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## Who is not coming to clinic? A predictive model of excessive missed appointments in persons with multiple sclerosis



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## ABSTRACT

**Background:** Missed appointments can have negative effects on several facets of healthcare, including disruption of services, worse patient health outcomes, and increased costs. The influence of demographic and clinical factors on missed appointments has been studied in a number of chronic conditions, but not yet in multiple sclerosis (MS). Engagement in healthcare services is a particular concern with this population, given the complexity of the condition. Furthermore, excessive missed appointments has emerged as a risk factor for suboptimal adherence to disease modifying therapies (DMTs), prompting further exploration into this issue and whether a tool could be developed to triage possible interventions for persons with MS on DMTs who are missing their appointments. As such, this study aimed to investigate the rate and factors associated with missed appointments among a large national sample of persons with MS and develop a predictive model of excessive missed appointments.

**Methods:** Administrative data from 01/01/2013 to 12/31/2015 were extracted from the VA MS Center of Excellence Data Repository. Variables not related to excessive missed appointments, defined as missing more than 20% of scheduled appointments, in bivariate analyses ( $p > 0.20$ ) were excluded. Remaining baseline co-occurring conditions, demographic, and healthcare utilization variables were entered into a logistic regression model, using a backward elimination criteria of  $p < 0.05$ . Calibration and discrimination of the model were assessed. An initial predictive score was generated based on the value of the variable and its  $\beta$ -value from the final model.

**Results:** The number of missed appointments ranged from 0 to 84 over a two-year period. Over 59% missed at least one appointment, though only 4.28% had excessive missed appointments. Seven variables were retained in the model: adherence to DMTs, age, distance, histories of post-traumatic stress disorder, congestive heart failure, and chronic obstructive pulmonary disease, and emergency visits. Predictive scores ranged from -6.42 to 0.96 ( $M = -2.61$ ,  $SD = 1.15$ ). The final model had good discrimination, calibration, and fit.

**Conclusions:** By using this model and accompanying score, clinicians could have a good chance of predicting individuals who will miss more than 20% of their appointments and triaging interventions.

### 1. Introduction

Missed appointments are a significant concern of the healthcare community due to disrupted medically necessary healthcare services

and their association with worse healthcare outcomes, higher rates of multi-morbidity and mortality, and increased direct and indirect healthcare costs (Hussain-Gambles et al., 2004; Macharia et al., 1992; McQueenie et al., 2019; Nguyen et al., 2011). As a result of missed

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appointments, healthcare providers can have unfilled appointment times, which can result in clinical inefficiency and financial losses (Moore et al., 2001). For instance, Kheirkhah et al. (2015) calculated that during the 2008 fiscal year, the marginal cost of missed appointments using the actual cost per encounter at a Veterans Affairs (VA) medical center in Houston, Texas was \$14.58 million, with an average cost of \$196 per Veteran. While the rates of missed appointments vary greatly between patient populations and types of clinics, it has been reported that rates of missed appointments range from 5% to 55% in primary care clinics in the US (George and Rubin, 2003). In studies that have focused on individuals receiving services through the VA, the mean “no show” rate has ranged from 8.4% to 25.7% (Boos et al., 2016; Kheirkhah et al., 2015). Missed appointments can be a source of frustration for healthcare providers, which can result in the development of negative attitudes toward those patients (Hussain-Gambles et al., 2004).

The influence of demographic and clinical factors on missed appointments has been studied in a number of chronic conditions. For instance, in HIV, younger age, less severe disease course, and aspects of social support were predictive of non-attendance (Bodenlos et al., 2007; Boffill et al., 2011; Catz et al., 1999). In contrast, persons with schizophrenia who have higher levels of psychopathology have been noted to be less likely to keep their appointments (Daniels et al., 2014). Other factors, such as having an established outpatient clinician, issues related to the individual's primary support group, and leaving against medical advice, were predictors of appointment attendance post-psychiatric hospitalization (Compton et al., 2006). Financial factors, such as higher copayments for appointments and medications, have also been shown to be associated with more missed appointments in the hypertension and diabetes populations (Karter et al., 2004; Nwabuo et al., 2014).

Surprisingly, little is known about appointment adherence in multiple sclerosis (MS), an unpredictable and progressive demyelinating central nervous system disorder that affects approximately one million individuals in the United States alone (Wallin et al., 2019). The onset of MS typically occurs in young adults, especially women, and progresses over essentially a normal life span. The disease can result in multiple physical, cognitive, and emotional impairments. These impairments can lead to other conditions, which may complicate care and negatively affect health-related quality of life (Marrie and Hanwell, 2013). These difficulties, particularly fatigue and mobility, may also be barriers to receiving needed healthcare services (Chiu et al., 2017).

In other populations, excessive missed appointments can be an indicator that individuals are not up-to-date with preventative health

services or of a worsening clinical presentation (Mitchell and Selmes, 2007; Nguyen et al., 2011). In MS, persons who have excessive missed appointments have been shown to be less adherent to their disease modifying therapies (DMTs) (Gromisch et al., 2019). As such, missed appointments may be an easy “red flag” for clinicians to detect persons with MS who may not be adherent to their MS-related treatment and are at-risk for a decline in functioning due to disruption of services. DMTs in particular are an important component of MS care given their known efficacy to reduce disease progression and disability (Burks et al., 2017; Freedman, 2006; Tsivgoulis et al., 2015). The association between medication adherence and appointment attendance is not unique to persons with MS, as it is a well-known problem in other populations (Karter et al., 2004; Nwabuo et al., 2014; Ogedegbe et al., 2007).

Given the dearth of information on missed appointments in the MS population and its role as a potential risk factor for suboptimal DMT adherence, this study aimed to investigate the rate of excessive missed appointments among a large national sample of persons with MS. In addition, this study examined the demographic and clinical factors, adherence to DMTs, impairments associated with MS, and other co-occurring conditions that were related to missed appointments and created an initial clinical prediction model and accompanying score to target interventions at those with the most missed appointments.

## 2. Methods

### 2.1. Participants

Data for this study were extracted from a large national sample of individuals in a unified national health care system, the VA MS Center of Excellence Data Repository, which is housed on the Corporate Data Warehouse (CDW) server. It is composed of U.S. Veterans receiving services at any VA medical center. A similar dataset was used in another study (Gromisch et al., 2019); however, that study focused on an explanatory model of DMT adherence, while the current study's aims were to examine factors associated with missed appointments and develop a predictive model. Based on the case-finding starting point (ICD-9 code 340), there were 49,204 Veterans in the Repository at the time of data extraction. That number was narrowed down by excluding Veterans who did not have at least one outpatient visit (not restricted to MS-related visits) in 2013, were deceased in 2015, and/or were not prescribed a DMT (i.e., teriflunomide, natalizumab, interferon beta-1a, interferon beta-1b, dimethyl fumarate, fingolimod, or glatiramer acetate) (Fig. 1). The individuals who did not meet the three inclusion

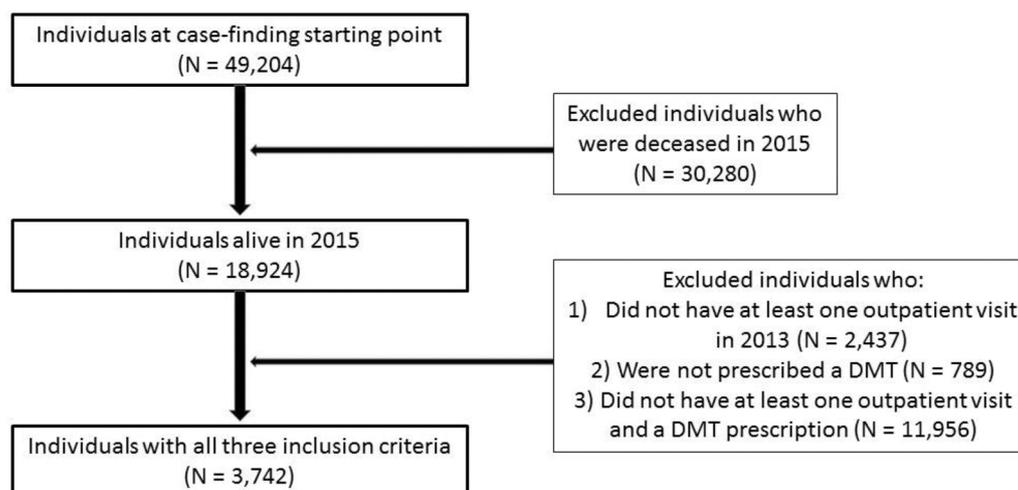


Fig. 1. Flowchart of participant selection from the VA MS Center of Excellence Data Repository. DMT: disease modifying therapy; VA: Veterans Affairs.

criteria were older ( $t(4952.20) = 35.28, p < 0.001$ ) and had a higher percentage of men ( $\chi^2(1) = 60.94, p < 0.001$ ). Similar inclusion criteria have been previously used with a high probability of successfully identifying individuals with a definite diagnosis of MS (Culpepper et al., 2006).

## 2.2. Procedures

Data extraction was conducted on a 24-month period between 01/01/2013 and 12/31/2015. Appointment adherence was calculated by dividing the number of missed appointments to any clinic by the total number of scheduled appointments over the 24-month period. Overall appointment attendance, rather than adherence to MS-specific appointments, was examined to understand whether missed appointments as a whole were a problem in this population. Furthermore, given that the VA is an integrated medical setting, information derived from this study could be useful in care coordination of patients (e.g., letting a nurse case manager know that someone is less likely to follow up on appointments referred by the MS clinic as well as those referred to the MS clinic). Cancelled appointments were not included in the definition of missed appointments, as this has been previously noted to be a different behavior from "no showing" to an appointment (Karter et al., 2004; Ogedegbe et al., 2007). Participants were categorized as having excessive missed appointments if they missed more than 20% of their appointments, based on the previously used definition of less than 80% for suboptimal adherence to medication (Osterberg and Blaschke, 2005; Siegel et al., 2008; Turner et al., 2007, 2009).

The demographics included age, gender, marital status, and service connection (a VA determined benefit for Veterans for an illness or injury that was sustained or worsened from their active military service). Participants' distance from their closest VA was calculated using the centroids of their residential zip codes (Turner et al., 2013). A proxy variable for participants' disease duration was calculated using the first date of a diagnostic code for MS in the CDW, ranging as far back as 1998, and the first date of the current data extraction.

Pharmacy records were used to determine adherence to DMTs, which was defined in greater detail in another study (Gromisch et al., 2019). Briefly, suboptimal adherence was characterized as refilling prescribed DMTs less than 80% of the time over five time intervals (i.e., 3 months, 6 months, 12 months, 18 months, and 24 months). Treatment switches were noted when participants began a different DMT within 90 days of the last refill of their initial DMT (Reynolds et al., 2010). Only DMT refills were examined for the purposes of defining medication adherence. Although participants could potentially be on other medications for symptom management or a co-occurring condition, DMTs are the primary treatment for MS that have several benefits for persons with MS (Burks et al., 2017; Freedman, 2006; Halpern et al., 2011; Tsivgoulis et al., 2015). Furthermore, they are often expensive (Hartung et al., 2015) and can result in significant side effects (National Multiple Sclerosis Society, 2018), which can negatively influence adherence.

The presence of co-occurring medical and psychiatric conditions were determined by corresponding ICD-9 codes from prior to 01/01/2013, which were reviewed and confirmed by all authors. If participants were issued one or more assistive devices (e.g., cane, walker, wheelchair, and electric wheelchair) per their records, they were noted as needing ambulatory assistance. This disability variable was then dichotomized (i.e., wheelchair versus no wheelchair). Healthcare utilization was noted based on CPT codes for emergency room (ER), observational, and inpatient services during the 24-month period. This study was approved by the Institutional Review Boards (IRB) at VA Puget Sound Health Care System and VA Connecticut Healthcare System.

## 2.3. Statistical analyses

Descriptive statistics were run to characterize the sample. Differences between suboptimal appointment adherence groups were determined using chi-squares for categorical variables and *t*-tests for continuous variables. Variables that appeared to not be related to suboptimal appointment attendance ( $p > 0.20$ ) were excluded from the model. The remaining baseline comorbidities, demographic, and healthcare utilization variables were entered into the logistic regression model, using a backward elimination criteria of  $p < .05$  in order to find the optimal fit for a prediction model (Sainani, 2014). A backward elimination process was selected over forward entry as this method is less likely to remove variables implicated in suppression effects (Field, 2009). Linearity, independence of errors, and multicollinearity were assessed through the interaction between continuous predictors and their log transformation, Durbin-Watson test, and variance inflation factor (VIF), respectively. Calibration of the model was assessed using the Hosmer and Lemeshow test, and its discrimination was evaluated with the optimism-corrected c-statistic using bootstrap analysis ( $n = 2000$ ).

An initial predictive score was generated based on the value of the variable and its  $\beta$ -value from the final model. A receiver-operating-characteristic (ROC) analysis was run to determine the sensitivity and specificity of the scores, which was used to calculate the likelihood ratios (i.e., sensitivity/1-specificity). The optimal cut-off score for detecting suboptimal appointment attendance was established based on the Youden index (Youden, 1950). A calibration curve was also generated for the final model. The analyses were conducted using SAS Enterprise 7.1, with the exception of the optimism-corrected c-statistic and calibration curve which were created using R 3.5.1

## 3. Results

A total of 3742 participants were included in the sample (Table 1). The number of missed appointments ranged from 0 to 84 across the 24-month period, with an average of 2.76 (SD = 5.52). Over 59% ( $n = 2214$ ) missed at least one appointment during this time, with the mean "no-show" rate over the 24-month period being 4.74% (range: 0–60%). Only 4.28% of the sample ( $n = 160$ ) had excessive missed appointments. These individuals were younger, lived closer to the VA, had been in the VA for MS care for fewer years, and were less likely to be married or issued a wheelchair. They had lower rates of hypertension and hyperlipidemia, but higher rates of mood, personality, psychotic (e.g., schizophrenic disorders), post-traumatic stress (PTSD), other anxiety (e.g., generalized anxiety), tobacco, alcohol, and other substance use disorders. Compared to participants who missed 20% or fewer of their appointments, they were nearly two times more likely to have suboptimal DMT adherence.

A total of 22 variables were entered into the logistic regression based on the bivariate analyses with the dichotomized missed appointments variable as the outcome: DMT adherence, age, marital status, distance from the VA, wheelchair issuance, disease duration proxy, usage of ER and observational services, hyperlipidemia, hypertension, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), diabetes, and thyroid, mood, personality, psychotic, PTSD, anxiety, tobacco, alcohol, and other substance use disorders. Seven of these variables were retained in the model (Table 2). All assumptions for the logistic regression were met and less than 3% of the standardized residuals had an absolute value of 2. The model was a significant fit of the data ( $\chi^2(7) = 164.84, p < 0.001$ ). It had an optimism-corrected c-statistic of 0.78 (95% CI: 0.75, 0.82), indicating good discrimination (Fig. 2), and a non-significant Hosmer and Lemeshow test ( $\chi^2(8) = 6.73, p = 0.567$ ), indicating good calibration.

An initial predictive score was calculated by multiplying the  $\beta$ -value

**Table 1**  
Demographics of overall sample and by appointment adherence groups.

	Total sample (n = 3742)	> 20% no show rate (n = 160)	≤ 20% no show rate (n = 3582)	p value
<i>Demographics</i>				
Age (years)	55.67 ± 11.54 (23–90)	48.69 ± 12.23 (23–76)	55.98 ± 11.41 (23–90)	< 0.001
Years in the VA for MS care	7.57 ± 4.38 (0–14.31)	6.44 ± 4.43 (0–13.26)	7.63 ± 4.38 (0–14.31)	0.001
Gender (male)	78.11%	75.63%	78.22%	0.437
Married	59.42%	45.86%	60.02%	< 0.001
Service connected	71.03%	71.25%	71.02%	0.950
Issued a wheelchair	33.08%	24.38%	33.47%	0.017
Distance from the closest VA (miles)	47.76 ± 46.95 (0.36–374.30)	36.45 ± 32.64 (0.81–126.90)	48.25 ± 46.70 (0.36–374.30)	< 0.001
<i>Co-occurring conditions</i>				
Congestive heart failure	3.05%	5.00%	2.96%	0.142
Coronary artery disease/peripheral artery disease	21.08%	18.75%	21.19%	0.459
Hypertension	54.57%	46.25%	54.94%	0.031
Hyperlipidemia	65.29%	49.38%	66.00%	< 0.001
Diabetes	17.72%	13.75%	17.90%	0.179
Thyroid disease	13.82%	9.38%	14.01%	0.096
Chronic obstructive Pulmonary disease	21.94%	26.88%	21.72%	0.123
Malignancies	14.00%	15.00%	13.96%	0.710
Acid peptic disease	8.07%	10.00%	7.98%	0.360
Crohn's disease	1.44%	1.25%	1.45%	0.834
Renal disease	3.79%	4.38%	3.77%	0.695
Liver failure	2.86%	2.50%	2.88%	0.780
Human immunodeficiency virus	0.37%	0.63%	0.36%	0.595
Glaucoma	19.88%	18.13%	19.96%	0.569
Epilepsy	4.73%	5.00%	4.72%	0.869
Traumatic brain injury	6.49%	8.75%	6.39%	0.237
Mood disorders	60.07%	70.00%	59.63%	0.009
Personality disorders	4.81%	10.63%	4.55%	< 0.001
Psychotic disorders	5.75%	10.00%	5.56%	0.018
Anxiety disorders	33.86%	44.38%	33.39%	0.004
Post-traumatic stress disorder	17.48%	30.00%	16.92%	< 0.001
Alcohol-related disorders	12.08%	19.38%	11.75%	0.004
Drug-related disorders	9.06%	17.50%	8.68%	< 0.001
Tobacco use disorders	34.18%	43.75%	33.75%	0.009
Pain disorders	62.77%	59.38%	62.93%	0.363
Cognitive disorders	18.12%	20.00%	18.03%	0.528
Sleep disorders	35.84%	33.13%	35.96%	0.465
Treatment adherence				
< 80% DMT adherence	44.12%	78.13%	42.60%	< 0.001
Number of treatment switches	0.20 ± 0.47 (0–5)	0.17 ± 0.42 (0–2)	0.20 ± 0.47 (0–5)	0.471
<i>Healthcare utilization</i>				
At least one inpatient visit	9.38%	9.38%	9.38%	0.998
At least one ER visit	31.83%	26.25%	32.08%	0.122
At least one observational visit	1.68%	3.13%	1.62%	0.148

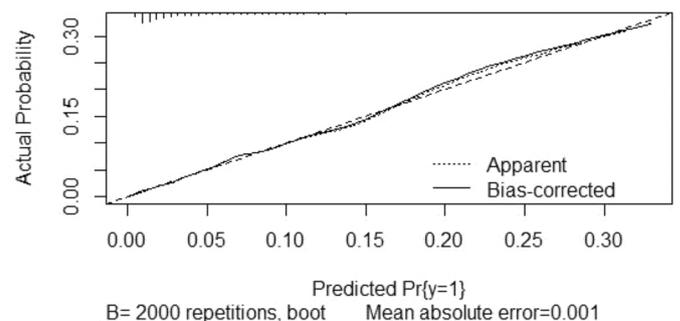
DMT: disease modifying therapy; ER: emergency room; VA: Veterans Affairs medical center.

**Table 2**  
Retained predictor variables for suboptimal appointment attendance.

Variable	β-value	Odds ratio (95% CI)	p value
DMT adherence (1 = < 80%)	1.53	4.61 (3.13, 6.99)	< 0.001
CHF (1 = Yes)	0.88	2.41 (1.02, 5.02)	0.028
COPD (1 = Yes)	0.46	1.58 (1.06, 2.31)	0.021
Age (continuous)	-0.05	0.95 (0.94, 0.97)	< 0.001
Distance from VA (continuous)	-0.01	0.99 (0.99, 1.00)	< 0.001
PTSD (1 = Yes)	0.50	1.65 (1.13, 2.39)	0.009
ER Use (1 = At least one visit)	-0.74	0.48 (0.32, 0.69)	< 0.001

CHF: Congestive heart failure; COPD: Chronic obstructive pulmonary disease; DMT: disease modifying therapy; ER: emergency room; PTSD: Post-traumatic stress disorder; VA: Veterans Affairs medical center.

by the value of the variable, which were either dichotomous (DMT adherence, histories of a PTSD, CHF, and COPD, and ER use) or continuous (age and distance from the VA), and summing all six together: (DMT adherence\*1.53) + (history of CHF\*0.88) + (history of COPD\*0.46) + (age\*-0.05) + (distance from the VA\*-0.01) + (history of PTSD\*0.50) + (ER use\*-0.74). The scores for the sample



**Fig. 2.** Calibration curve for appointment attendance predictive model.

ranged from -6.42 to 0.96 ( $M = -2.61$ ,  $SD = 1.15$ ). These scores were plotted against their corresponding likelihood ratio (i.e., how much more likely an individual is to have excessive missed appointments, which was calculated by dividing sensitivity by 1-specificity for each score) (Fig. 3). For instance, a 65-year-old individual who lives 11 miles from the VA, takes his DMT at least 80% of the time, has no

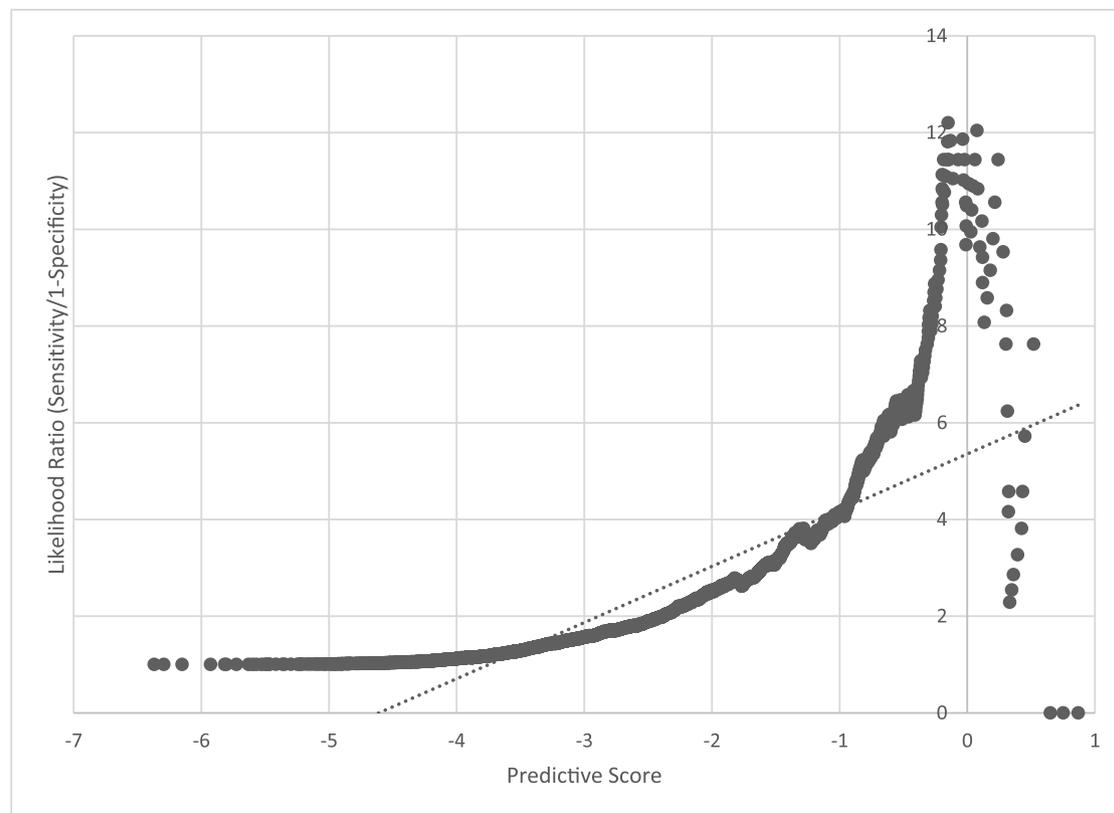


Fig. 3. Scatterplot of likelihood ratio (sensitivity/1-specificity) by predictive score.

histories of CHF, COPD, or PTSD, and has had at least one ER visit would have a score of  $-4.10$ , which has a corresponding likelihood ratio of  $1.09$ . A 72-year-old, DMT adherent, individual who lives 50 miles away with none of the other risk or protective factors would also have the same score. On the other hand, an individual with a score of  $-0.39$  (i.e., a 42-year-old who lives 28 miles from the VA with suboptimal DMT adherence and a history of COPD) would be nearly six and a half times more likely to have excessive missed appointments. As such, participants with fewer risks and/or more protective factors had lower likelihoods of missing more than 20% of their appointments.

If clinicians wish to use a cut-off score for determining who is most likely to have suboptimal appointment attendance, the optimal score was  $-2.03$ , which yielded a sensitivity of 75% and a specificity of 70% and a likelihood ratio of 2.50. An example of a profile with this score would be a 59-year-old individual who lives 37 miles away from the VA with suboptimal DMT adherence, a history of PTSD, and at least one ER visit.

#### 4. Discussion

This study is the first to examine the rate of missed appointments in the MS population, using a large national sample of persons with MS who use the VA. In addition, factors associated with excessive missed appointments were explored and used to develop a clinical prediction model and score. More than 59% of the sample had at least one missed appointment, but only 4.28% met the criterion for excessive missed appointments, meaning they missed more than 20% of their scheduled appointments. Of the 22 predictors entered into the logistic regression, seven were retained in the model: four risk (histories of PTSD, CHF, and COPD, and suboptimal DMT adherence) and three protective factors (older age, further distance from the VA, and ER use). Adherence to DMTs had the highest  $\beta$ -value (1.53), highlighting the important connection between medical appointments and medication management. The resulting prediction score from the model showed that as

individuals had a greater number of risk factors and/or fewer protective factors, their likelihood of having excessive missed appointments increased. If using a cut-off score to predict adherence,  $-2.03$  and greater demonstrated good to fair sensitivity (75%). However, it has a moderate false positive rate—30%—meaning that the model predicts poor appointment attendance in those who have excessive missed appointments well, but it has a tendency to predict more problems with appointment attendance than truly exist. While clinicians will need to keep this caveat in mind when using this prediction tool, it should be noted that in screening a population of limited size for a health behavior, the benefits of identifying those in need to additional assistance is high and the risks associated with misclassification, particularly false positives, are modest.

Having at least one missed appointment was prevalent within this sample, though the average “no show” rate was only 4.74%, with 4.28% of the sample having excessive missed appointments. This number is lower than previous numbers for primary care and VA clinics (Boos et al., 2016; George and Rubin, 2003; Kheirkhah et al., 2015). That being said, none of those studies investigated persons with MS specifically. While some of these predictors, such as age and presence of a mental health diagnosis, have been previously been associated with appointment attendance in different populations (Boos et al., 2016; Dantas et al., 2018; Moore et al., 2001), others are in contrast to prior studies, which may be due to differences in the patient population and/or setting. For instance, both CHF and COPD have been associated with fewer missed appointments among Veterans who did not have MS (Daggy et al., 2010). One explanation for the difference may be that persons with MS who also have CHF and COPD struggle to keep their appointments as they have the additional burden of multiple chronic conditions, such as additional or worsening symptoms that may keep them from attending an appointment or difficulty managing a more complex treatment regimen.

Three separate studies found that either greater distance was predictive of missed appointment (Daggy et al., 2010) or distance from

their clinics was not significantly related to missed appointments (Boos et al., 2016; Moore et al., 2001), while the current study showed that individuals living closer to the VA were more likely to miss their appointments. As mobility and accessibility are potential barriers for persons with MS (Chiu et al., 2017), individuals living further away may invest more time and energy into planning their appointments, which might increase their likelihood of attendance. In addition, if a VA is located in an area with fewer socioeconomic and psychosocial resources, this may influence individuals who live closer's ability to attend their appointments. Another difference is that individuals in a community clinic who had excessive missed appointments were more likely to use emergency services (Nguyen et al., 2011), which is in contrast to this sample. While the direction of this relationship is surprising, given that ER usage was a risk factor for suboptimal DMT adherence (Gromisch et al., 2019), one possibility is that individuals who sought emergency services received follow-up reminders to attend their outpatient appointments (Ritchie et al., 2000). Besides further investigating these phenomena, it will be important to replicate this study to determine whether there are similar rates of excessive missed appointments and if these factors are predictive of appointment attendance among persons with MS who receive care in different settings (e.g., community hospital), as well as non-veterans with MS.

The findings from the current and accompanying study (Gromisch et al., 2019) suggest a strong relationship between appointment attendance and DMT adherence among persons with MS, though there are likely different underlying phenomenon contributing to each of these health-related behaviors. While the patient-provider relationship likely affects multiple health-related behaviors, its influence might be strongest in terms of attending appointments, which requires face-to-face interactions. For instance, persons with MS have reported that feeling like their providers are not listening to their needs is a barrier to receiving healthcare service (Chiu et al., 2017). Research in other populations have suggested additional interpersonal factors, such as perceived reasons for non-attendance and resulting attitudes, that may be influencing appointment attendance. In one study of primary care providers, those surveyed indicated that missed appointments were a problem in several of their practices, with many blaming patients due to their forgetfulness or that they "couldn't be bothered" to attend the appointment (Hussain-Gambles et al., 2004). In the subsequent focus groups, the providers noted that while patients' embarrassment might contribute to why they do not cancel an appointment instead of "no showing," many stated that this behavior was due to a lack of responsibility or ignorance. Furthermore, providers endorsed developing negative attitudes towards these patients.

However, a corresponding study with patients (Neal et al., 2005) showed that the largest reason they missed their appointments was because of forgetfulness, with only one individual noted that "I couldn't be bothered." A separate qualitative study involving patients noted that anticipatory fear and feeling disrespected contributed to missed appointments (Lacy et al., 2004). Attachment styles may also play a role. Ciechanowski et al. (2006) found that among persons with diabetes, missed primary care visits were more likely in individuals with dismissing or fearful attachment styles. The authors recommended different approaches for reducing missed appointments in these individuals, such as offering same day appointments to patients and educating providers on attachment theory so their approaches can be tailored towards patients' needs. Another approach may be through fostering self-management skills, such as forming collaborative partnerships with healthcare providers (Lorig and Holman, 2003), which may assist with potential interpersonal issues. Furthermore, these programs can use techniques such as motivational interviewing and cognitive behavioral strategies (Rae-Grant et al., 2011; Shevil and Finlayson, 2009), which can help promote positive behavioral changes. As such, follow-up studies should consider investigating the interpersonal contributors to missed appointments in the MS population, which may help further explain the directional relationship between

appointment attendance and DMT adherence and inform strategies to keep these at-risk patients engaged in treatment.

Besides behavioral approaches, a potential technology-based intervention is the use of appointment reminders. Through a systematic review of general hospital-based appointments, Hasvold and Wootton (2011) found a 39% reduction in the rate of missed appointments when manual reminders were used (e.g., a phone call made by a medical staff member) versus a 29% reduction with automated reminder (e.g., short message service; SMS). They did not find a strong effect on the time between when the reminder was sent and the appointment; however, all reminders were sent within a week. Another meta-analysis and systematic review, which only focused on SMS reminders, found that the likelihood of appointment attendance increased by 50% when compared to no appointment reminders (Guy et al., 2012). That being said, there are several factors that may negatively influence reminders' effectiveness, such as the accuracy of patients' records, the reminder not being received, and barriers to understanding the reminder (e.g., cognitive impairment) (McLean et al., 2016). As a recent study showed that 86.1% of persons with MS use a smartphone, tablet, or both (Marrie et al., 2019), using technology to improve adherence has potential. Since missing appointments can potentially have a negative impact on health status, efforts to optimize attendance among persons with MS need to be investigated further.

There are limitations to consider when interpreting the results of this study. While internal validation was done with this prediction model via bootstrapping, it will be important to conduct further external validation in order for it to be ready to implement in a clinical setting. Future research may investigate whether the rate of missed appointments among persons with MS varies between clinics and confirm this model for MS-specific appointments. As individuals who were not on any DMTs for the duration of the study were excluded, this may have resulted in an underestimation of the rate of missed appointments. Furthermore, these findings may not be applicable to persons with MS who are not on a DMT. Although the causal relationship between DMT adherence and appointment attendance is unclear, it is possible that these individuals could have worse appointment attendance because they might not need medication refills as regularly. Other factors that could theoretically be associated with appointment attendance in the MS population that have been studied in other populations, such as time until appointment, financial costs, beliefs regarding treatment, race/ethnicity, socioeconomic status, and condition-related knowledge (Karter et al., 2004; Mitchell and Selmes, 2007; Nwabuo et al., 2014), were not included and may be considered in future studies. Finally, given that this model was tested and validated using Veterans with MS who use the VA, who as a whole had a greater percentage of men and high prevalence of medical and psychiatric co-occurring conditions, these findings may not generalize to the civilian MS or non-VA Veteran populations.

## 5. Conclusions

Missed appointments can have negative effects on both healthcare outcomes and costs in general (Karter et al., 2004; Kheirkhah et al., 2015; Nwabuo et al., 2014; Ogedegbe et al., 2007), and often individuals who need additional help with self-management are not attending them (Osterberg and Blaschke, 2005). Overall, while more than half of this large national sample of persons with MS missed at least one appointment during a two-year period, only 4.28% were considered as having excessive missed appointments. Missing appointments and adherence to DMTs were highly associated, although it still remains unclear what the causal relationship is between these two health-related behaviors. This model and accompanying score represent a first step towards developing a tool that will help clinicians better predict who is likely to miss more than 20% of their appointments, thus allowing them to develop and triage interventions that may improve their appointment attendance and adherence to MS-related treatments.

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## Declaration of Competing Interest

None.

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## References

- Bodenlos, J.S., Grothe, K.B., Whitehead, D., Konkle-Parker, D.J., Jones, G.N., Brantley, P.J., 2007. Attitudes toward health care providers and appointment attendance in HIV/AIDS patients. *J. Assoc. Nurses AIDS Care* 18 (3), 65–73.
- Bofill, L., Waldrop-Valverde, D., Metsch, L., Pereyra, M., Kolber, M.A., 2011. Demographic and psychosocial factors associated with appointment attendance among HIV-positive outpatients. *AIDS Care* 23 (10), 1219–1225.
- Boos, E.M., Bittner, M.J., Kramer, M.R., 2016. A profile of patients who fail to keep appointments in a Veterans Affairs primary care clinic. *WMJ* 115, 185–190.
- Burks, J., Marshall, T.S., Ye, X., 2017. Adherence to disease-modifying therapies and its impact on relapse, health resource utilization, and costs among patients with multiple sclerosis. *CEOR* 9, 251.
- Catz, S.L., McClure, J., Jones, G., Brantley, P., 1999. Predictors of outpatient medical appointment attendance among persons with HIV. *AIDS Care* 11 (3), 361–373.
- Chiu, C., Bishop, M., Pionke, J., Strauser, D., Santens, R.L., 2017. Barriers to the accessibility and continuity of health-care services in people with multiple sclerosis: a literature review. *Int J MS Care* 19 (6), 313–321.
- Ciechanowski, P., Russo, J., Katon, W., Simon, G., Ludman, E., Von Korff, M., Young, B., Lin, E., 2006. Where is the patient? The association of psychosocial factors and missed primary care appointments in patients with diabetes. *Gen Hosp Psychiatry* 28 (1), 9–17.
- Compton, M.T., Rudisch, B.E., Craw, J., Thompson, T., Owens, D.A., 2006. Predictors of missed first appointments at community mental health centers after psychiatric hospitalization. *Psychiatr. Serv.* 57 (4), 531–537.
- Culpepper, W., Ehrmantrout, M., Wallin, M., Flannery, K., Bradham, D., 2006. Identification of the VHA MS surveillance registry. The problem of case finding from administrative databases. *J Rehabil Res Dev* 43, 17–24.
- Daggy, J., Lawley, M., Willis, D., Thayer, D., Suelzer, C., DeLaurentis, P.-C., Turkcan, A., Chakraborty, S., Sands, L., 2010. Using no-show modeling to improve clinic performance. *Health Informatics J* 16 (4), 246–259.
- Daniels, K., Loganathan, M., Wilson, R., Kasckow, J., 2014. Appointment attendance in patients with schizophrenia. *Clin. Pract.* 11 (4), 467.
- Dantas, L.F., Fleck, J.L., Oliveira, F.L.C., Hamacher, S., 2018. No-shows in appointment scheduling—a systematic literature review. *Health Policy (New York)* 122 (4), 412–421.
- Field, A., 2009. *Discovering Statistics Using SPSS*, 3rd edition. Sage Publications Ltd, London, UK.
- Freedman, M.S., 2006. Disease-modifying drugs for multiple sclerosis: current and future aspects. *Expert Opin Pharmacother* 7 (sup1), S1–S9.
- George, A., Rubin, G., 2003. Non-attendance in general practice: a systematic review and its implications for access to primary health care. *Fam Pract* 20 (2), 178–184.
- Gromisch, E.S., Turner, A.P., Leipertz, S.L., Beauvais, J., Haselkorn, J.K., 2019. Risk factors for suboptimal medication adherence: development of an explanatory model for disease modifying therapy use. *Arch Phys Med Rehabil.*
- Guy, R., Hocking, J., Wand, H., Stott, S., Ali, H., Kaldor, J., 2012. How effective are short message service reminders at increasing clinic attendance? A meta-analysis and systematic review. *Health Serv Res* 47 (2), 614–632.
- Halpern, R., Agarwal, S., Borton, L., Oneacre, K., Lopez-Bresnahan, M.V., 2011. Adherence and persistence among multiple sclerosis patients after one immunomodulatory therapy failure: retrospective claims analysis. *Adv Ther* 28 (9), 761.
- Hartung, D.M., Bourdette, D.N., Ahmed, S.M., Whitham, R.H., 2015. The cost of multiple sclerosis drugs in the US and the pharmaceutical industry: too big to fail? *Neurology* 84 (21), 2185–2192.
- Hasvold, P.E., Wootton, R., 2011. Use of telephone and SMS reminders to improve attendance at hospital appointments: a systematic review. *J Telemed Telecare* 17 (7), 358–364.
- Hussain-Gambles, M., Neal, R.D., Dempsey, O., Lawlor, D.A., Hodgson, J., 2004. Missed appointments in primary care: questionnaire and focus group study of health professionals. *Br J Gen Pract* 54 (499), 108–113.
- Karter, A.J., Parker, M.M., Moffet, H.H., Ahmed, A.T., Ferrara, A., Liu, J.Y., Selby, J.V., 2004. Missed appointments and poor glycemic control: an opportunity to identify high-risk diabetic patients. *Med Care* 110–115.
- Kheirkhah, P., Feng, Q., Travis, L.M., Tavakoli-Tabasi, S., Sharafkhaneh, A., 2015. Prevalence, predictors and economic consequences of no-shows. *BMC Health Serv Res* 16 (1), 13.
- Lacy, N.L., Paulman, A., Reuter, M.D., Lovejoy, B., 2004. Why we don't come: patient perceptions on no-shows. *Ann. Family Med.* 2 (6), 541–545.
- Lorig, K.R., Holman, H.R., 2003. Self-management education: history, definition, outcomes, and mechanisms. *Ann. Behav. Med.* 26 (1), 1–7.
- Macharia, W.M., Leon, G., Rowe, B.H., Stephenson, B.J., Haynes, R.B., 1992. An overview of interventions to improve compliance with appointment keeping for medical services. *JAMA* 267 (13), 1813–1817.
- Marrie, R.A., Hanwell, H., 2013. General health issues in multiple sclerosis: comorbidities, secondary conditions, and health behaviors. *Continuum (Minneapolis)* 19 (4, Multiple Sclerosis), 1046–1057.
- Marrie, R.A., Leung, S., Tyry, T., Cutter, G.R., Fox, R., Salter, A., 2019. Use of eHealth and mHealth technology by persons with multiple sclerosis. *Mult Scler Relat Disord* 27, 13–19.
- McLean, S.M., Booth, A., Gee, M., Salway, S., Cobb, M., Bhanbhro, S., Nancarrow, S.A., 2016. Appointment reminder systems are effective but not optimal: results of a systematic review and evidence synthesis employing realist principles. *Patient Prefer Adherence* 10, 479.
- McQueenie, R., Ellis, D.A., McConnachie, A., Wilson, P., Williamson, A.E., 2019. Morbidity, mortality and missed appointments in healthcare: a national retrospective data linkage study. *BMC Med* 17 (1), 2.
- Mitchell, A.J., Selmes, T., 2007. Why don't patients attend their appointments? Maintaining engagement with psychiatric services. *Adv. Psychiatr. Treat.* 13 (6), 423–434.
- Moore, C.G., Wilson-Witherspoon, P., Probst, J.C., 2001. Time and money: effects of no-shows at a family practice residency clinic. *Family Med.* 33 (7), 522–527.
- National Multiple Sclerosis Society, 2018. *Disease-modifying therapies for MS*. <https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-The-MS-Disease-Modifying-Medications.pdf>. (Accessed September 17 2018.).
- Neal, R.D., Hussain-Gambles, M., Allgar, V.L., Lawlor, D.A., Dempsey, O., 2005. Reasons for and consequences of missed appointments in general practice in the UK: questionnaire survey and prospective review of medical records. *BMC Fam Pract* 6 (1), 47.
- Nguyen, D.L., DeJesus, R.S., Wieland, M.L., 2011. Missed appointments in resident continuity clinic: patient characteristics and health care outcomes. *J Grad Med Educ* 3 (3), 350–355.
- Nwabuo, C.C., Dy, S.M., Weeks, K., Young, J.H., 2014. Factors associated with appointment non-adherence among African-Americans with severe, poorly controlled hypertension. *PLoS ONE* 9 (8), e103090.
- Ogedegbe, G., Schoenthaler, A., Fernandez, S., 2007. Appointment-keeping behavior is not related to medication adherence in hypertensive African-Americans. *J Gen Intern Med* 22 (8), 1176–1179.
- Osterberg, L., Blaschke, T., 2005. Adherence to medication. *New Engl. J. Med.* 353 (5), 487–497.
- Rae-Grant, A.D., Turner, A.P., Sloan, A., Miller, D., Hunziker, J., Haselkorn, J.K., 2011. Self-management in neurological disorders: systematic review of the literature and potential interventions in multiple sclerosis care. *J Rehabil Res Dev* 48 (9), 1087.
- Reynolds, M.W., Stephen, R., Seaman, C., Rajagopalan, K., 2010. Persistence and adherence to disease modifying drugs among patients with multiple sclerosis. *Curr Med Res Opin* 26 (3), 663–674.
- Ritchie, P., Jenkins, M., Cameron, P., 2000. A telephone call reminder to improve outpatient attendance in patients referred from the emergency department: a randomised controlled trial. *Aust N Z J Med* 30 (5), 585–592.
- Sainani, K.L., 2014. Explanatory versus predictive modeling. *PM&R* 6 (9), 841–844.
- Shevil, E., Finlayson, M., 2009. Process evaluation of a self-management cognitive program for persons with multiple sclerosis. *Patient Educ Couns* 76 (1), 77–83.
- Siegel, S.D., Turner, A.P., Haselkorn, J.K., 2008. Adherence to disease-modifying therapies in multiple sclerosis: does caregiver social support matter? *Rehabil Psychol* 53 (1), 73.
- Tsivgoulis, G., Katsanos, A.H., Grigoriadis, N., Hadjigeorgiou, G.M., Heliopoulos, I., Papathanasopoulos, P., Kiliadreas, C., Voumvourakis, K., Dardiotis, E., 2015. The effect of disease modifying therapies on disease progression in patients with relapsing-remitting multiple sclerosis: a systematic review and meta-analysis. *PLoS ONE* 10 (12), e0144538.
- Turner, A., Kivlahan, D., Sloan, A., Haselkorn, J., 2007. Predicting ongoing adherence to disease modifying therapies in multiple sclerosis: utility of the health beliefs model. *MSJ* 13 (9), 1146–1152.
- Turner, A.P., Chapko, M.K., Yanez, D., Leipertz, S.L., Sloan, A.P., Whitham, R.H., Haselkorn, J.K., 2013. Access to multiple sclerosis specialty care. *PM&R* 5 (12), 1044–1050.
- Turner, A.P., Williams, R.M., Sloan, A.P., Haselkorn, J.K., 2009. Injection anxiety remains a long-term barrier to medication adherence in multiple sclerosis. *Rehabil Psychol* 54 (1), 116.
- Wallin, M.T., Culpepper, W.J., Campbell, J.D., Nelson, L.M., Langer-Gould, A., Marrie, R.A., Cutter, G.R., Kaye, W.E., Wagner, L., Tremlett, H., 2019. The prevalence of MS in the United States: a population-based estimate using health claims data. *Neurology*. <https://doi.org/10.1212/WNL.0000000000007035>.
- Youden, W.J., 1950. Index for rating diagnostic tests. *Cancer* 3 (1), 32–35.