Reviewer's report

Title: Relating relapse and T2 lesion changes to disability progression in multiple sclerosis: A systematic literature review and regression analysis

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Reviewer: Robert Zivadinov

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Fahrbach et al.

This systematic literature review was conducted in MEDLINE (via PubMed) and EMBASE to identify randomized trials published in English from 1993- November 2010 evaluating DMTs in adult MS patients using keywords for CIS, RRMS, and SPMS combined. Eligible studies were required to report outcomes of relapse and T2 lesion changes or disease progression in CIS, RRMS, or SPMS patients receiving DMTs and have a follow-up duration of at least 22 months. 33 studies satisfied those criteria. Regression analysis determined there is a substantive clinically and statistically significant association between concurrent treatment effects in relapse rate and in EDSS and between EDSS measures and T2-LV. Based on these results the authors suggested that treatment differences in relapse reduction and T2 lesions are significantly related to differences in disease progression over the first two years of treatment.

Several comments are offered:

1. Would it be possible to search the literature and add studies that eventually meet the criteria for years 2011 and 2012?

2. The results of the study are important and expand upon our understanding of the impact of T2 lesion variables in relation to disability progression. The Discussion should compare the results of this study and other similar studies, especially those using meta-analysis.

3. In that sense, can authors comment on the methodological differences in studies using meta-analysis vs. the systematic review analysis techniques. If this Reviewer understood correctly, the authors did not have access to the raw data, which was the case in some previous meta-analysis studies. How could these affect study findings?