# Predicting ongoing adherence to disease modifying therapies in multiple sclerosis: utility of the health beliefs model

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# Predicting ongoing adherence to disease modifying therapies in multiple sclerosis: utility of the health beliefs model

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***Objective*** To evaluate ongoing adherence to disease modifying therapies (DMT) among individuals with multiple sclerosis and test the utility of the Health Beliefs Model (HBM) to predict adherence.
***Design*** Telephone survey completed at baseline with monthly telephone follow-up for 6 months.
***Setting*** Veterans Health Administration.
***Participants*** Eighty-nine veterans with MS actively enrolled in a regional VA MS outpatient clinic currently prescribed DMT.
***Measures*** Demographic information. Selected items from the Adherence Determinants Questionnaire (ADQ) and Barriers to Care Scale (BACS).
***Results*** Adherence in this population of ongoing DMT users was relatively high (over 80% achieved 80% adherence at follow-up time points). Logistic regression and hierarchical multiple regression analyses controlling for demographics and disease duration were employed to examine the relationship of HBM constructs of perceived susceptibility, severity, benefits, and barriers to DMT adherence and satisfaction at 2-, 4- and 6-month follow-up. Of the four HBM constructs, only perceived benefits uniquely predicted both outcomes across multiple time points.
***Conclusion*** Sustained adherence to DMT remains a challenge for an important minority of individuals with MS. The Health Beliefs Model provides insight into psychosocial mechanisms that maintain adherence behavior. In particular, focus upon the perceived benefits of ongoing DMT therapy may be a promising focus for future interventions. *Multiple Sclerosis* 2007; **13**: 1146–1152. http://msj.sagepub.com

**Key words:** health beliefs; medication adherence; multiple sclerosis

Several medications show promise in slowing the progression of relapsing forms of multiple sclerosis (MS) and, as a result, delaying the onset of new disability. These medications, commonly called disease modifying therapies or DMTs, include three preparations of beta interferon (inteferon beta-1a [Avonex], interferon beta-1a [Rebif], and interferon beta-1b [Betaseron]), as well as glatiramer acetate (Copaxone). The DMTs have an important impact on the MS disease process by reducing the development of new lesions in the central nervous system, the frequency of acute exacerbations, and both physical and cognitive impairment, although the specific benefits differ somewhat between medications [1].

Despite the apparent benefits of DMT use, rates of adherence are often variable and in some cases low. Rates of medication drop-out or loss to follow-up during clinical trials, though typically below 10%, have reached as high as 33.9% [2]. Survey data suggest that as many as 45% of individuals with MS have discontinued the use of a DMT [3]. Little published information is available, however, about ongoing

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adherence among current users of DMT. All forms of the medication are injectable and require training in set-up, administration, and management of side effects. DMT use does not provide direct relief of MS-related symptoms, nor are there practical proximal biomoarkers that measure and reinforce medication efficacy, as with blood pressure in the case of anti-hypertensives. As a result, DMT users are faced with a treatment regimen that is comparatively complex and aversive with few immediate and tangible benefits.

The Health Beliefs Model (HBM) [4] provides an important framework for understanding the psychosocial factors that may contribute to medication adherence. Originally developed in the field of public health, the HBM asserts that the decision to engage in preventive health behaviors is influenced by four important perceptions: 1) the perceived *severity* of an illness, 2) the perceived *susceptibility* of the individual to that illness, 3) the perceived *benefits* associated with a health behavior to address the illness, and 4) the perceived *barriers* to engaging in the health behavior. HBM perceptions have been shown to predict a broad variety of health behaviors including mammography screening [5], the use of child safety restraints [6] and most commonly adherence to medication regimens for other chronic diseases such as diabetes [7,8] and hypertension [9].

The present study was conducted to further understanding of adherence to disease modifying therapies, a class of medications that provides significant obstacles to sustained use, but which represents a potential opportunity to delay disability in MS. Our primary goals were threefold, and included examining rates of ongoing adherence among a sample of current DMT users, exploring the relationship of patient demographic and medication factors to DMT use, and most importantly, testing the hypothesis that the constructs articulated in the Health Beliefs Model would predict adherence to DMT over time.

## Methods

### Participants

Participants were recruited from veterans receiving outpatient services for MS at a VA regional medical center as part of a larger project examining medication adherence in MS. Inclusion criteria included a diagnosis of MS, current use of one of four DMTs to slow disease progression (inteferon beta-1a [Avonex], interferon beta-1a [Rebif], interferon beta-1b [Betaseron], or glatiramer acetate [Copaxone]), and active participation in medication administration. Individuals who received their injections primarily from an injection clinic nurse or a caregiver were excluded. Participants were enrolled by the study coordinator during a regularly scheduled clinic visit, or in response to a mailing. Of 113 eligible participants, 94 veterans were consented, of which 90 (80.0% of total eligible) completed baseline assessment. Of the consented participants, two withdrew prior to the completion of the baseline assessment and two could not be contacted prior to the end of the enrollment period. One participant withdrew after baseline, leaving a final study sample of 89.

### Procedure

Potential participants' medical records were prescreened to confirm that they were currently taking a DMT. They were then approached by the study coordinator during a regularly scheduled clinic appointment to ask if they would be interested in enrolling in a study examining barriers to medication adherence. Participants were informed that all study information was confidential and would not be shared with clinical providers. Additional screening was conducted to verify that DMT was self-administered at least some of the time, and that there was a telephone number where the person could be reached. Consenting individuals were later contacted to complete a one-hour baseline interview over the phone, which included questions about demographics, history of DMT use and health beliefs. The baseline interview also contained a brief cognitive assessment containing tests of verbal memory, attention, and verbal fluency [11]. Ten-minute telephone follow-up interviews were conducted once a month for 6 months and contained questions that included past month adherence to DMT and satisfaction with DMT. Results of 2-, 4- and 6-month follow-up are presented here. For individuals who did not complete a 2-month, 4-month or 6-month follow-up interview, information was substituted from the immediately previous month (1, 3 or 5) when it was available. All study procedures were approved by the local institutional review board.

### Measures

#### *Demographic and disease information*

Gender, race (Caucasian versus non-Caucasian), age, education level, marital status (currently married versus all other), household income, years since diagnosis of MS, and length of time on current DMT medication were all obtained from single item queries in the baseline interview. Current DMT type was extracted from participants' medical records. Due to limited sample size, DMT type was dichotomized for regression analyses to reflect the use of

an interferon-based medication (inteferon beta-1a [Avonex], interferon beta-1a [Rebif], interferon beta-1b [Betaseron]) or glatiramer acetate (Copaxone).

### *Cognitive status*

Cognitive status was assessed using the Short-D test (a verbal learning and memory task) from the Screening Examination for Cognitive Impairment (SEFCI) [11]. Participants were read a list of 10 unrelated nouns and asked to recall as many as they could. Three such learning trials were given. After 12 minutes, participants were again asked to remember as many words as they could. The number of correct responses in this delayed-recall trial was the study variable.

### *Health beliefs*

Health belief constructs of perceived MS *susceptibility* and adherence *benefits* were assessed with scales adapted from the Adherence Determinants Questionnaire (ADQ) [12]. The ADQ susceptibility scale consisted of two items measuring patient perceptions of susceptibility to MS such as 'my body will fight off MS in the future'. Response values ranged from 1 = strongly disagree to 5 = strongly agree. Items were reverse scored to produce a total score where higher values reflected greater perceived susceptibility. Adherence benefits were measured using the ADQ utility scale containing two items reflecting benefits of DMT use including 'The benefits outweigh any difficulty I might have in following it' with similar response values producing a total score where higher values reflected greater perceived benefit. MS *severity* was measured with a single item mobility performance subscale from the North American Research Consortium on Multiple Sclerosis (NARCOMS) registry [13]. Possible scores ranged from 0 = normal to 6 = total gait disability. Perceived *barriers* to adherence were assessed with a measure adapted from the Barriers To Care Scale (BACS) [14]. The BACS barriers scale consisted of three items such as 'long distances to medical facilities and personnel'. Response values ranged from 1 = no problem at all to 4 = major problem. Internal consistency of the scales ranged from acceptable for susceptibility ($\alpha = 0.63$) and barriers ($\alpha = 0.61$) to good for benefits ($\alpha = 0.84$).

### *Satisfaction*

Satisfaction with DMT use was measured with a single item created for this study. Participants were asked 'how satisfied are you with your DMT right now?' with response values ranging from 1=not at all to 5 = extremely.

### *DMT adherence*

Adherence to DMT medications was assessed with a single self-report question adapted from HIV adherence literature [15]. Participants were asked, 'People often have difficulty taking their medications for one reason or another. How many times have you missed taking your DMT in the past month?' DMT adherence was defined as the percent adherent over the past month (total doses taken divided by total prescribed doses). Individuals were identified as 'adherent' if they reported taking 80% or more of their medication and non-adherent if they reported taking less than 80%. For descriptive purposes, a secondary variable was also created reflecting total missed doses. DMT medications are taken at different frequencies ranging from once per week (interferon beta-1a [Avonex]) to once per day (glatiramer acetate). As a result, it was necessary to create a common metric for missed doses across medications. Standard weightings corresponding to a 30-day month were computed for each medication. A missed dose of once per week interferon beta-1a (Avonex) was given a weight of 7.5 such that total non-adherence (four doses) $\times 7.5 = 30$. A missed dose of daily glatiramer acetate was given a weight of 1 such that total non-adherence (30 doses) $\times 1 = 30$ as well.

## Data analytic strategy

Our primary aim was to examine the utility of the health beliefs model to predict adherence to DMT medication and satisfaction with DMT medication at the 2-, 4- and 6-month follow-up time periods. Towards this end, we conducted regression analyses with predictor variables that were identical across outcomes and across time points. Logistic regression was used to examine adherence. Hierarchical multiple regression analysis was used to examine satisfaction. For the multiple regression analysis, participant age, gender and race were entered as demographic factors on Step 1. Years since diagnosis of MS, length of time on DMT, DMT type and cognitive status were entered as disease- and medication-related factors on Step 2. Finally, to examine their unique contribution to the prediction of medication adherence and satisfaction, variables reflecting the four separate components of the health beliefs model (susceptibility, severity, benefits, and barriers) were entered on Step 3. For the logistic regression analysis, the same variables were entered simultaneously.

## Results

Participants were predominantly male ($n = 71$, 79.8%), Caucasian ($n = 74$, 83.1%) and married ($n = 55$, 61.8%), with a mean age of 51.42 (SD = 9.27) years and a mean education level of 14.77 (SD = 2.23) years. More than half ($n = 56$, 64.4%) reported total household income over $30 000 per year. Overall, the sample population was highly representative of the larger population of VHA veterans with MS [10].

Participants reported they had been diagnosed with MS for a mean of 11.79 (SD = 7.95) years and had been taking their current DMT medication for a mean of 3.43 (SD = 3.29) years. All four medications were represented in the sample with 20 (22.5%) currently taking inteferon beta-1a (Avonex), eight (9%) taking interferon beta-1a (Rebif), 19 (21.3%) taking interferon beta-1b (Betaseron) and 42 (47.2%) taking glatiramer acetate (Copaxone).

### Sample characteristics at baseline

On the cognitive status screening measure, participants recalled a mean (SD) of 5.36 (2.65) of the 10 items presented in the learning trials. Examining the four components of the Health Beliefs Model, participants endorsed high levels of disease susceptibility, *M* (SD) = 3.79 (0.84) where possible values ranged from 1 to 5, and moderate levels of illness severity, *M* (SD) = 3.18 (1.71), with range of 0 to 6. They endorsed significant benefits of sustaining health behavior (adherence to DMT medication), *M* (SD) = 4.16 (0.74) with range of 1 to 5, and comparatively moderate barriers to sustaining health behavior, *M* (SD) = 1.63 (0.72) with range of 1 to 4.

### DMT adherence and satisfaction at 2-, 4- and 6-month follow-up

A total of 67 (75.2%) participants completed interviews at 2-month follow-up. Eighty (90.0%) completed interviews at 4 months, and 85 (95.5%) completed interviews at 6-month follow-up. Overall rates of DMT adherence were reasonably high, with 80% adherence or better achieved by 59 (88.1%) individuals at 2-month follow-up, 69 (86.3%) at 4-month follow-up and 74 (87.1%) at 6-month follow-up. Put differently, individuals missed a mean of 3.10 (SD = 7.56) standardized doses per month at 2-month follow-up, 3.07 (SD = 7.29) doses at 4-months and 3.01 (SD = 7.27) doses at 6-months. Satisfaction with DMT use was high at 2-month follow-up, *M* (SD) = 4.12 (1.09); 4-months, *M* (SD) = 3.85 (1.25); and 6-months, *M* (SD) = 4.19 (1.17). No participant stopped or switched DMT medications during the study period.

### Predicting Adherence to DMT at follow-up

Demographic, disease and medication variables rarely predicted DMT adherence at any follow-up time point. In the fully adjusted model (see Table 1) increasing age was associated with a greater likelihood of 80% or better adherence at the 4-month time point. More years with an MS diagnosis was associated with poorer adherence also at the 4-month time point OR (95%CI) = 0.83 (0.72–0.96).

**Table 1** Logistic regression predicting DMT adherence at follow-up

| | Adherence to DMT (2 months) OR (95% CI) | Adherence to DMT (4 months) OR (95% CI) | Adherence to DMT (6 months) OR (95% CI) |
|---|---|---|---|
| Variable | | | |
| Gender (male) | 34.50 (0.92–1291.0) | 2.77 (0.18–42.43) | 1.25 (0.13–12.12) |
| Race (white) | 0.44 (0.00–43.21) | 0.80 (0.06–11.06) | 0.42 (0.05–3.59) |
| Age | 1.06 (0.92–1.22) | 1.14 (1.01–1.29)* | 0.99 (0.90–1.08) |
| Years with MS | 0.88 (0.73–1.07) | 0.83 (0.72–0.96)* | 0.90 (0.81–1.01) |
| DMT type (interferon) | 0.00 (0.00–0.00) | 0.10 (0.01–1.01) | 0.20 (0.03–1.41) |
| Time on DMT | 1.29 (0.84–1.99) | 1.18 (0.84–1.64) | 1.25 (0.89–1.75) |
| Cognitive status | 0.99 (0.60–1.62) | 1.37 (0.86–2.16) | 0.75 (0.51–1.12) |
| HBM susceptibility | 0.25 (0.04–1.57) | 0.23 (0.04–1.31) | 0.49 (0.14–1.71) |
| HBM severity | 1.40 (0.58–3.37) | 2.29 (1.02–5.13)* | 1.59 (0.89–2.87) |
| HBM benefits | 3.52 (0.80–15.46)† | 4.07 (1.23–13.44)* | 2.49 (1.01–6.17)* |
| HBM barriers | 1.26 (0.22–7.18) | 0.67 (0.18–2.52) | 0.50 (0.16–1.55) |

Note. n = 67 (2 months) 80 (4 months) and 85 (6 months). All variables adjusted for all other variables in the model. Adherent to DMT = 80% adherent or better for each follow-up. Cognitive Status = short D delayed recall score. HBM = health beliefs model. †<0.09; *<0.05.

*P*-value obtained from the Wald statistic.

**Table 2** Hierarchical multiple regression predicting DMT satisfaction at follow-up

| | DMT satisfaction (2 months) | | | DMT satisfaction (4 months) | | | DMT satisfaction (6 months) | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | β | $R^2_{cha}$ | $R^2_{total}$ | β | $R^2_{cha}$ | $R^2_{total}$ | β | $R^2_{cha}$ | $R^2_{total}$ |
| 1) Demographics | | 0.08 | 0.08 | | 0.06 | 0.06 | | 0.09 | 0.09 |
| Gender (male) | −0.24 | | | −0.23 | | | −0.21 | | |
| Race (white) | 0.13 | | | −0.01 | | | 0.20 | | |
| Age | 0.17 | | | 0.10 | | | 0.14 | | |
| 2) Disease/medication | | 0.07 | 0.15 | | 0.03 | 0.09 | | 0.09 | 0.18 |
| Years with MS | 0.15 | | | 0.04 | | | 0.22 | | |
| DMT type (interferon) | −0.03 | | | −0.07 | | | 0.20 | | |
| Time on DMT | 0.12 | | | 0.17 | | | 0.10 | | |
| Cognitive status | −0.18 | | | 0.08 | | | −0.15 | | |
| 3) Health beliefs | | 0.29*** | 0.44*** | | 0.24*** | 0.33*** | | 0.21*** | 0.39*** |
| HBM susceptibility | −0.15 | | | −0.09 | | | 0.07 | | |
| HBM severity | −0.02 | | | −0.13 | | | −0.28* | | |
| HBM benefits | 0.55*** | | | 0.49*** | | | 0.45*** | | |
| HBM barriers | −0.02 | | | −0.01 | | | 0.15 | | |

Note. *n = 67 (2 months) 80 (4 months) and 84 (6 months)*. Each group of variables was entered on a separate step in the order specified in the table. Cognitive status = short D delayed recall score. HBM = health beliefs model. β = standardized regression weights. $R^2_{cha}$ = *r*-squared value for the individual regression step. $R^2_{total}$ = total *r*-squared value for the model at that step. *$P < 0.05$; ***$P < 0.001$.

Of the four individual HBM constructs, susceptibility, illness severity, benefits, and barriers, only perceived benefits of medication use were associated with a greater likelihood of 80% or better adherence at 4 months OR (95%CI) = 4.07 (1.23–13.44) and 6 months, OR (95% CI) = 2.49 (1.01–6.17), also trending towards significance at 2 months OR (95%CI) = 3.52 (0.08–15.46), $P < 0.09$. Greater perceived benefits at baseline were associated with greater likelihood of adherence at follow-up (see Table 1). Severity was also associated with greater adherence at 4 months.

### Predicting Satisfaction with DMT at follow-up

Demographic and disease/medication variables did not predict DMT satisfaction at any follow-up time points. Health beliefs did predict satisfaction significantly, accounting for 29% of the unique variance in this outcome at 2 months, $F_{\text{cha}}(4.55)\ 5\ 7.23$, $P < 0.001$, 24% of the unique variance in this outcome at 4 months, $F_{\text{cha}}(4.68)\ 5\ 6.12$, $P < 0.001$, and 21% of the unique variance in this outcome at 6 months, $F_{\text{cha}}(4.72)\ 5\ 6.40$, $P < 0.001$. Again, of the individual HBM constructs, only perceived benefits of medication use predicted satisfaction at 2 months, β = 0.55, $P < 0.001$; 4 months, β=0.49, $P < 0.001$; and 6 months, β = 0.45, $P < 0.001$; with greater perceived benefits at baseline associated with greater satisfaction at follow-up (see Table 2). Severity also predicted satisfaction at 6 months.

## Discussion

Adherence to DMT in this sample of sustained users was relatively high. Most individuals with MS missed approximately three standardized doses of their medication per month, but 80% or greater adherence was achieved by over 80% of participants at all three follow-up time points. These findings are encouraging when contrasted with medication adherence in general, which is often estimated to be no more than 50% [16–18] and is usually lower in chronic illness [19]. One significant difficulty with all DMTs is that there is no clear indication of the level of adherence necessary to sustain treatment efficacy. This is partly due to the fact that MS-related disability unfolds slowly over time, and the measurement of outcome using global disability rating scales does not allow for more subtle yet possibly clinically-meaningful distinctions in functioning.

Demographic characteristics of individuals with MS, including age, gender and race, did not predict DMT adherence or satisfaction in this study. Results are consistent with findings in the broader adherence literature that often these factors do not have a direct impact on medication behavior [20]. Overall, disease and medication-related variables such as years with MS and cognitive status, as well as time on DMT and DMT type, also were not associated with adherence and satisfaction, a result that is partially supported by the available evidence on DMT adherence [21,22]. Data from one time point suggest that older individuals and those who have been diagnosed with MS longer may be less likely

to adhere to their DMT medication, but evidence for this observation was not consistent across follow-up.

As hypothesized, the Health Beliefs Model did predict both DMT adherence and satisfaction prospectively after controlling for all other variables. Only one of the four HBM constructs, however, was individually significant across multiple time points. The two disease perception variables, MS susceptibility and severity, did not consistently predict our outcomes. There are several reasons why this may be the case. From a clinical perspective, our sample was composed of individuals with MS who had been diagnosed an average of over 11 years, and for whom the risk and extent of disease and disability was both immediate and well known. This situation is substantially different from the most common applications of the HBM in which the potential health consequences of behavior are more distal, such as mammography screening or even adherence to medication for hypertension management. From a psychometric perspective, there are many instances in the literature in which perceived illness severity has been unrelated to health behavior [23], calling into question the predictive validity of this particular HBM construct. The failure of perceived barriers to predict adherence in this study was unexpected. Most participants did endorse at least some barriers to DMT adherence. Again, this result may be due to the characteristics of our study sample. People reported that they had been taking their current DMT an average of almost three and a half years. It is possible that most individuals with MS, though faced with ongoing challenges to adherence, had learned to overcome them by the time of entrance into the study.

The perceived benefits of adherence to DMT emerged as the most important HBM construct in our sample, independently predicting medication adherence and satisfaction over repeated follow-up occasions. Similar results have been found in one prior study examining DMT interruption. In a retrospective chart review, perceived lack of efficacy was identified as the number one reason for stopping or switching medications [24]. Together these findings suggest that a critical element for ongoing adherence to DMT is the belief that medication use will continue to have a positive impact on the MS disease process. Put differently, patients must perceive their continued efforts will be rewarded with better health outcomes.

This study has several limitations worthy of note. The relatively small sample size precluded a meaningful comparison of adherence rates and predictors between each DMT individually. The sample was limited to veterans with MS, who are typically older, more disabled and predominantly male [10], and may not generalize to the larger population of individuals with MS. The adherence variable employed in this study was based upon self-report, which may be subject to bias because of social desirability or errors in recall, particularly for individuals with some cognitive impairment. Nonetheless, to our knowledge, this study represents the first examination of ongoing adherence to DMT, and longitudinal predictors of missed doses among sustained users. As evidence of the long term efficacy of DMT accumulates, brief feedback highlighting health benefits of ongoing use may represent an important opportunity to improve adherence. Such an intervention may have multiple benefits, including the potential to increase motivation and self-efficacy of individuals with MS to become more proactive participants in their care.

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