two aspects of this study make these data particularly unique. The first is that the study focuses on patients perceptions and HRQoL rather than MD/clinical or laboratory based measures; the second is the large population of patients who have provided data for this study. The authors’ goals are clearly stated, and the questions they seek to answer have not been well-explored in the MS literature. As such this paper includes findings that should be of interest to those who follow patients with relapsing-remitting MS. As the authors acknowledge, the study is not without limitations – data are retrospective in nature, and rely on patient recall. There also are other limitations to the study that the authors do not address in the manuscript (see below).

Despite these limitations, the data provide a perspective that is lacking in other studies regarding this topic, and the results presented in this paper highlight the need for: a) more in-depth patient-oriented studies regarding side effects of corticosteroids and impact of corticosteroid treatment on patient HRQoL; b) the process by which health care providers decide to treat vs. observe MS patients experiencing a relapse; and c) patterns of health care utilization by MS patients experiencing relapses and the factors leading to a patient’s decision to consult or not consult a health care provider when they are experiencing a relapse.

The title is appropriate to the subject matter presented, and the abstract is well-written and appropriate. However, there are some issues relating to statistical analysis and presentation of results that must be addressed before this paper is ready for publication. All of these issues are ones that can be fixed, and assuming that these issues are adequately addressed in the revised manuscript, the resulting paper could make a valuable contribution to the field. However, a final decision regarding publication can not be reached until these issues are addressed.

I. Major compulsory revisions: Before a decision of publication can be reached,
authors must address the issues below.

Statistical Analysis & Results:

Use of Pearson chi-square and logistic regression (LR) are a reasonable approach to statistical analyses given the questions the authors have examined in this study. The authors provide a detailed explanation of how they re-coded their outcome variables to meet the dichotomous outcome variable requirement of LR. However information regarding other important aspects of the logistic regression analyses are lacking, presentation of LR results are not sufficiently well-developed and are somewhat disorganized.

1) At the very least, authors should include a table or tables summarizing LR results which include OR’s, CIs and P-values and possibly beta coefficients for each variable included in final models for the different outcome/dependent variables assessed using LR. Also, a list of all variables included in each backward elimination model tested should be included in the footnotes for the table (s) summarizing LR results, as well as the final best model for each LR analysis. This would make it easier for the reader to follow the LR results discussed in the text.

2) Another concern has to do with the testing of underlying assumptions for the LR models. While LR is more robust than multiple linear regression, there are still some underlying assumptions that apply. In particular, the LR model to be tested should have little or no multicollinearity - i.e. the independent predictor variables entered into the model should be independent from one another. It is possible that the authors did the appropriate testing to insure that none of the independent variables included in the full backward elimination model were correlated with each other to a degree that would be problematic. However, the information provided in the manuscript is not sufficient to determine whether or not multicollinearity was adequately assessed. Based on existing literature, for example, it would not be surprising to find that time since last relapse was correlated with number of total/lifetime relapses.

3) Did authors test for any interactions between independent variables in predicting outcomes?

Other major compulsory revisions/items that warrant further exploration/elaboration

4) In this study, male gender was associated with less self-reported symptom improvement. Numerous studies have reported differences in utilization of health care resources by gender across a wide variety of diseases and medical conditions. Was the distribution of males vs. females similar in the observation only vs. IVMP, or oral prednisone treatment groups? Were the age distributions, time since last relapse and/or number of relapses similar for males vs. females? Were males as likely as females to have follow-up with a physician after a relapse? More or less likely to seek treatment for relapse at an urgent care center rather than a physician’s office?
5) Based on the information provided in paragraph 3.2 of the results section, it appears that the majority of patients had contact with a health care provider regarding their relapse before a treatment decision was made. The categories mentioned include examination by a physician, a physician’s assistant or nurse, and/or phone consultation, along with investigation for a UTI, and MRI or other imaging study. It is also appropriately noted that patients could choose more than one option. Were there other options not mentioned in the paper? E.g. were patients given the option “did not consult a health care provider” or “None of the above?” If these were not options, can it be assumed that all patients self-reported some kind of communication with a health care provider regarding their relapse? If “did not consult a health care provider” and/or “none of the above” were options, what percent of patients indicated that they did not consult a health care provider regarding their relapse, or checked “None of the above” and did not check any other option? Authors should indicate in the text whether “no care” or “none of the above” were choices on the questionnaire, and if they were, what percent of patients chose these options.

6) The age distribution of patients participating in the study is provided in table 1. However, it does not appear from the description provided in 2.3- Statistical Analysis that the association between age and either LR outcome variable or age and/or other independent variables was evaluated as part of this study. Given that the data are available, it would be helpful to know whether age was associated with type of treatment (e.g., were older individuals more or less likely to be treated with observation only?) and treatment response. Also, was there any difference in the age distribution between males and females?

II. Discretionary Revisions

The authors provide a nice discussion regarding the limitations of the study, including the retrospective nature of data collection and reliance on patient recall and limitations of the questionnaire that was used to generate the data for this study. They also note the large number of patients included in the analysis, which is a definite strength of this study. They do note in the first paragraph of the Results section (3.1) that 10,688 (63.4%) of the 16,590 patients who were sent the questionnaire responded (meaning approximately 34.6% of patients who were sent a questionnaire did not respond.) It would be appropriate to mention this as a limitation of the study in the discussion section, and perhaps provide a short summary of the selection bias (if any) that might be introduced by not having data on 34.6% of patients who were sent a questionnaire.

This is an interesting paper. I look forward to seeing the revised manuscript.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests.