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Comorbidity and persistence of disease-modifying therapy use for relapsing remitting multiple sclerosis

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Among individuals with multiple sclerosis (MS), comorbidity reduces the likelihood of initiating disease modifying therapy (DMT) and may increase the risk of discontinuing DMT due to lack of tolerability but not lack of efficacy.

We aimed to describe the relationship between comorbidity and persistence to initial DMT along with reasons for discontinuation.

We identified individuals with relapsing remitting multiple sclerosis (RRMS) or clinically isolated syndrome (CIS) starting a platform DMT (interferon-β, glatiramer acetate, teriflunomide, dimethyl fumarate) as initial therapy in the province of Nova Scotia, Canada from 2001 to 2016. Cases were identified using a database maintained at the only clinic providing specialty MS care in a province with universal publicly-funded healthcare. Comorbidity was determined by linkage of MS cases to provincial health administrative data using validated definitions based on International Classification of Disease (ICD)-9/ICD-10-CA codes. The comorbidities of interest included hypertension, hyperlipidemia, diabetes, chronic lung disease, ischemic heart disease, epilepsy, inflammatory bowel disease, any mental health disorder. We tested the association between comorbidity and persistence to initial DMT using multivariable Cox proportional hazards models.

We included 1464 individuals with RRMS/CIS in the analysis. Median age at MS diagnosis was 36.6 years (IQR 29.3-44.6) with median delay from MS diagnosis to DMT initiation of 0 years (IQR 0-2). Median duration of DMT persistence was 4 years (95%CI: 4-4). The number of comorbidities was not associated with DMT persistence. Mental health comorbidity was associated with an increased risk of discontinuing DMT (hazard ratio 1.20; 95%CI: 1.02-1.41). Risk of DMT discontinuation for lack of tolerability was increased in the presence of $\geq$2 comorbidities (odds ratio 1.72; 95%CI: 1.05-2.82). Comorbidity was not associated with DMT discontinuation for lack of efficacy.

Individuals with higher comorbidity burden, and particularly mental health comorbidity should be monitored for barriers to continuing DMT after treatment initiation.