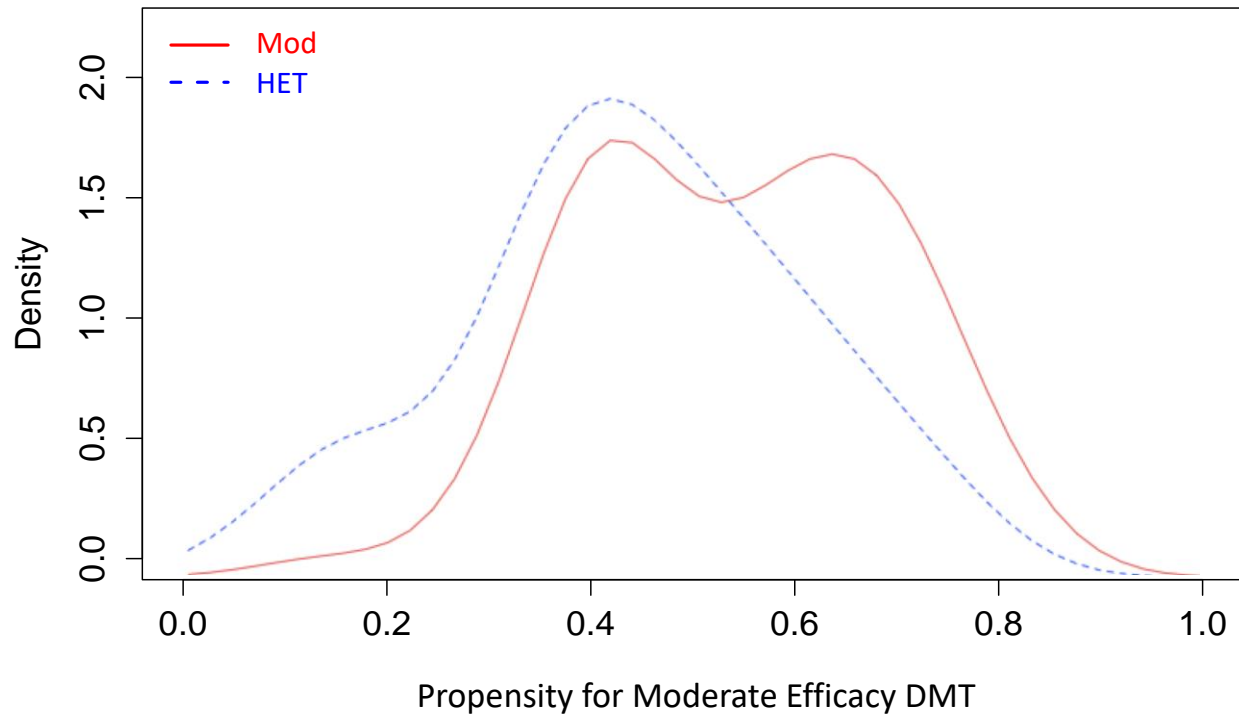
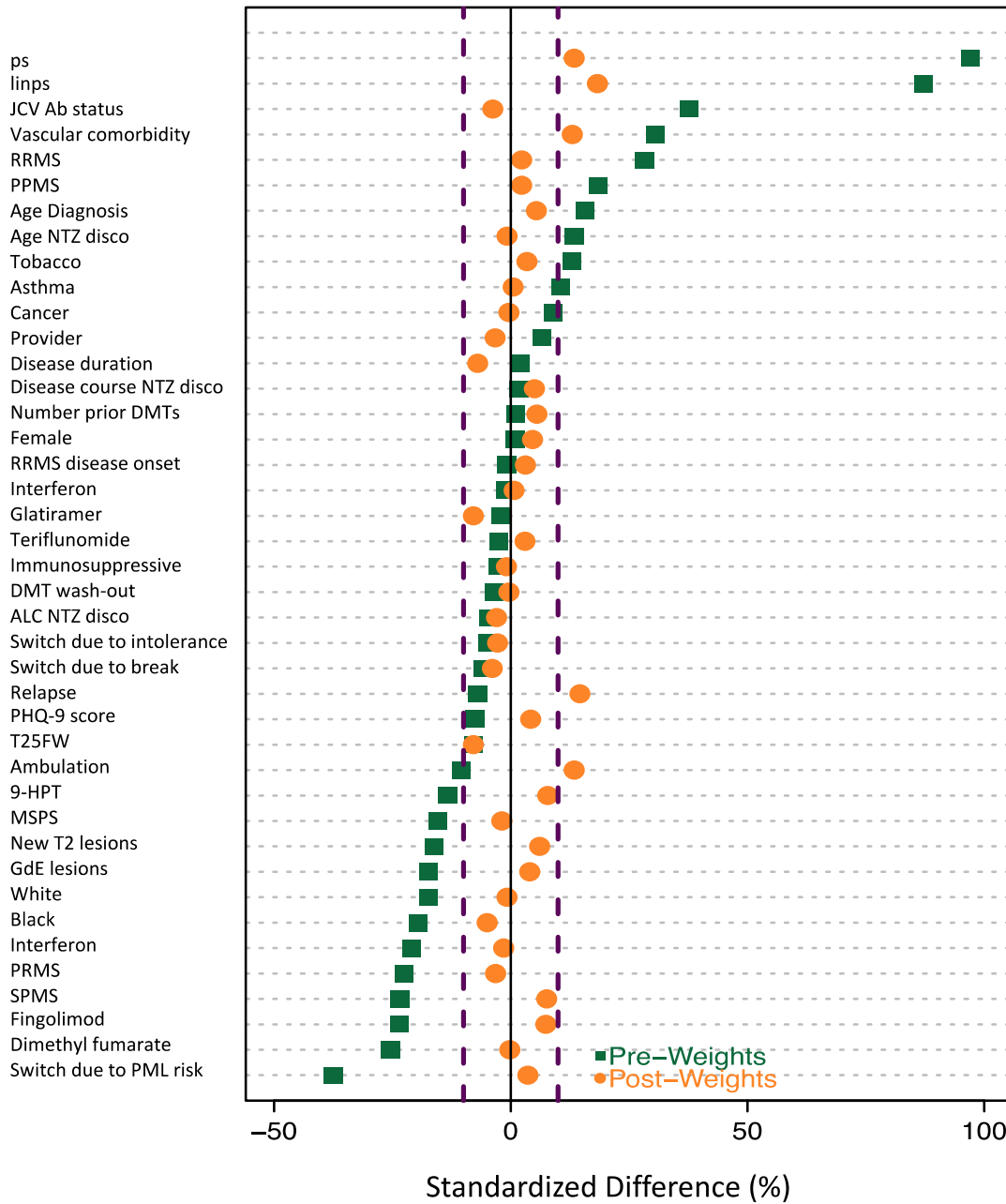


Supplemental Material**eFigures****Figure e-1.** Propensity Score Density Plot.

The propensity score (PS) model appropriately assigned higher PS to Mod DMT vs. HET, and there was sizeable overlap of PS between the two treatment groups. This finding confirmed adequate comparability between groups and further confirmed the appropriateness of using PS adjustment prior to making conclusions on treatment effect differences between our cohorts.

Abbreviations: HET, high efficacy DMT; Mod, moderate efficacy DMT.

Figure e-2. Absolute Standardized Difference Plot: Pre and Post ATT Weighting.



Absolute standardized difference plot comparing baseline covariates between NTZ switchers to Mod DMT vs. HET before and after average treatment effect on the treated (ATT) weighting using the linear propensity score in a double robust approach. Positive values represent higher standardized effect sizes for Mod DMT. Variables include ps (continuous), linps (continuous), JCV Ab status (positive, negative, indeterminate), vascular comorbidity (hypertension,

hyperlipidemia, diabetes mellitus), RRMS (present, absent), PPMS (present, absent), age at diagnosis (continuous), age at NTZ discontinuation (continuous), tobacco use (present, absent), asthma (present, absent), cancer (present, absent), provider (treating healthcare provider at CCLRCBH or Mellen Center), disease duration (continuous), disease course at NTZ discontinuation (RRMS, SPMS, PPMS), number of prior DMTs (continuous), female (present, absent), RRMS disease course at disease onset (present, absent), interferon beta-1a (prior use; present, absent), glatiramer acetate (prior use; present, absent), teriflunomide (prior use; present, absent), immunosuppressive (prior use; present, absent), DMT wash-out (continuous), ALC at NTZ discontinuation (continuous), switch due to NTZ intolerance (present, absent), switch due to NTZ breakthrough disease (present, absent), relapse before and during NTZ use (present, absent), PHQ-9 score (continuous), T25FW (continuous), ambulation (none, unilateral, bilateral, wheelchair), 9-HPT (continuous), MSPS (continuous), new T2 lesions before and during NTZ use (present, absent), GdE lesions before and during NTZ use (present, absent), white (yes, no), black (yes, no), interferon beta-1b (prior use; present, absent), PRMS disease course at disease onset (present, absent), SPMS disease course at disease onset (present, absent), fingolimod (prior use; present, absent), dimethyl fumarate (prior use; present, absent), switch due to PML risk on NTZ (present, absent).

Abbreviations: 9-HPT, nine-hole peg test; ALC, absolute lymphocyte count; DMT, disease modifying therapy; GdE, gadolinium-enhancing; JCV Ab, John Cunningham virus antibody; linps, linear propensity score; MSPS, Multiple Sclerosis Performance Scale; NTZ, natalizumab; PHQ-9, Patient Health Questionnaire-9; PML, progressive multifocal leukoencephalopathy; PPMS, primary progressive MS; PRMS, progressive relapsing MS, ps, propensity score; RRMS, relapsing remitting MS; SPMS, secondary progressive MS; T25FW, timed twenty-five foot walk.