BACKGROUND

• Multiple sclerosis (MS) is a chronic, debilitating condition that affects approximately 400,000 persons in the U.S. and 2.5 million worldwide. 1

• While disease-modifying therapies (DMTs) are promising for reducing relapses and delaying disease progression, the clinical effectiveness may be limited by patients’ level of adherence. 2

• Adherence to DMTs is low in MS patients, with estimates ranging from 41 to 88 percent. 3

OBJECTIVE

• The objective of this study was to review and summarize the methodologies currently used to measure adherence to oral and injectable DMTs in MS patients.

METHODS

• A systematic literature search for measures used to assess adherence to DMTs in MS patients was conducted in the following databases: PubMed, CINAHL, PsychINFO, and Cochrane Library.

• The publication time frame was from January 2004 to January 2015. Figure 1 provides the keywords that were used to search the databases.

• Two reviewers (AVT and CC) independently screened abstracts for relevance and applied full inclusion/exclusion criteria to full-text articles. Disagreements were resolved through discussions and with the help of two additional reviewers (TM and CMB).

• Inclusion criteria:

  • Focused on at least one of the following: F.D.A.-approved DMTs; interferon beta-1a, interferon beta-1b, peginterferon beta-1a, glatiramer acetate, fingolimod, teriflunomide, and dimethyl fumarate

  • Authors of DMT adherence as either a primary or secondary outcome

  • Provided details of the methods used to calculate adherence level or proportion of adherers/non-adherers

  • Published in a peer-reviewed journal

  • Published from 2004 to time of review

• Exclusion criteria:

  • Only assessed adherence to natalizumab, mitoxantrone, and/or a non-FDA-approved DMT

  • Exclusions (n = 43) of additional reviewers (TM and CMB).

• The search strategy used to assess adherence to MS DMTs is included in Table 1.

RESULTS

• Figure 2 provides an overview of the the search strategy

• A total of 40 articles were included in the final review

• Cross-sectional, randomized, and controlled, and prospective observational studies (n=25 studies)

  • Almost all (88%) of cross-sectional, randomized controlled, and prospective observational studies used self-reported measures of adherence.

  • Two studies captured adherence through an electronic auto injection device.

  • A few studies (n=3) use more than one method to measure adherence.

  • None of the studies assessed adherence to oral DMTs.

  • Most (n=11) retrospective database studies used medication possession ratio (MPR), one study used proportion of days covered (POC), and three used both MPR and POC.

  • The sources of data included medical/pharmacy claims data (n=13), an MS registry database (n=1), and an industry-sponsored MS support program (n=1).

Table 2. Summary of Strengths and Weaknesses of Adherence Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Definition</th>
<th>Strength</th>
<th>Weakness</th>
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<tbody>
<tr>
<td>Adherence diary</td>
<td>Patient records date and time of each injection over a period of time (e.g., one month) in a diary (e.g., calendar style diary)</td>
<td>No need to recall over the past month; Provides date and time of each injection</td>
<td>Manipulate adherence level</td>
</tr>
<tr>
<td>Medication Event Monitoring System (MEMS)</td>
<td>Needle disposal bottles with MEMS cap electronic capture of adherence (e.g., percentage days not covered by DMT)</td>
<td>Objective; Good reliability and validity; Accurate; Captures medication use exactly/day/day for each needle dispensed</td>
<td>Manipulate adherence level</td>
</tr>
<tr>
<td>MPR</td>
<td>Rate of DMT supply/need</td>
<td>Not available for all DMTs</td>
<td>Not available for all DMTs</td>
</tr>
<tr>
<td>MDR</td>
<td>DMT adherence measured as time (e.g., frequency)</td>
<td>Only captures a potential confounding reason for non-adherence</td>
<td></td>
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Table 1. General Characteristics of Articles Included in Review (n=40)

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Cross-sectional, randomized controlled, and prospective observational studies</th>
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<tbody>
<tr>
<td>Retrospective database studies</td>
<td>25 (62.5)</td>
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<tr>
<td>Type of Disease Modifying Therapy</td>
<td>Injectable only 38 (95.0) Injectable and oral 2 (5.0)</td>
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REFERENCES

