Multiple Sclerosis and Related Disorders 18 (2017) 218–224

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

The impact of treatment adherence on clinical and economic outcomes in multiple sclerosis: Real world evidence from Alberta, Canada

Brittany Gerber[a,*], Tara Cowling[a], Guanmin Chen[b], Michael Yeung[c], Pierre Duquette[d], Paola Haddad[e]

[a] Medlior Health Outcomes Research Ltd., 160 Quarry Park Blvd. SE, Suite 300, Calgary, AB, Canada T2C 3G3
[b] University of Calgary, Calgary, Alberta, Canada
[c] University of Calgary, Multiple Sclerosis Clinic, Calgary, Alberta, Canada
[d] Notre Dame Hospital, Université de Montréal, Montreal, Canada
[e] Novartis Pharmaceuticals Canada Inc., 385, boulev. Bouchard, CDN, Dorval, Quebec, Canada H9S 1A9

ARTICLE INFO

Keywords:
Multiple sclerosis
Disease-modifying therapy
Adherence
Utilization
Costs

ABSTRACT

Background: Approximately 1 in 400 Albertans has multiple sclerosis (MS). The current study objective was to determine the real-world impact of adherence to disease-modifying therapies (DMTs) on healthcare utilization and costs among MS patients utilizing administrative data from the Alberta health system in Canada.

Methods: MS patients were identified using a validated case definition (≥ 1 inpatient record or ≥ 5 practitioner claims within 2 years) and the study index DMT was defined as the first claim for a DMT between 1 April 2011 and 31 March 2014. Treatment adherence was calculated using medication possession ratio (MPR), and patients with MPR ≥ 80% were considered adherent; healthcare utilization and costs were explored using multivariable negative binominal regression and logistic regression models.

Results: The majority of the 2864 MS patients identified were females, aged 35–55 years old. Overall, 66% of patients were adherent. Compared to non-adherent patients, adherent patients had fewer ambulatory care visits (all-cause: 8.8 vs 10.9, $p = 0.0012$; MS-related: 4.3 vs 5.3; $p = 0.001$), physician visits (all-cause: 15.1 vs 18.2, $p = 0.0001$; MS-related: 3.6 vs 4.4; $p = 0.0001$), and hospitalizations (all-cause: 5.2% vs 10.2%, $p < 0.0001$; MS-related: 1.2% vs 2.5%, $p = 0.0088$). After adjusting for potential confounding factors adherent patients had approximately 20% less physician visits (MS-related: IRR 0.82 (0.79,0.86), $p < 0.0001$; all-cause: IRR 0.83 (0.81,0.85), $p < 0.0001$) and ambulatory care visits (MS-related IRR 0.80 (0.77,0.84), $p < 0.0001$; all-cause: IRR 0.82 (0.80,0.84), $p < 0.0001$) and approximately 50% fewer hospitalizations (MS-related: OR 0.50 (0.28–0.89), $p < 0.0001$; all-cause: OR 0.48 (0.35–0.64), $p < 0.0001$) than non-adherent patients.

Conclusions: The current study found a significant impact of non-adherence to MS therapy on increased health system utilization. These findings demonstrate the importance of treatment adherence on clinical decision-making for patients with MS.

1. Introduction

Multiple sclerosis (MS), a chronic autoimmune disease, is characterized by recurrent inflammatory attacks of the central nervous system myelin and causes progressive neurological disability (Finkelsztejn, 2014). Symptoms include extreme fatigue, loss of balance, impaired speech and vision, paralysis and cognitive dysfunction (Alberta Health, 2013). The Canadian Institute for Health Information estimates 93,500 Canadians have multiple sclerosis (MS) (Canadian Institute for Health Information CIHI, 2014). With approximately 340 out of every 100,000 people in Alberta being diagnosed with MS, the province has one of the highest prevalence rates in the world (Alberta Health, 2013).

Disease Modifying Therapies (DMTs) are the current standard of care in Canada for treating MS, with the aim of slowing disease progression, reducing the number and severity of relapses, and maintaining quality of life (Hart and Bainbridge, 2016; Steinberg et al., 2010a; Bergvall et al., 2013; Freedman et al., 2013a). Several DMT are now available in Canada and the selection is typically dependent on prior treatment, severity of disease, and access to therapies within each

* Corresponding author.
E-mail addresses: brittany.gerber@medlior.com (B. Gerber), tara.cowling@medlior.com (T. Cowling), guchen@ucalgary.ca (G. Chen), Michael.Yeung@albertahealthservices.ca (M. Yeung), pierre.duquette.1@umontreal.ca (P. Duquette), paola.haddad@novartis.com (P. Haddad).

http://dx.doi.org/10.1016/j.msard.2017.10.001
Received 1 June 2017; Received in revised form 29 September 2017; Accepted 4 October 2017

province (Freedman et al., 2013b). The Canadian Multiple Sclerosis Working Group recommend IFN-1a, IFN-1b, and glatiramer acetate as first line treatments for the management of relapsing-remitting MS; fingolimod and natalizumab as second line treatments; and mitoxantrone, alemtuzumab, cladribine (IV), and cyclophosphamide as third line treatments (Freedman et al., 2013a). However, since these recommendations were made, new medications have been made available.

While the efficacy of DMTs has been demonstrated in clinical trials, these medications can only achieve maximum benefits if patients adhere to their treatment (Evans et al., 2016). Patient adherence to treatment is critical for achieving the maximum benefits of DMTs; whereas a lack of adherence can lead to treatment failure, increased hospitalizations and relapse rates, and higher costs to the health system (Alberta Health, 2013; Patti, 2010; McKay et al., 2016). Current evidence suggests that improved treatment adherence may be one of the best strategies for managing MS (He et al., 2012); however, patient adherence to DMTs is known to be challenging (McKay et al., 2016; World Health Organization, 2013). Barriers to treatment adherence among MS patients include: perceived efficacy concerns, adverse events, inconvenience and needle phobia (associated with injectable DMTs). There are also concerns with cognitive impairment, such as memory function and depression, on the proper and timely administration of treatment (Patti, 2010). Given that a lack of adherence can lead to treatment failure (World Health Organization, 2013), there may be implications for the health system, particularly in terms of healthcare resource utilization (Guo et al., 2016). As new MS treatments are developed, a comprehensive understanding of adherence rates and the impact of adherence on clinical and economic outcomes is of particular interest.

With a rich source of administrative data captured by a centralized provincial health system, Alberta, Canada offers a unique opportunity to retrospectively explore the impact of treatment adherence on healthcare resource utilization. The current study examined treatment patterns, including adherence, discontinuation and switching, as well as the impact of adherence to prescribed DMTs on health care utilization among patients with MS in Alberta using patient data captured from the Alberta Ministry of Health (Alberta Health) and Alberta Health Services (AHS) administrative databases.

2. Methods

2.1. Data source

This retrospective observational study was conducted using health administrative data from Alberta, Canada from the fiscal year 2002–2014. The following data sources were used in this study. 1) Population Registry, which includes basic demographic and geographic information for Albertans who are registered with the Alberta Health Care Insurance Plan; 2) Discharge Abstract Database (DAD), which includes information from inpatient stays within Alberta such as services, diagnoses, and length of stay; 3) National Ambulatory Care Reporting System (NACRS), which includes facility-based ambulatory care information on services and diagnoses (e.g. emergency department visits); 4) Practitioner Claims, which include fee-for-service claims from physicians and other providers (e.g. specialists) for insured health services; 5) Pharmaceutical Information Network (PIN) data, which captures dispensing information, including prescription drugs, days supplies and dosage in Alberta; and 6) Alberta Blue Cross Pharmacy Claims, which captures pharmacy data for Albertans covered through Alberta Blue Cross, primarily senior citizens. This study was approved by the Health Research Ethics Board of Alberta.

2.2. Study population

Data was linked from DAD, Practitioner Claims, and the Population Registry from April 1, 2002 to March 31, 2014 (i.e., fiscal year) using unique identifiers provided by Alberta Health. MS patients were then identified using a validated case definition of ≥ 1 hospital separation OR ≥ 5 physician office person-day visits based on ICD-10-CA and ICD-9-CM respectively (ICD-9/10 codes 340/G35) in a two-year period (Widdifield et al., 2015). Multiple claims of MS-related physician visits on the same day were counted once.

The date of the first dispense for a DMT between April 1, 2011 and March 31, 2014 in PIN data was defined as the Study Index Date. The medications for the first dispense for a DMT in the study period include interferon beta-1b (drugs identification number (DIN): 02169649, 02237319, 02337819); interferon beta-1a (DIN: 02237320, 02269201, 02318261, 02318253); glatiramer acetate (DIN:02245619); natalizumab (DIN:02286386); fingolimod (DIN: 02365480); teriflunomide (DIN:02416328) and dimethyl fumarate (DIN: 02404508). The pre-index period was defined as the 365 days prior to the study index date, and the follow-up period was defined as the period from the study index date to 365 days past the study index date.

2.3. Study variables

Patient's age (grouped as < 35, 35–55, 55–65, and ≥ 65 years old for our analyses), gender, and geographic location at study index date were identified using Registry data. Comorbidities were examined using the Charlson Comorbidities Index (CCI), calculated using validated ICD-9 and ICD-10 coding algorithms (Charlson et al., 1987; Deyo et al., 1992; Halfon et al., 2002; Quan et al., 2005) from the DAD and Practitioner Claims datasets in the 365 days prior to the study index date. In addition, comorbidities, including depression, anxiety, hypertension, bipolar disorder, chronic lung disease, hyperlipidemia, diabetes, epilepsy, stroke, and ischemic heart disease were identified using ICD-9-CM and ICD-10-CA codes (Marrie et al., 2013a, 2013b, 2013c, 2012).

DMTs were grouped by mode of index DMT administration: oral (fingolimod, teriflunomide, dimethyl fumarate), injection (interferon beta-1b, interferon beta-1a, glatiramer acetate) and infusion (natalizumab). For patients who switched from one mode of administration to another, the first identified DMT at the baseline was used to group the DMT as an oral, injection or infusion.

2.4. Outcomes

Data extracted from the PIN dataset included the DIN, dispense date, and days supplied. The drug records in PIN from the 365 days following the study index date were included. Duplicate records with the same service date and same DIN were excluded. Adherence was assessed using Medication Possession Ratio (MPR) in the 365 days following the study index date. MPR was calculated using the total number of days supply of the DMT during the persistence period divided by the number of days between the first prescription fill and the last refill plus the days' supply of the last refill. Those with an estimated MPR of ≥ 80% were considered adherent, and those with an estimated MPR of < 80% were considered non-adherent. The threshold of ≥ 80% was selected as it is widely used in adherence research, including studies with MS populations (Evans et al., 2016; Osterberg and Blaschke, 2005; Simpson et al., 2006; Karve et al., 2009; Raimundo et al., 2013). Treatment discontinuation was examined based on a ≥ 60 day gap in drug claims prior to resuming therapy during the follow-up period. For patients with more than two gaps of > 60 days, only the first gap and date was counted. For patients who switched to a different mode of administration during the follow-up period, MPR was calculated only based on the DMT for the first drug administration mode, and the data were truncated at the last date of refill for this drug. In addition, treatment switching in the one year follow-up period, and treatment patterns across the study period were explored. Treatment switching between the different modes of administrations was counted; however, due to the small number of patients with multiple switches during the