**e-Methods**

Supplement to: **Defining Benign/Burnt-out MS and Discontinuing Disease Modifying Therapies**

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**METHODS**

**Study Population**. We searched electronic databases to identify KPSC members with last dispensed date of an MS DMT (interferon-betas, IFN-beta; glatiramer acetate, GLAT; fingolimod; teriflunomide; dimethyl fumarate; natalizumab or rituximab) between 1/1/2012 and 12/31/2016 and reviewed the complete EHR to confirm that the following inclusion criteria were met: 1) confirmed MS diagnosis per 2017 criteria13; 2) discontinuation of treatment with any MS DMT between 1/1/2012 and 12/31/2016 for at least 3 months and for reasons other than death, membership termination or initiating chemotherapy; 3) 50 years of age or older at the time of DMT discontinuation; and 4) suspected benign/burnt-out MS at the time of discontinuation.

To identify patients with suspected benign/burnt-out MS at DMT discontinuation, we required 1) documentation of a stable neurological exam for at least 5 years, 2) the absence of progressive MS and 3) the absence of active RRMS. Progressive MS was defined as documentation of progressively worsening neurological deficits (e.g. weakness, spasticity, ataxia, tremor and/or cognition), independent of relapses for at least 1 year at any time in the disease course. To account for potential discrepancies between documented subjective complaints (e.g. fatiguing leg weakness), the neurologist’s physical exam findings (e.g. progressively worsening spasticity and ataxia) and/or the MS subtype documented by the neurologist (RRMS in this example), we *a priori* decided to rely on the documented physical exams (in this case the patient would be classified as SPMS). Active RRMS was defined as patients with a relapse or MRI disease activity within 1 year prior to DMT discontinuation. Relapses were defined as the occurrence, reappearance or worsening of symptoms of neurological dysfunction lasting for 48 hours or more and needed to be documented by a treating physician during a physical exam. Symptoms that occurred within 1 month of each other were part of the same relapse.

**Additional Data Collection Details.** Data were extracted by manually reviewing the EHR through the end of the study period. Variables extracted were date of symptom onset, date of diagnosis, date of last visit, relapse history, DMT start and stop dates, physical exam findings, use of walking assist devices, cognitive impairment and expanded disability status scale (EDSS) scores. EDSS is not used routinely in community-based practices. Thus, for those with missing EDSSs (n=115), MS-related disability was obtained from neurologists’ notes and other potentially MS-related visits (e.g. ophthalmology, physical therapy, urology, psychiatry). Patients were classified as no disability (normal/near normal exams, EDSS=0-2.0), some disability but fully ambulatory (EDSS equivalent 2.5-3.5), some ambulatory impairment (EDSS equivalent 4.0-5.5) and cane, walker or wheelchair-dependent (EDSS ≥6.0).