

Appendix

Assuming an $\alpha = 0.001$ to account for multiple analyses, $\beta = 0.10$, confounders explain 20-40% of the variance in HRQoL,¹ if we consider that it would be clinically relevant if comorbidity explains 5% or more of the variance considering up to 20 comorbidity variables, then the necessary sample size is 674. Accounting for 20% drop-out our required sample size was 808 (total across all 4 sites).

1. Turpin KV, Carroll LJ, Cassidy JD, Hader WJ. Deterioration in the health-related quality of life of persons with multiple sclerosis: the possible warning signs. *Mult Scler* 2007;13:1038-1045