

**DEBATE: ARE THE PRESENT OUTCOME MEASURES FOR ASSESSING THE EFFICACY OF DISEASE MODIFYING THERAPIES CLINICALLY RELEVANT? – NO**

**George Ebers**

*UK*

First let me concede that relapses do have some clinical relevance to patients. They are frightening, they remind the patient that they have the disease and cause temporary disability. A minority of patients will experience permanent disability from relapses although it is quite infrequent that this is severe. Many of the anecdotes told about severe devastating relapses were actually cases of NMO.

However it is not relapses which cause the main social medical and economic impact of multiple sclerosis. This is determined almost entirely by the development of the progressive course of the disease and the subsequent consequences of this.

I spent a quarter of a century collecting the natural history of a population-based group of patients in London Ontario. To do this I had to see 20-30 MS patients a week over this duration and I believe I have as much practical experience with the disease as anyone.

Accordingly the systematic study of these patients allowed us to evaluate the standard outcome measures used in clinical trials. It was clear that relapse frequency does not associate with long term disability and in this we have avoided the sissy outcomes of half and one point changes in DSS and have focussed on time to cane, bed, or dead.

These studies show that relapse frequency excepting for a modest effect in the first two years does not associate with long term outcome, in fact after the second year relapses are associated with slightly better and significantly better outcome.

Similarly we have studied the long term outcome in patients in clinical trials particularly the one with the pivotal study of beta Interferon. This put us in the position of being able to evaluate the relationship between the outcome measures studied in trial versus hard disability endpoints. We were able to show that none of the end points which have been used strongly associate with long term outcome since all these are overridden or trumped by the progressive course. Future studies need to focus on the harder outcomes and patients should not be promised long term benefits unless these have in fact been demonstrated. No treatment has been shown to impact on long term disability.