

# Patient-reported financial barriers to adherence to treatment in neurology

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**Objective:** Many effective medical therapies are available for treating neurological diseases, but these therapies tend to be expensive and adherence is critical to their effectiveness. We used patient-reported data to examine the frequency and determinants of financial barriers to medication adherence among individuals treated for neurological disorders.

**Patients and methods:** Patients completed cross-sectional surveys on iPads as part of routine outpatient care in a neurology clinic. Survey responses from a 3-month period were collected and merged with administrative sources of demographic and clinical information (eg, insurance type). We explored the association between patient characteristics and patient-reported failure to refill prescription medication due to cost in the previous 12 months, termed here as “nonadherence”.

**Results:** The population studied comprised 6075 adults who were presented between July and September 2015 for outpatient neurology appointments. The mean age of participants was 56 (standard deviation: 18) years, and 1613 (54%) were females. The patients who participated in the surveys (2992, 49%) were comparable to nonparticipants with respect to gender and ethnicity but more often identified English as their preferred language (94% vs 6%,  $p<0.01$ ). Among respondents, 9.8% ( $n=265$ ) reported nonadherence that varied by condition. These patients were more frequently Hispanic (16.7% vs 9.8% white,  $p=0.01$ ), living alone (13.9% vs 8.9% cohabitating,  $p<0.01$ ), and preferred a language other than English (15.3% vs 9.4%,  $p=0.02$ ).

**Conclusion:** Overall, the magnitude of financial barriers to medication adherence appears to vary across neurological conditions and demographic characteristics.

**Keywords:** outcomes, adherence, cost

## Introduction

There is a growing armamentarium of effective medical therapies to treat neurological diseases.<sup>1,2</sup> National guidelines have discussed ten US Food and Drug Administration (FDA)-approved disease-modifying therapies for multiple sclerosis, >20 FDA-approved antiepileptic drugs for seizure prophylaxis, and 23 drugs involved in stroke prevention, including novel oral anticoagulants.<sup>3-5</sup> Most of these therapies are expensive and adherence is critical to their effectiveness.<sup>6-8</sup>

Medication adherence depends on many factors, including affordable access to drugs, which varies by drug type and insurance-benefit design. For instance, Medicare beneficiaries obtain outpatient drug coverage through the Part D program, which is administered by private insurance plans, i.e., Part D drug plans. The formulary protections of these plans apply to formulary inclusion, but not tier placement. The resulting differences in out-of-pocket payments can be challenging for beneficiaries with limited

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incomes or impaired cognition.<sup>9</sup> In addition, since adherence depends mainly on patient reporting and perception, it has been demonstrated that many patients who claim to have been adherent to their medications are in fact not.<sup>10,11</sup> According to a recent study on therapeutic drug monitoring in consecutive emergency hospital admissions for seizures, >40% of nonadherent patients claimed to have been adherent when further asked about medication failure.<sup>12</sup>

Medication nonadherence has been shown to seriously hurt health outcomes in neurology, and hence efforts to understand the causes and solutions to this problem have become increasingly important. Some studies have shown a moderate association between drug choice, adherence, and satisfaction with treatment.<sup>7,13</sup> Previous studies of medication nonadherence in neurology have been limited to population-wide databases and reliable claims-based algorithms.<sup>14–24</sup> These large-scale approaches to the evaluation of medication adherence using retrospective electronic health records (EHRs) abstraction or claims data have missed critical information and fallen short in representing the real-world complexity.<sup>25</sup> In an effort to capture more accurate, specific, and informative data on medication nonadherence, systematic collection of patient-reported outcomes offers great promise.<sup>26,27</sup>

The term “patient-reported outcomes” refers to data directly collected from patients such as self-administered surveys and other attempts to quantify patients’ behavior and their subjective experience of health. Patient-reported data have been shown to correlate with and augment more typical clinical measurements, proving useful in the assessment of treatment outcomes and determinants of health.<sup>28–31</sup>

This study examined the frequency and determinants of financial barriers to medication adherence among individuals treated for neurological disorders using patient-reported data.

## Patients and methods

### Participants

This study was a retrospective review of data collected as part of a quality improvement project implemented in Neurology Ambulatory clinical practices that began in July 2015 and continues to date. Since July 2015, all ambulatory neurology patients in the outpatient waiting room aged 18+ years have been offered an iPad survey upon arrival at the office, except for unaccompanied non-English speakers, whose eligibility was determined by front desk staff based on the patient’s observed inability to understand very simple survey directions. The front desk staff had received standard institutional training to determine patients’ ability to read and sign check-in-related

documents (eg, insurance-driven pre-office forms). All patients were given the opportunity to verbally opt out of the survey and were reminded that the quality of their care would not be adversely affected by survey completion. Patients who arrived late for appointments or had other essential tasks to complete prior to the physician visit were at times unable to complete the survey prior to the end of the office visit. Although longitudinal data were captured for patients with several visits during this period, only the first visit was included in the analysis.<sup>7,32,33</sup>

### Procedures and measurements

This study combines information from the survey merged by deterministic linkage using the medical record number to administrative and clinical data gathered using a Research Patient Data Registry (RPDR) query tool.

### Survey

In ambulatory neurology clinics, patients were checked in by front desk staff before being seen by the provider. After determining patient appropriateness, the front desk staff handed patients an iPad tablet pre-loaded with the survey questions. Patients completed the survey in the waiting room. Before beginning, they were prompted to read and agree to an informed consent disclaimer, which they signed on the Apple iPad2 (Apple, CA, USA) screen. A report summarizing the patients’ survey responses became available in the EHR immediately upon completion, and providers were encouraged to review this information with the patient.

The survey had four parts – an introduction, demographic questions, and the medication adherence question, “How often in the past 12 months did you decide not to fill or refill your prescription because the medicines cost too much?” with the answers “often”, “sometimes”, “never”, and “prefer not to answer”. After this question, the survey included an additional questionnaire to measure global health function, which is not the focus of this article and is detailed in the Supplementary materials.

### RPDR query tool

We anticipated that not all patients would be able to participate in the survey. To determine the primary predictors of participation and examine the potential for selection bias, we gathered additional demographic information using the Partners Healthcare Clinical data registry for all arriving patients (both participating and nonparticipating in the survey) seen in the Ambulatory Neurology clinics during the study time frame. The RPDR is a clinical data registry that aggregates data from sources throughout the Partners

Healthcare System (PHS), including the medical record, reports, claims, and administrative systems. Queried variables included age, gender, preferred language, insurance status, ethnicity, marital status, and clinic type (eg, general neurology vs subspecialty area).

Results of the RPDR query identified patients scheduled for an ambulatory neurology clinical visit from July 2015 to September 2015. A member of the study staff reviewed the RPDR query output to exclude ineligible patients or encounters. Eligible encounters were the patients >18 years of age seen at the neurology outpatient clinic (main campus only), who had a first visit or were established patients who came for a follow-up visit within the study time frame (subsequent visits were excluded). There were 6075 eligible visits.

## Statistical analysis

We defined cost-related medication nonadherence as an answer of “often” or “sometimes” to the question “How often in the past 12 months did you decide not to fill or refill a prescription because the medicines cost too much?”.

We performed univariate comparisons of the baseline characteristics of the adherence groups using two-group two-sided *t*-tests for continuous variables and chi-square tests for categorical variables. In multivariable analysis, we utilized logistic regression models to assess the associations between sociodemographic and clinical characteristics associated with the report of cost-related medication nonadherence. The independent variables were selected based on prior knowledge and examination of the distribution of the univariate analysis. Conservatively, no step-wise approach was used.

To address the potential for selection bias in our respondents, we performed univariate analysis of covariates associated with survey participation (participants vs nonparticipants, including age, gender, ethnicity, preferred language, insurance type, marital status, and clinic type).

We used SAS Studio®, version 9.4 for statistical analysis.

This study was conducted under a protocol approved by the Partners Healthcare Institutional Review Board.

## Results

A total of 2992 out of 6075 patients participated in the survey and 2716 fully completed the survey questions, yielding a participation rate of 49% and a completion rate of 45% (Figure S1). The mean age of participants was 56 (SD: 18) years and 1613 (54%) were females. Respondents were comparable to nonrespondents with respect to gender and ethnicity. Survey responders more often identified English as their preferred language (90.6%,  $p=0.02$ ; Table S1).

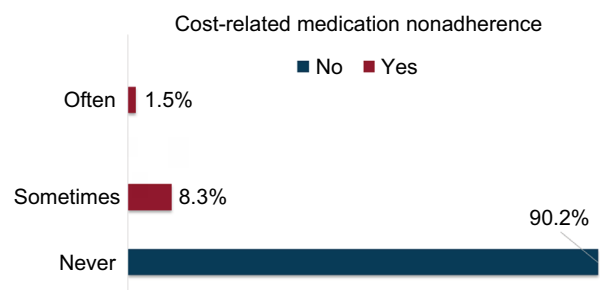
Among the participants, 9.8% ( $n=265$ ) of patients reported cost-related medication nonadherence. More specifically, nonadherent patients “often” (40 or 15.1%) or “sometimes” (225 or 84.9%) failed to fill or refill a prescription (Figure 1).

Table 1 summarizes the distribution of sociodemographic indicators among nonadherent vs adherent patients. Patients who reported cost-related nonadherence were younger (mean age:  $53\pm 16$  years vs  $56\pm 18$  years,  $p<0.01$ ), more often Hispanic (16.7% vs 9.8%,  $p<0.01$ ), had a native language that was not English (22% vs 9.4%,  $p=0.02$ ), and were not currently partnered (single, separated, divorced, or widowed vs married; 11.9% vs 8.5%,  $p<0.01$ ).

In multivariable analysis, care in subspecialty clinics, compared to general neurology clinic as the reference, was associated with higher rates of patient-reported nonadherence. Stroke clinical patients had twice the odds ratio (OR) of nonadherence (OR = 2.09, 95% CI: 1.05–4.16), and memory disorder clinical patients had more than threefold increase (OR = 3.73, 95% CI: 1.31–10.59; Figure S2). A sensitivity analysis using both marital status and cohabitation in a multivariable logistic regression did not significantly impact the reported results.

## Discussion

We have presented a cross-sectional study of cost-related medication nonadherence to use in a patient-reported survey conducted in a large cohort of neurology patients. Our results suggest that the prevalence of financial barriers to medication adherence is modest (<10%). These findings were consistent with those presented in the study of Campbell et al,<sup>34</sup> who found that trouble affording medications was the fourth leading reason for medication nonadherence among elderly patients.



**Figure 1** Proportion of survey respondents who endorsed cost-related medication nonadherence by category.

**Notes:** 9.8% ( $n=265$ ) patients reported cost-related medication nonadherence (red bars) and 90% ( $n=2451$ ) patients did not (blue bar). Approximately 1% ( $n=40/2716$ ) of patients said “often” and 8% ( $n=225/2715$ ) said “sometimes” they would fail to refill or fill a prescription.

**Table 1** Demographic and clinical characteristics of patients with vs without cost-related nonadherence to medications

	Cost-related non-adherence		p-Value
	No	Yes	
Number of patients, N=2716 (%)	N=2451 (90)	N=265 (10)	
Mean age in years (SD)	56 (18.33)	53 (16)	0.001
Gender (%), N=2715			0.02
Male	1143 (91.7)	104 (8.34)	
Preferred language (%)			0.02
English	2329 (90.6)	243 (9.4)	
Ethnicity (%), N=1687			0.01
Non-Hispanic	1386 (90.2)	151 (9.8)	
Marital status (%), N=2603			0.004
Single, separated, divorced, widowed	943 (88.1)	128 (11.9)	
Married	1401 (91.5)	131 (8.5)	
Cohabitation (%)			0.004
Single	372 (86.1)	60 (13.9)	
Shared	2022 (91.1)	197 (8.9)	
Prefer not to answer	57 (87.7)	8 (12.3)	
Education (%)			0.08
Grade school	91 (90.1)	10 (9.9)	
High school or GED	853 (89.8)	97 (10.2)	
Bachelor's degree	739 (89.7)	85 (10.3)	
Master's degree or higher	667 (92.4)	55 (7.6)	
Prefer not to answer	101 (84.9)	18 (15.1)	
Insurance status (%)			0.38
Public insurance	833 (91.0)	83 (9.0)	
Private insurance	1618 (89.9)	182 (10.1)	
Employment (%), N=2715			0.11
Employed full time	801 (89.7)	92 (10.3)	
Employed part time	264 (90.4)	28 (9.6)	
Retired	916 (92.1)	79 (7.9)	
Unemployed	373 (88.0)	51 (12.0)	
Prefer not to answer	97 (87.4)	14 (12.6)	
Survey respondent (%), N=2715			0.01
Patient	2065 (89.7)	238 (10.3)	
Proxy	386 (93.7)	26 (6.3)	
Clinic type (%)			<0.0001
Ataxia	30 (93.8)	2 (6.2)	
Epilepsy	163 (94.2)	10 (5.8)	
General neurology	1060 (88.6)	137 (11.4)	
Memory disorders	225 (96.6)	8 (3.4)	
Movement disorders	395 (92.5)	32 (7.5)	
Motor neuron disorders	49 (89.1)	6 (10.9)	
Neurobehavioral disorders	130 (85.0)	23 (15.0)	
Sleep disorders	166 (83.4)	33 (16.6)	
Stroke	233 (94.3)	14 (5.7)	

**Notes:** The comparison between the group of patients that reported cost-related medication non-adherence (Yes) and the group of patients that did not (No). We used two-sided t-tests to calculate p-values to compare the mean values of patient age between the groups. We used the chi-squared test of independence to calculate the p-values to test whether the categorical variables were associated with increased rates of adherence.

**Abbreviation:** GED, General Education Diploma.

However, the comparison of our cost-related non-adherence rates with the current literature is limited by the general lack of congruence in the way adherence is measured and reported. Most other medication adherence studies have either evaluated patients in controlled settings with small sample sizes or used claims data to measure patient prescription refills. In comparison, our survey describes the patient report of the burden of financial barriers to medication adherence.<sup>35,36</sup>

In addition, to reduce potential for both recall and interviewer bias, we collected data from patients immediately before their clinical visits. We believe that collecting data from patients immediately before their clinical visits yielded more accurate results because the patients were already prompted to think about their health problems and medications in use. Also, having to complete the survey in the waiting room allowed the patients to have ready access to staff members and clarify the meaning of any question they found hard to interpret. In comparison, this would not be possible in a paper-based form sent out after clinic.<sup>37-41</sup> Of note, our participation and completion rates (49% and 45%, respectively) were similar to the rates obtained in previous similar studies.<sup>42-46</sup>

A second interesting finding was that patients seen at the memory disorders clinic, which includes primarily patients with Alzheimer's disease and related dementias who were almost always accompanied by a care giver, were especially vulnerable to financial barriers to medication adherence, even after adjusting for pertinent socioeconomic factors. This finding is particularly concerning because these patients tend to be older, and medication adherence by older patients is lower compared to younger patients due to increased side effects as well.<sup>47-49</sup> These older- and cognitively impaired adults are clinically vulnerable due to concurrent medical illnesses and drug interactions.<sup>47-49</sup> Studies have shown that the number and types of co-morbidities, such as depression, are predictors of cost-related nonadherence.<sup>36,37</sup> This is especially striking since most of these patients are Medicare eligible and so would not be expected to have large out-of-pocket expenses for many tests, procedures, or hospitalizations.

Observational retrospective studies using claims data (prescription fills) have suggested that drug-benefit design and tier strategies (i.e., prescription drug coverage) may also affect adherence to treatment.<sup>50</sup> Adding complexity to this problem, McWilliams et al<sup>19</sup> showed that Medicare beneficiaries with low cognitive function were less responsive to the generosity of Medicare Advantage benefits in their decisions (i.e., multiple and complex insurance plan benefit choices negatively impacted seniors with impaired decision making). Our study findings build upon the existing literature

and highlight the complex interaction of multiple socioeconomic and clinical factors in cost-related nonadherence.<sup>35</sup>

In this study, patients from socially disadvantaged backgrounds, such as Hispanics and non-English speakers, also appear to be more likely to report having financial barriers to medication adherence.<sup>51</sup> Our study supports other groups that have presented data on how people of lower socioeconomic status and ethnic minorities report higher rates of cost-related medication nonadherence.<sup>37,47,52–57</sup>

While many studies focused on examining the adherence to a specific medication, we asked a broad question about any medication, which allowed for a cross-clinic comparison.<sup>58</sup> In the case of patients with Alzheimer's disease in our memory disorders clinic, our study findings remain consistent with studies about the recent rising costs of neurology prescription drugs, which ultimately indicates more out-of-pocket spending for this population.<sup>5</sup> For example, an analysis of Medicare Part D data revealed that neurologists comprised only 1.2% of prescribing providers but expenditures with neurology-prescribed medications were the third highest of all specialties. Medications for multiple sclerosis, epilepsy, and Alzheimer's disease and related dementias were the major drivers of the exceptional costs (\$5 billion in 2013).<sup>5</sup>

Finally, this study is aligned with the existing literature that suggests that patient reporting and the linking of multiple sources of data have been shown to improve the accuracy of research findings.<sup>59,60</sup>

This study had many important limitations. Most notably, the trade-off in asking a broad medication adherence question and absence of data from chart abstraction is that we may not have captured the specific medication that is the principal reason for the financial barrier in each clinical scenario. For instance, aspirin is an important medication prescribed for patients with stroke. This medication is relatively of low cost and is classified as Tier 1, designating medications that are largely covered, according to the most common insurance policies. For patients with stroke, we believe that the culprit might be the related medications often prescribed in patients with stroke, such as anticoagulants and medications for hypertension, hyperlipidemia, and pain management.<sup>58,61</sup>

In addition, other broad wordings that serve as a limitation of our study were such as the categorical scale with frequency options (eg, "often", "sometimes", and "never"). The meanings of these frequency words can vary among individuals. Perhaps, an open-ended question could yield a more specific measurement (eg, "How many days in a month would you miss a medication?"). However, the likelihood that a patient would be able to provide an accurate numerical value with respect to adherence over the past 12 months would be low.

Therefore, we considered categorical scales easier to respond and opted to use simple frequency words.

A second major limitation was that we were unable to distinguish between patients who declined to participate and patients who were not approached, due to the aforementioned exclusion criteria and administrative errors. The absence of these data prevents further characterization of potentially confounding participant vs nonparticipant differences. In addition, we excluded unaccompanied non-English speakers and unaccompanied patients with severe cognitive impairment. Both the criteria were determined after a patient-handed survey based on self-reported or observed inability to follow basic survey directions. Also, 275 patients (9%) started the survey but did not complete the medication adherence question. The reasons for leaving the survey incomplete include the early call from the treating physician (eg, when there is <10 minutes of waiting time from check-in to the encounter with the physician), fatigue (eg, patients get tired and give up), and distractions (eg, patients answer phone calls and leave the survey aside). Another limitation that exists with the study population is that the research team did not consider other impairments, such as visual impairment, as one of the exclusion criteria due to the fact that patients were likely to visit with a designated proxy. Because the patients were self-answering the survey in the context of a busy neurology clinic, we were unable to track specific reasons for survey exclusion and incompleteness.

This study has limited generalizability to nonacademic medical centers as is common to many similar studies.<sup>11,22</sup> However, it is hoped that the findings are more generalizable due to the high participation and completion rates. We did not identify patients who were nonadherent because of nonfinancial reasons, and therefore the comparison arm of our analysis includes some patients who were nonadherent due to other reasons.

Next, this study did not prospectively capture adherence following the prescription of a specific medication, making causal association in our study impossible. The clinical value of our study was demonstrated in the secondary analysis. As outlined earlier, this study made note of a potential association between patients being seen in certain clinics that may prescribe more expensive medications, such as those for patients with Alzheimer's disease and related dementias, suggesting that they may have a higher cost-sharing burden.

Finally, residual measured and unmeasured confounding may exist, such as the cost per drug tier in each patient's insurance coverage formulary. We would expect that the patients with cost-related nonadherence would have been most often prescribed medications in the highest cost tier, as described in previous studies.<sup>62</sup> However, we were not able to examine if nonadherence was related to drug tier and co-pay as we did

not have reliable access to each patient's pharmacy benefit to determine these interactions.

Despite these limitations, this study offers opportunities to improve outcomes in neurology patients through medication adherence and drive health policy in neurology. There are many possible future studies and solutions to the issues we have outlined. 1) Patients could be encouraged to reduce their medication costs by requesting generic medications or using mail order pharmacies. 2) More assistance for patients in navigating health insurance and therapeutic choices might reduce nonadherence to medication regimens among patients with neurological conditions. 3) Value-based drug pricing (varying payments for medications based on outcomes or magnitude of clinical benefits) may be another means of engaging patients, physicians, and payers toward improving adherence and outcomes.

Our study also sought to improve the discussions between patients and treating physicians about prices of medications. We present the medication adherence question to the patients before their visit in order to prompt the patients to discuss any prescription filling problems with the treating physician during the encounter. However, patients still have difficulty starting this conversation and may only realize the amount of co-pay when they go to pick up their refill after the clinical visit. We encourage quality improvement strategies, such as using electronic notifications of answers to the cost-related nonadherence question, in order to encourage the physicians to incite these discussions about financial issues. Future studies should also integrate patient-reported information into insurance-benefit designs in order to measure the actual ratio of adherence to out-of-pocket spending, per patient and by treatment period.

## Conclusion

This study suggests that while the overall level of poor adherence due to costs is limited, cost-related barriers to medication adherence appear to be concentrated among the most cognitively- and socioeconomically vulnerable patients. Multiple strategies are needed to prospectively identify these vulnerable patients and to alter prescribing practices to enhance affordability and thereby long-term efficacy.

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## Author contributions

LMVRM conceptualized and designed the study. LMVRM, ELS, and VMJ performed data collection. LMVRM and VMJ performed the database management and statistical analysis. LMVRM, JH, and VMJ drafted the original manuscript. LMVRM, JH, MPS, DBH, and LHS significantly reviewed and revised the manuscript. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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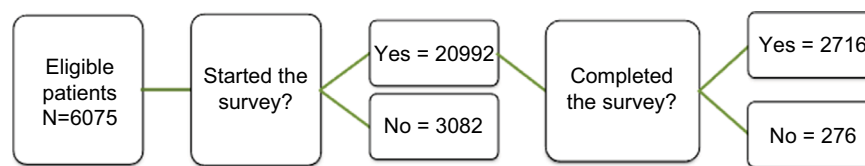


## Supplementary materials

### Additional survey details

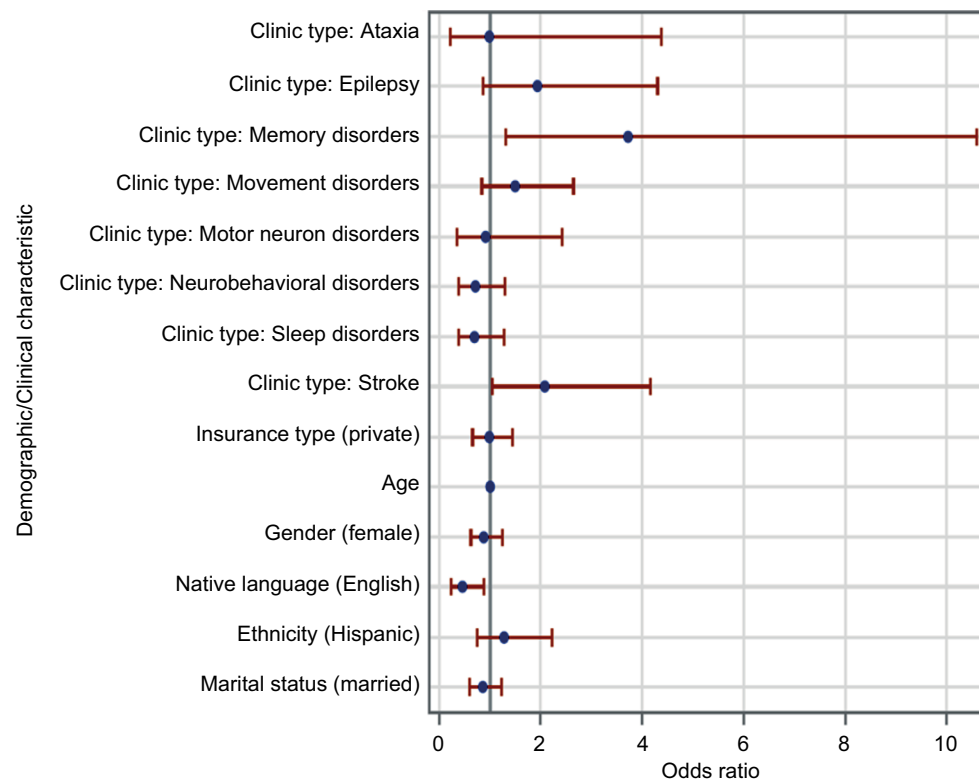
The survey was administered on an Apple iPad2 (Apple, Cupertino, CA, USA), with a plastic cover to allow for easy grip and identification in the busy outpatient setting of a major academic neurology clinic. The survey questions were built using the Tonic for Health platform (Tonic Solutions Inc., CA, USA), a survey software tool that allowed intuitive survey construction, and integration with the Apple iPad iOS (version 8 and beyond) and the hospital's electronic health record (EHR). All data were stored in a repository compliant with the hospital's privacy policies.

In addition to the measures described in the main manuscript, we also collected the NIH PROMIS-10. The NIH PROMIS-10 is a short form that measures a patient's perceived physical and mental health. The PROMIS-10 has been validated in populations with different neurological diseases (eg, stroke, epilepsy, and Parkinson's disease) as well as without neurological diseases and attempt to measure patient-reported physical and mental function.<sup>1</sup>



**Figure S1** Survey attrition.

**Note:** It demonstrates the attrition from 6075 to 2716 patients.



**Figure S2** Demographic and clinical predictors of cost-related medication nonadherence.

**Notes:** It graphically represents the logistic regression using demographic and clinical characteristics in the model to predict the odds of cost-related medication nonadherence. Red line represent 95% CIs. The patients whose preferred language was English (OR: 0.46 [0.25–0.87]), the patients seen at the memory disorders clinic (OR: 3.72 [1.3–10.6]), and the patients seen at the stroke clinic (OR: 2.1 [1.0–4.2]) had higher odds for reporting cost-related medication nonadherence.

**Abbreviations:** CI, confidence interval; OR, odds ratio.

**Table S1** Characteristics of the eligible population by survey participation

	Survey participation		p-Value
	No, N (Column %)	Yes, N (Column %)	
Total, n=6075	3082	2992	
Mean age (years ± SD)	57±19	56±18	0.0260
Gender			0.6676
Male, n=2781	1403 (45.52)	1387 (45.48)	
Female, n=3292	1679 (54.48)	1613 (53.93)	
Ethnicity			0.1357
Non-Hispanic, n=3354	1677 (88.92)	1677 (90.40)	
Hispanic, n=387	209 (11.08)	178 (9.60)	
Preferred language			<0.0001
English, n=5624	2805 (90.98)	2819 (94.22)	
Non-English, n=451	278 (9.02)	173 (5.78)	
Insurance			<0.0001
Medicare, Medicaid, and MassHealth, n=2391	1369 (44.40)	1022 (34.16)	
Private, n=3684	1714 (55.60)	1970 (65.84)	
Marital status			0.0069
Single, n=2510	1307 (45.70)	1203 (42.15)	
Married, partnered, n=3204	1553 (54.30)	1651 (57.85)	
Clinic type			<0.0001
Ataxia, n=117	82 (2.66)	35 (1.17)	
Epilepsy, n=520	327 (10.61)	193 (6.45)	
General neurology, n=2489	1168 (37.89)	1321 (44.15)	
Memory, n=473	222 (7.20)	251 (8.39)	
Movement, n=1057	584 (18.94)	473 (15.81)	
Neuromuscular, n=291	232 (7.53)	59 (1.97)	
Neurobehavioral, n=376	202 (6.55)	174 (5.82)	
Sleep, n=224	0 (0)	224 (7.49)	
Stroke, n=528	266 (8.63)	262 (8.76)	

**Notes:** Two-sided t-tests were used to calculate p-values to compare the mean values of patient age between the groups. The chi-squared test of independence was used to calculate the p-values to test whether the categorical variables were associated with increased rates of adherence.

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