A Systematic Review of Factors Associated with Disease MODIFYing Therapies (DMTs) in Patients with Multiple Sclerosis

Andrew V. Thach, MS,1 Carolyn M. Brown, PhD,2 Viviana Herrera, MS,2 Rahul Sasane, PhD,2

1College of Pharmacy, The University of Texas at Austin /Novartis Pharmaceuticals Corporation

**Background**

- Prior adherence to disease-modifying therapies (DMTs) in patients with multiple sclerosis (MS) is a well-established problem with downstream economic and clinical consequences.1, 2
- Understanding the factors associated with adherence to DMTs may help to guide interventions and strategies.

**Study Model**

Figure 1. World Health Organization Medication Adherence Model (WHOMAM)3

**Objective**

- To identify factors significantly associated with adherence to DMTs in patients with MS, particularly focusing on factors that may be modifiable

**Methods**

- **Databases:** PubMed, CINAHL, PsychInfo, and Cochrane Library
- **Publication Timeframe:** Inception of each database through June 2015
- **Search string:** ([“multiple sclerosis”] AND (“medication adherence” OR “adherence” OR “compliance” OR “concordance”) AND (“immunomodulatory” OR “disease modifying” OR “therapy” OR “interferon-beta-1b” OR “interferon-beta-1a” OR “peginterferon-beta-1a” OR “glatiramer acetate” OR “fingolimod” OR “dimethyl fumarate” OR “alemtuzumab” OR “mitoxantrone” OR “natalizumab”)
- **Inclusion criteria:**
  - Assessed adherence to DMTs approved for MS patients
  - Published in English
- **Exclusion criteria:**
  - Treated impact of an intervention (e.g., psychosocial program)
  - Meeting abstracts, letters, cases, reports, reviews, and theses/dissertations
- **Procedures**
  - All titles and abstracts reviewed for initial eligibility
  - Full-text and reference list review of all initially eligible articles
- **Final list of articles based on pre-defined inclusion and exclusion criteria**
  - Final set of articles reviewed to determine factors significantly associated with adherence to DMTs, which were subsequently organized into five broad domains of WHOM MAM

**Results**

**Discussion**

- **Most of the social and economic-related factors were patients’ demographic characteristics (e.g., age, gender, race, university education, marital status), with age (50.0% of studies) being the most frequently reported factor associated with DMT adherence.
- The most frequently reported condition-related factor was disease duration (39.2% of studies).
- Several MS-related symptoms and comorbidities were also common, including headaches, mood and anxiety disorders, fatigue, depression, and memory.
- Among therapy-related factors, the most frequently reported factor was the specific type of DMT that the patient was prescribed (51.0% studies).
- **Inclusion criteria:**
  - Assessed adherence to DMTs approved for MS patients
  - Published in English
- **Exclusion criteria:**
  - Treated impact of an intervention (e.g., psychosocial program)
  - Meeting abstracts, letters, cases, reports, reviews, and theses/dissertations
- **Procedures**
  - All titles and abstracts reviewed for initial eligibility
  - Full-text and reference list review of all initially eligible articles
- **Final list of articles based on pre-defined inclusion and exclusion criteria**
  - Final set of articles reviewed to determine factors significantly associated with adherence to DMTs, which were subsequently organized into five broad domains of WHOM MAM

**Limitations**

- **Although this study reported several factors significantly associated with DMT adherence, causation cannot be assumed.**
- Directionality of relationships for several factors (i.e., adherence causing factor or factor causing adherence) cannot be assumed due to limitations of study designs (e.g., cross-sectional) and statistical tests (e.g., bivariate analyses).
- Considerable effort was made to include all relevant articles; however, it is possible that some eligible studies and findings were unintentionally missed or omitted.

**Conclusion**

- Poor adherence to DMTs is a significant issue in MS patients that may increase the number and severity of relapses and may result in more rapid progression of the disease.
- Several modifiable and non-modifiable factors put patients at risk for DMT nonadherence across all five domains of the WHOM MAM (including social and economic, healthcare system, condition, therapy, patient factors).
- Compared to other domains of the WHOM MAM, condition-related factors may be the most difficult to modify. Patient-related factors were among the most modifiable, which suggests that focusing on patient-related factors in DMT adherence interventions and strategies may be the most effective.
- Future strategies and interventions aimed at improving patients’ OTM adherence should target these modifiable risk factors.

**References**


**Disclosure**

- This study was funded by a research grant from Novartis Pharmaceuticals Corporation.