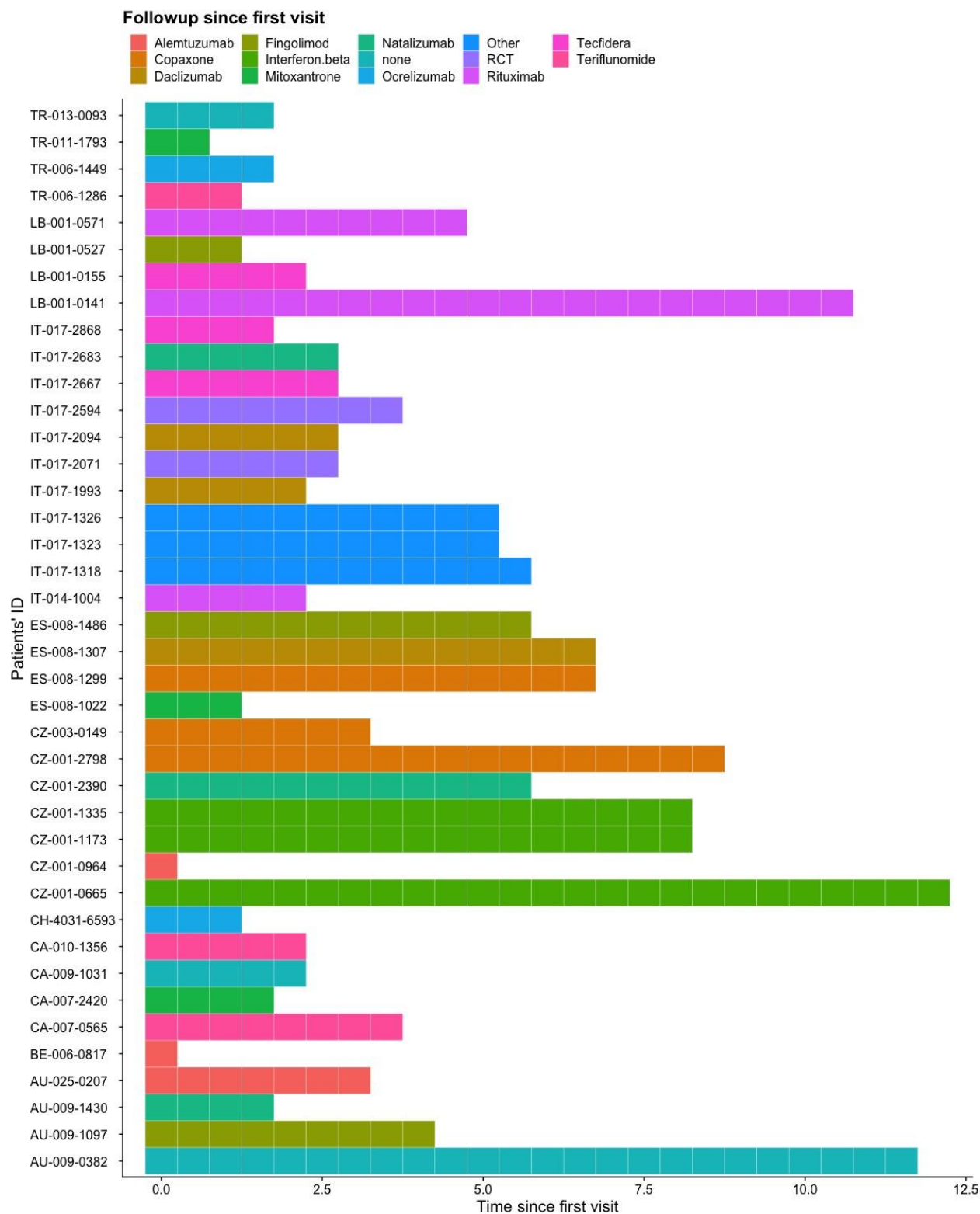


**Online supplement****Supplementary Table 1.** Comparison of patients eligible for and excluded from the present study.

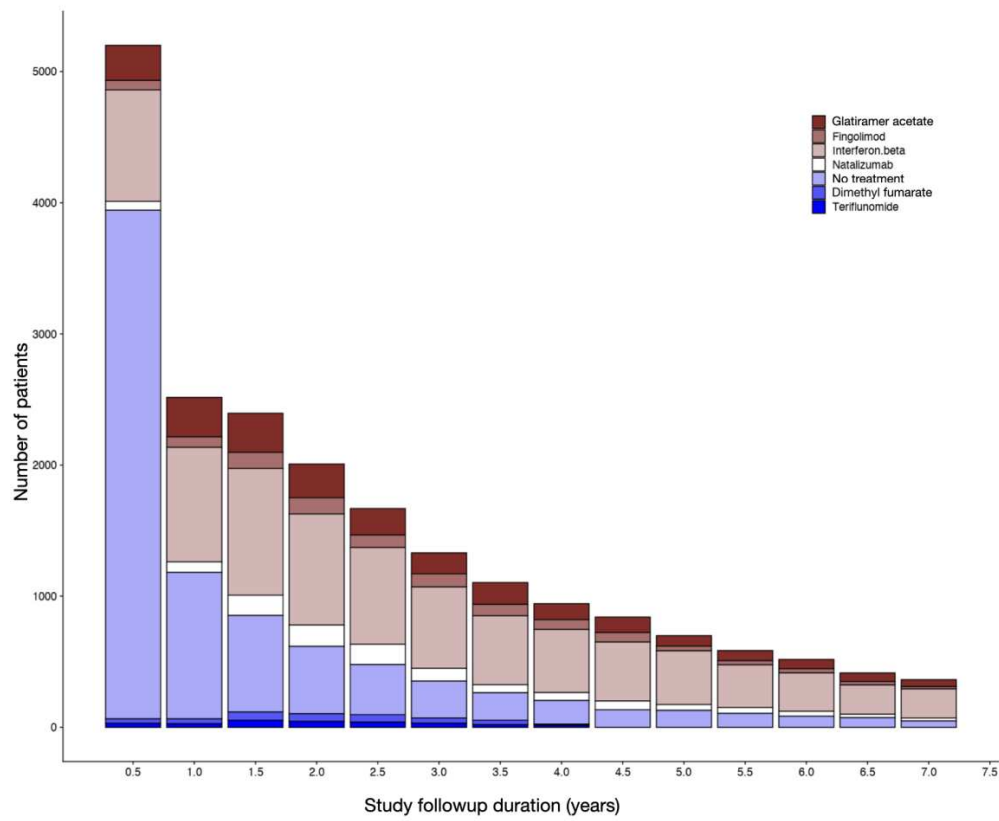
	<b>Excluded (n=38574)</b>	<b>Included (n=23236)</b>
Age first visit, Mean (SD)	39.1 (12.6)	36.3 (10.5)
Female sex	26899 (69.7%)	16685 (71.8%)
MS duration at baseline, Median [Q1, Q3]	7.53 (8.59)	6.21 (6.82)
Disability		
EDSS 0-3.5	22094 (57.3%)	20236 (87.1%)
EDSS 4-5.5	5086 (13.2%)	2230 (9.6%)
EDSS 6-9.5	6087 (15.8%)	770 (3.3%)
Missing	5307 (13.8%)	0 (0%)
Presence of new/enlarging/enhancing cerebral MRI lesions during the last 12 months	913 (2.4%)	1314 (5.7%)
Receiving disease modifying therapy at baseline	9736 (25.2%)	15068 (64.8%)

**Supplementary table 2:** Summary of the study protocol

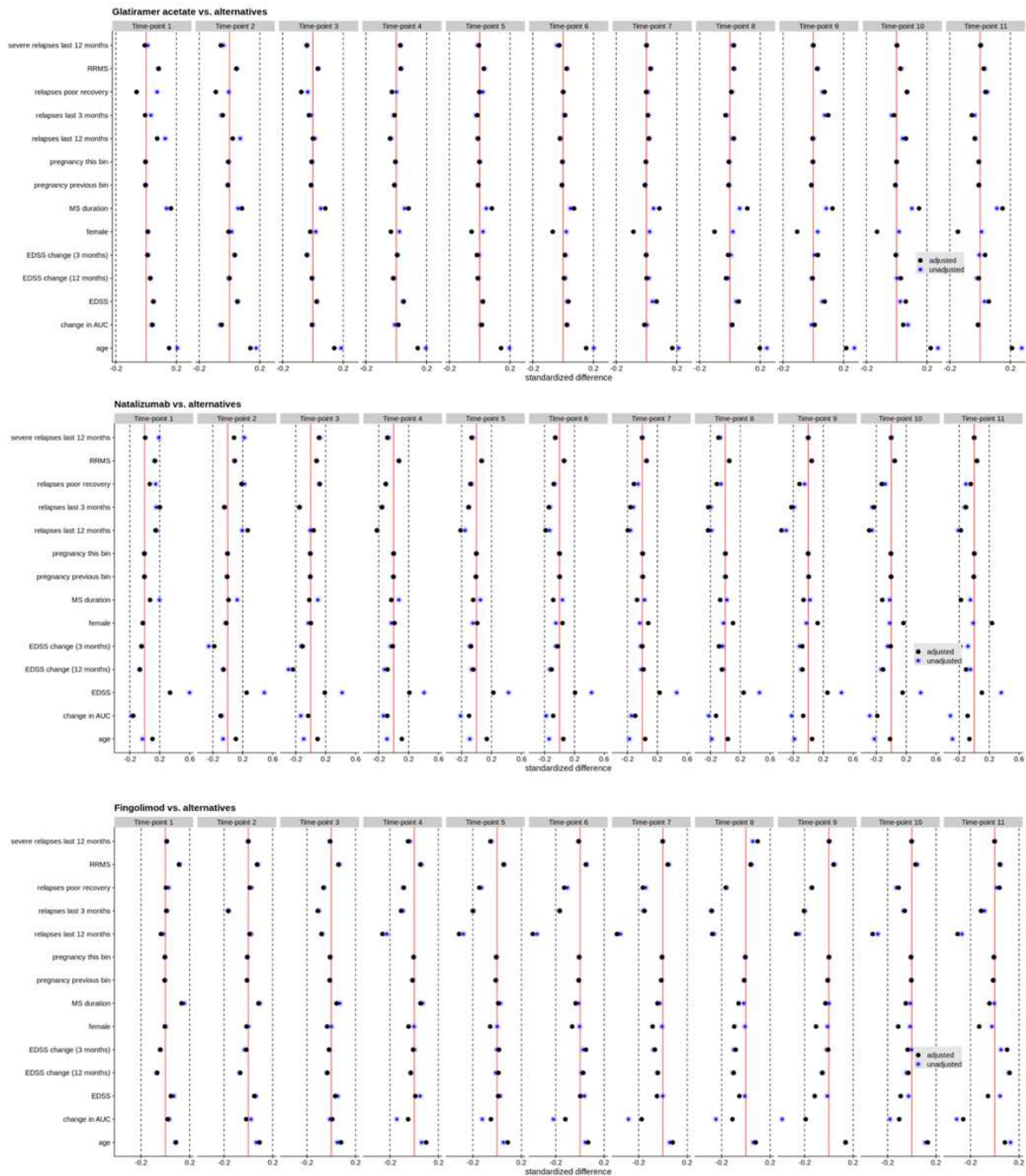
<b>Protocol component</b>	<b>Description</b>
inclusion criteria	clinically isolated syndrome or definite multiple sclerosis
treatment strategies	patients may contribute 6-month periods to either the treated (where exposed to disease modifying therapy for $\geq 15$ days during the given period) or the untreated pseudo-cohort (where exposure to disease modifying therapy during the given period $< 15$ days)
assignment procedures	non-random assignation of therapy by treating neurologists
follow-up period	follow-up $\geq 1$ year, $\geq 3$ disability scores with $\geq 1$ score recorded per year
outcomes	<ul style="list-style-type: none"><li>• 12-month confirmed disability worsening events (increase in EDSS by 1 step; 1.5 step if baseline EDSS=0 and 0.5 steps if baseline EDSS<math>&gt;5.5</math>)</li><li>• 12-month confirmed disability improvement events (decrease in EDSS by 1 step; 1.5 steps if baseline EDSS<math>\leq 1.5</math> and 0.5 steps if baseline EDSS<math>&gt;6</math>)</li><li>• relapses</li></ul>
causal contrast of interest	per-protocol effect
analysis	proportional hazards models of multiple events with robust estimation of variance and inverse probability of treatment weights to adjust for fixed and time-dependent confounders and intermediates of outcomes; this analysis plan implies that data on the adjustment factors are available

**Supplementary figure 1.** An example of the included follow-up.

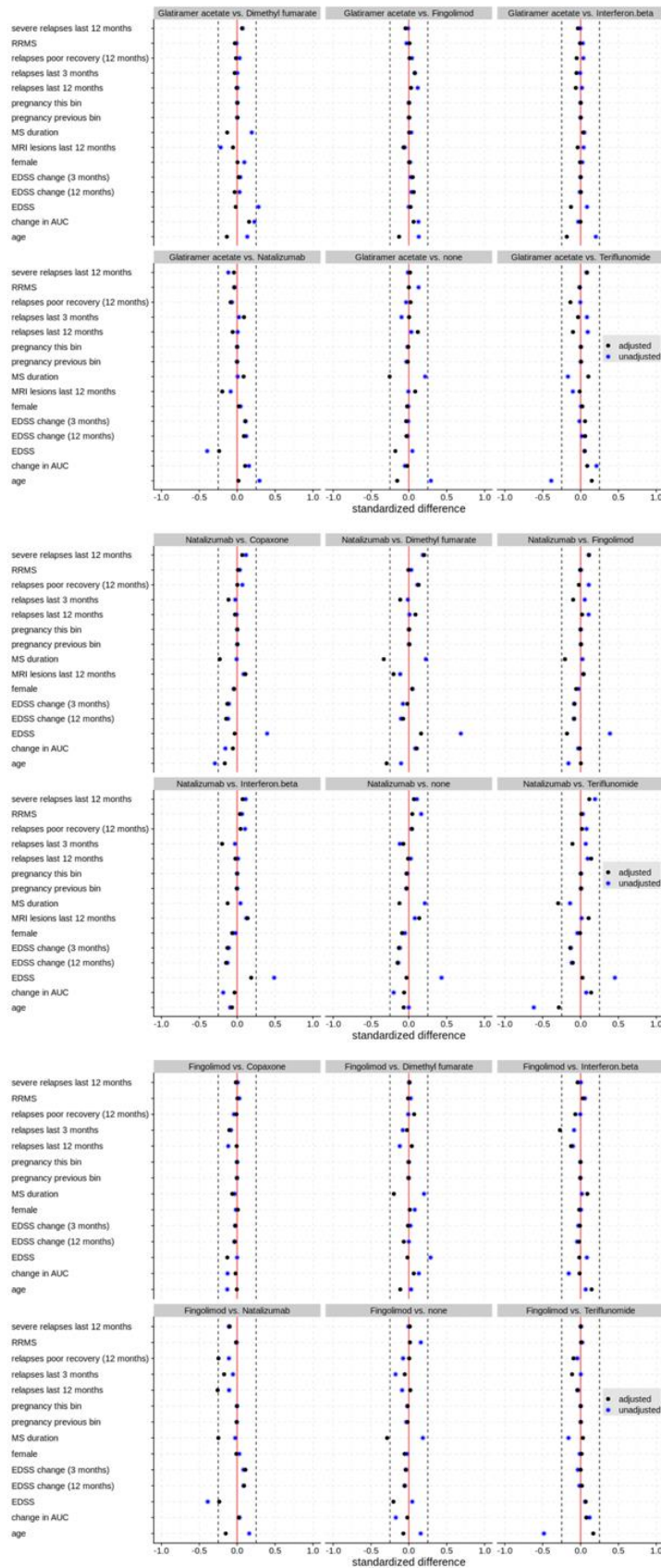
Only patients followed-up with prospective data entry commencing after 1st January 2006 were included. One treated / untreated epoch per patient was included. Patients were censored at the change of their treatment status.

**Supplementary figure 2.** Attrition of the number of patients over time for each therapy

**Supplementary Figure 3:** Covariate balance over time, the presented example shows the three reference treatments



**Supplementary figure 4:** Weighted and unweighted covariate balance measured with standardized difference between glatiramer acetate and alternative treatment groups in an ATT model.



**Supplementary figure 5:** Comparison of multiple therapies (ATE) among patients with recorded MRI data.

