ARE PLACEBO-CONTROLLED CLINICAL TRIALS STILL ETHICAL/NECESSARY IN RRMS?

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The evidence that you can actually teach or convey ethical principles has never been substantiated. Ethics derive from the inner voice that tells an individual what is right or wrong and in the case of medicine what is in the best interests of the patient.

Clinical trials of multiple sclerosis have been uniform in utilising invalidated outcome measures. This has occurred to a degree to which it is difficult to find parallels in medicine in general. To be sure, it is a difficult disease with long term outcomes being the ones that patients fear, whereas trials have focussed in on short term outcomes with no established relationship to things that really matter. Multiple sclerosis has gone through a very long series of false dawns and therapeutic claims over the last century which has been overly optimistic as a general rule.

We have recently evaluated the outcomes which have been used for evaluating past trials leading to drug approval and current trials.

It is not a pretty sight. It is quite clear from natural history studies that relapses have very little if anything to do with long term outcome. Similarly MRI measures have been thoroughly evaluated within large datasets and found to be similarly non-predictive for meaningful outcomes. The measures of disability used in trials certainly don't measure unremitting disability as investigators and their industry supporters have claimed.

With respect to therapies and prospective trials, at the very least, patients can be told what they can reasonably expect. This is at substantial odds from what is commonly done in recruiting patients for trials. It then becomes a dialogue between patient and physician as to what is in the patient's best interests. If drugs have no risk then there is the inconvenience only to be considered of being in a trial. However if drugs have substantial risk and this is quantifiable then it must be stacked up against any quantifiable benefit for the outcomes that really matter to patients.

The widespread embracing of dubious and poorly validated outcomes by some MS investigators, often in contexts where there are egregious conflicts of interest, threaten academic credibility not to mention long term professional autonomy. For those who think this is secure all that is necessary is to review events of the past three decades in the US.

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