Impact of insurance status on migraine care in the United States
A population-based study

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ABSTRACT
Objective: To determine whether insurance status is associated with differential outpatient treatment of migraine in the United States.

Methods: We analyzed 11 years of data from the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (1997-2007), which survey patient visits to doctors' offices, hospital outpatient departments, and emergency departments (EDs) in the United States. We used logistic regression to determine whether insurance status was associated with the prescription of standard migraine therapy, defined as 1) a triptan or dihydroergotamine and 2) a prophylactic agent.

Results: We identified 6,814 individual patient visits for migraine, representing 68.6 million visits nationally. After controlling for age, gender, race/ethnicity, geographic location, and year, migraineurs with no insurance or Medicaid were less likely than the privately insured to receive abortive therapy [odds ratio (OR) for failure to receive medication 2.0 [95% confidence interval (CI) 1.3, 3.0] and 1.6 [95% CI 1.1, 2.3]] and prophylactic therapy [OR 2.0 [95% CI 1.3, 2.9] and 1.5 [95% CI 1.0, 2.1]]. Adding site of care to the regression model suggested that one mechanism for this discrepancy was the reliance of the uninsured on EDs for migraine care, a site where standard migraine care is often omitted [OR for failure to receive abortive and prophylactic medication in the ED relative to physicians' offices 4.8 [95% CI 3.8, 6.3] and 8.7 [95% CI 6.4, 11.7]].

Conclusions: The uninsured, and those with Medicaid, receive substandard therapy for migraine, at least in part because they receive more care in emergency departments and less in physicians' offices. Neurology® 2010;74:1178-1183

GLOSSARY
AAN = American Academy of Neurology; CI = confidence interval; DHE = dihydroergotamine; ED = emergency department; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; NAMCS = National Ambulatory Medical Care Survey; NCHS = National Center for Health Statistics; NHAMCS = National Hospital Ambulatory Medical Care Survey; NSAID = nonsteroidal anti-inflammatory drug; OPD = outpatient department; OR = odds ratio.

Migraine headache is common, affecting 18% of American women and 6% of men. The condition disables over half its sufferers, reducing both quality of life and productivity. A large survey of migraineurs found that 91% reported functional impairment from migraine; thus, most migraine is moderate to severe. Migraineurs lose 4 to 6 work days each year due to headache and cost American employers as much as $17 billion annually. Optimal migraine treatment is important for both patients and society.

The evidence-based practice parameter of the American Academy of Neurology (AAN) recommends a triptan or dihydroergotamine (DHE) as first-line therapy for moderate or severe migraine, based on their superiority to nonsteroidal anti-inflammatory drugs (NSAIDs), and older migraine-specific medications such as ergotamine/caffeine. Migraineurs prefer treatment that includes a triptan over an analgesic alone. The AAN recommends prophylactic therapy for patients whose migraines are frequent, severe, incompletely responsive to abortive

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therapy, or disabling. Prophylaxis has been shown to reduce the use of abortive medications, as well as physician and ED visits, making it a cost-effective element of migraine care.

Standard migraine therapy for most migraine, which is moderate to severe, thus consists of a triptan or DHE as abortive therapy plus a prophylactic medication for those patients with frequent or incompletely responsive migraines. We hypothesize that one of the factors influencing whether a patient receives standard migraine therapy in the ambulatory setting is health insurance. In this study, we examine a nationally representative sample of adult visits for migraine to ambulatory settings in the United States to assess the effect of insurance status on the receipt of standard migraine therapy.

**METHODS** Data source. We analyzed the National Hospital Ambulatory Medical Care Survey (NHAMCS) and the National Ambulatory Medical Care Survey (NAMCS). The National Center for Health Statistics (NCHS) conducts both NHAMCS and NAMCS: NHAMCS assesses ambulatory visits to hospital outpatient departments (OPD) and EDs, whereas NAMCS assesses ambulatory visits to office-based physicians. Both surveys use virtually identical questions and are designed to be nationally representative; jointly, they provide a comprehensive view of ambulatory care visits in the United States.

The surveys’ methodologies have been described elsewhere. In brief, the NHAMCS uses a 4-stage probability design to select geographic regions, hospitals within each region, clinics and emergency service areas within the hospitals, and patient visits within the service areas. Federal hospitals are excluded. Field representatives of the US Census Bureau train hospital staff to complete survey forms for visits during a randomly assigned, 4-week reporting period. Information is recorded on age, race/ethnicity, gender, expected sources of payment, 1 primary and 2 other diagnoses, medical professionals seen during the visit, and medications given or prescribed during the visit. NHAMCS also records hospital characteristics including ownership (government; voluntary, nonprofit or proprietary), region, and urban (metropolitan statistical area) vs nonurban (non-metropolitan statistical area) location. Unless it is hospital policy to ask patients for race/ethnicity, hospital personnel record race/ethnicity based on observations. Race is categorized as white, black/African American, Asian, Native Hawaiian/other Pacific Islander, American Indian, or Alaska Native. Hispanic ethnicity is coded separately. NHAMCS categorizes anticipated source of payment as private insurance, Medicare, Medicaid, worker’s compensation, self-pay, or no charge, as well as other, unknown, or blanket (which we combined into a single category). NHAMCS codes diagnoses based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

NAMCS is a survey of visits to physicians who are office-based, principally engaged in patient care, non-federally employed, and not practicing anesthesiology, pathology, or radiology. NAMCS employs a 3-stage design that selects geographic regions, physician practices in each region, and patient visits within each practice. During a randomly assigned, 1-week reporting period, each selected physician or office staff records data from patient visits. NAMCS collects patient data similar to that collected in NHAMCS, but also includes physician specialty.

**Study population**. We analyzed 11 years of NAMCS and NHAMCS data, from 1997–2007. Injectable sumatriptan became available in the United States in 1991 and oral sumatriptan in 1995; we began our data analysis a couple of years after this to ensure that knowledge and use of triptans would be widespread. We included all adult patient visits coded for either common or classic migraine, with or without intractability (ICD-9-CM codes 456.00, 456.01, 456.10, 456.11, 456.91, and 436.90); however, we excluded other forms and variants of migraine, as these diagnostic categories include conditions such as complicated and barbituric migraine in which a triptan or DHE might be contraindicated. The diagnosis of migraine was coded by the treating physician. We analyzed race/ethnicity in 4 mutually exclusive categories: non-Hispanic white, non-Hispanic black, Hispanic of any race, and all others.

The NHAMCS and NAMCS databases contain medication codes for drugs administered or prescribed at each visit. We considered patients to have received standard abortive therapy if they were given or prescribed any of the abortive medications listed in table 1. In a sensitivity analysis, we included the 2 drugs most commonly associated with visits for migraine, butalbital/ aspirin/caffeine and acetaminophen/dichloralphenazone/isometheptene, in our list of abortive medications.

For this study, we analyzed prophylactic medications recommended in the AAN’s latest practice guidelines on migraine, although we excluded NSAIDs because they are prescribed for many more nonmigraine indications than other prophylactic agents and are often given in EDs as an abortive treatment for migraine, confounding our assessment of their use for prophylaxis. We considered patients to have received prophylactic therapy if they were given or prescribed any of the prophylactic medications listed in table 1 or a medication with the generic code for “beta blocker.”

**Standard protocol approvals, registrations, and patient consents.** We obtained institutional review board approval for this study.

**Statistical analysis.** We performed a multivariate analysis on data from all visits associated with a diagnostic code for migraine, controlling for age, gender, race/ethnicity, region, urban vs rural location, and year of visit in order to analyze the effect of insurance status on the likelihood of receiving abortive and prophylactic migraine therapy. We then assessed the model for interaction between site of care and insurance, to see if stratification by site of care was indicated. Because the interaction term was nonsignificant, we proceeded to analyze the effect of site of care by adding this variable to the multivariate model. We also tested whether later year of visit predicted receipt of abortive or prophylactic therapy. All analyses account for the complex survey design. We used weights provided by the NCHS to yield national estimates. We performed these analyses using SAS version 9.0 (Cary, NC).

**RESULTS** A total of 6,814 ambulatory visits for migraine were made to EDs, OPDs, and physicians’ offices over the 11-year study period, representing 68.6 million (95% confidence interval [CI] 62.4 mil-
Table 3 shows the results of our multivariate analysis of data from all visits associated with a diagnostic code for migraine, controlling for insurance status, age, gender, race, region, urban vs rural location, and year of visit. In these models, both lack of insurance and Medicaid were associated with failure to receive standard migraine treatment. The uninsured and those with Medicaid were less likely than the privately insured to receive abortive treatment with a triptan or DHE (OR for failure to receive either medication 2.0 [95% CI 1.3, 3.0] and 1.6 [95% CI 1.1, 2.3]). The uninsured and those with Medicaid were also less likely than those with private insurance to receive prophylactic therapy (OR for failure to receive medication 2.0 [95% CI 1.3, 2.9] and 1.5 [95% CI 1.0, 2.1]).

Including site of care in the model reduced the association between insurance status and likelihood of receiving standard abortive and prophylactic medication, suggesting that the nationwide disparities in migraine care are driven, at least in part, by inadequate access to office-based care for uninsured and Medicaid patients. Those seen in the ED were much less likely than those seen in non-ED ambulatory settings to receive standard abortive treatment and standard prophylactic treatment (OR for failure to receive medication 4.8 [95% CI 3.6, 6.3] and 8.7 [95% CI 6.4, 11.7]). Nonetheless, for the uninsured, the trend toward substandard treatment remained substantial for both abortive therapy (OR 1.6 [95% CI 1.0, 2.5]) and prophylaxis (OR 1.5 [95% CI 1.0, 2.3]).

Age greater than 65 years was also associated with failure to receive these abortive therapies, perhaps because contraindications to triptans are common in the elderly, while Hispanics and those in the Midwest were less likely to receive prophylactic therapy. Addition of butalbital/acetaminophen/dichloralphenazone to the list of abortive medications did not change the relationship between uninsurance or Medicaid and the likelihood of failing to receive abortive treatment (OR for failure to receive medication 2.0 [95% CI 1.3, 2.9] and 1.4 [95% CI 1.0, 2.2]).

**DISCUSSION** In this study, we demonstrate that among those who seek care for migraine, the uninsured are less likely than the privately insured to receive standard migraine therapy. When standard therapy is defined as receiving a triptan or DHE and receiving a prophylactic medication. Our results are based on a nationally representative sample and are generalizable to the entire United States. Approximately 15% of the United States population, 45.7 million individuals, is currently uninsured. Given a

<table>
<thead>
<tr>
<th>Abortive medications</th>
<th>Prophylactic medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>Metoprolol</td>
</tr>
<tr>
<td>Naratriptan</td>
<td>Atenolol</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>Nadolol</td>
</tr>
<tr>
<td>Frostantriptan</td>
<td>Timolol</td>
</tr>
<tr>
<td>Eleptriptan</td>
<td>Verapamil</td>
</tr>
<tr>
<td>DHE 45 dihydroergotamine</td>
<td>Nimodipine</td>
</tr>
<tr>
<td>Valproate/divalproex sodium</td>
<td>Topiramate</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Amoxicilin</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Protriptyline</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Desipramine</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Oxcarbazepine</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Fluvaxamine</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Phenerazine</td>
</tr>
<tr>
<td>Riboflavin vitamin B2</td>
<td>Feverfew</td>
</tr>
<tr>
<td>Migrein</td>
<td>Cyproheptadine</td>
</tr>
<tr>
<td>Methysergide</td>
<td></td>
</tr>
</tbody>
</table>
forms of insurance is not the same as access to adequate care. In exploring mechanisms for these disparities, we found that site of care was critical, although the odds of substandard treatment for uninsured migraineurs remained somewhat elevated for both abortive and prophylactic therapy, suggesting that site of care is not the only explanation for the disparity in treatment. The uninsured are more likely than the privately insured to receive substandard treatment in large part because they are more likely to receive care for migraine in EDs rather than physician offices. Unfortunately, 20% of the uninsured (vs 3% of those with coverage) say their usual source of care is the ED; the uninsured are also much less likely than the insured to have a regular source of medical care.\(^{16}\)

While we cannot exclude the possibility that the uninsured have more severe headaches than the insured, we presume that they receive migraine care in the ED as a last resort. Our data add to prior evidence that migraine care in EDs is suboptimal. In a study of 219 patients presenting to an ED for headache, 47.5% of whom were diagnosed with migraine by a neurologist’s chart review, only 40.6% were asked to follow up with a physician and only 37.4% had any documented discharge medications.\(^{17}\)

The high cost of some migraine medications is another possible mechanism for some of the disparities we document. Injectable sumatriptan ($19/dose in 2009 prices) became available in the United States in 1991 and oral sumatriptan ($26/100 mg tablet) in 1995; no generic triptans were available during the years of our study. However, adding the less expensive butalbital/aspirin/caffeine ($1/tablet) and acetaminophen/dichloralphenazone/isometheptene ($0.73/tablet) to our list of abortive medications did not change the relationship of uninsurance and Medicaid coverage to substandard treatment, suggesting that the availability of moderately priced medications is not sufficient to reduce disparities in migraine care for those without private insurance.

The substandard treatment of migraine in the uninsured and Medicaid populations has significant financial implications. A study of the effect of initiating sumatriptan treatment in migraine patients found that over a 6-month follow-up period, sumatriptan reduced the total migraine disability time from 27.8 to 17.2 days per year. Quantifying the economic impact of this disability time based on national average wage rates, and taking into account migraine-related medical costs, this study estimated that sumatriptan use generated a net cost savings of $2,498 per patient per year.\(^{18}\)

Prior studies have documented that migraine care is often suboptimal in the United States; for example,

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Patient and provider characteristics of migraine headache visits to United States physician offices, hospital outpatient departments, and emergency departments, 1997-2007</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Office-based settings</strong></td>
<td><strong>Physician offices</strong></td>
</tr>
<tr>
<td><strong>(n = 2,244)</strong></td>
<td><strong>(n = 1,447)</strong></td>
</tr>
<tr>
<td><strong>Total weighted visits nationally</strong></td>
<td>53.1 million</td>
</tr>
<tr>
<td><strong>Age, weighted %</strong></td>
<td></td>
</tr>
<tr>
<td>18-40 years</td>
<td>42.6</td>
</tr>
<tr>
<td>41-65 years</td>
<td>51.1</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>6.3</td>
</tr>
<tr>
<td><strong>Race/ethnicity, %</strong></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>79.8</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>8.1</td>
</tr>
<tr>
<td>Hispanic, any race</td>
<td>8.3</td>
</tr>
<tr>
<td>Other</td>
<td>3.7</td>
</tr>
<tr>
<td><strong>Gender, %</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>83.6</td>
</tr>
<tr>
<td><strong>Anticipated source of payment, %</strong></td>
<td></td>
</tr>
<tr>
<td>Private insurance</td>
<td>71.5</td>
</tr>
<tr>
<td>Uninsured</td>
<td>6.2</td>
</tr>
<tr>
<td>Medicaid</td>
<td>8.4</td>
</tr>
<tr>
<td>Medicare</td>
<td>8.0</td>
</tr>
<tr>
<td>Worker’s compensation</td>
<td>0.1</td>
</tr>
<tr>
<td>Unknown payer</td>
<td>5.8</td>
</tr>
<tr>
<td><strong>Region, %</strong></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>16.5</td>
</tr>
<tr>
<td>Midwest</td>
<td>25.2</td>
</tr>
<tr>
<td>South</td>
<td>34.8</td>
</tr>
<tr>
<td>West</td>
<td>23.4</td>
</tr>
<tr>
<td><strong>Urban/rural location, %</strong></td>
<td></td>
</tr>
<tr>
<td>MSA</td>
<td>81.5</td>
</tr>
<tr>
<td><strong>Hospital owner, %</strong></td>
<td></td>
</tr>
<tr>
<td>Voluntary nonprofit</td>
<td>76.0</td>
</tr>
<tr>
<td>Government, nonfederal</td>
<td>21.0</td>
</tr>
<tr>
<td>Proprietary</td>
<td>3.0</td>
</tr>
<tr>
<td><strong>Provider type</strong></td>
<td></td>
</tr>
<tr>
<td>Neurologist</td>
<td>19.6</td>
</tr>
<tr>
<td>Primary care physician</td>
<td>67.9</td>
</tr>
<tr>
<td>Other</td>
<td>12.6</td>
</tr>
</tbody>
</table>

Abbreviation: MSA = medical provider located in a Metropolitan Statistical Area, as defined by the Office of Management and Budget.
Table 3 Multivariate odds that US adults will fail to receive standard migraine treatment, all ambulatory sites of care: National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, 1997–2007

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Abortive medication, odds ratio (95% CI)</th>
<th>Prophylactic medication, odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insurance status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Privately insured (ref)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Uninsured</td>
<td>2.0* [1.3, 3.0]</td>
<td>2.0* [1.3, 2.9]</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1.6 [1.2, 2.3]</td>
<td>1.5* [1.0, 2.1]</td>
</tr>
<tr>
<td>Medicare</td>
<td>1.6 [0.9, 2.7]</td>
<td>1.4 [0.9, 2.4]</td>
</tr>
<tr>
<td>Worker’s compensation b</td>
<td>3.4* [1.0, 11.5]</td>
<td>3.0 [0.4, 2.32]</td>
</tr>
<tr>
<td>Other</td>
<td>1.4 [0.8, 2.3]</td>
<td>1.8* [1.2, 2.7]</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (ref)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Male</td>
<td>0.8 [0.6, 1.1]</td>
<td>1.1 [0.9, 1.5]</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–40 y (ref)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>41–65 y</td>
<td>1.0 [0.8, 1.3]</td>
<td>0.8 [0.7, 1.1]</td>
</tr>
<tr>
<td>&gt;65 y</td>
<td>3.8* [1.7, 8.5]</td>
<td>0.8 [0.4, 1.4]</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white (ref)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.0 [7.1, 16]</td>
<td>2.1* [1.3, 3.2]</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>11.0 [7.1, 18]</td>
<td>1.1 [0.7, 1.7]</td>
</tr>
<tr>
<td>Other b</td>
<td>2.4* [1.1, 5.1]</td>
<td>2.1* [1.1, 3.9]</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast (ref)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Midwest</td>
<td>0.8 [0.6, 1.2]</td>
<td>1.5* [1.0, 2.2]</td>
</tr>
<tr>
<td>South</td>
<td>11.0 [0.8, 1.9]</td>
<td>1.3 [0.9, 1.9]</td>
</tr>
<tr>
<td>West</td>
<td>11.0 [0.7, 1.7]</td>
<td>1.2 [0.8, 1.7]</td>
</tr>
<tr>
<td>Urban/rural location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural (ref)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Metropolitan area</td>
<td>0.8 [0.6, 1.1]</td>
<td>0.7 [0.5, 1.1]</td>
</tr>
<tr>
<td>Year of visit c</td>
<td>1.0* [1.0, 1.1]</td>
<td>1.1* [1.0, 1.1]</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval; ref = reference group.
*Statistically significant result.
Results based on small numbers of visits.
Odds ratio equals the change for each successive year of visit.

while 25.7% of migraineurs met criteria for prophylaxis, only 13% were actually receiving it.1 Only 29% of migraineurs are very satisfied with their usual acute treatment.19 Our finding that Hispanics receive less prophylactic medication, regardless of insurance status, suggests that language barriers may also deter optimal migraine care. However, our data strongly suggest that absent or inadequate insurance is a major contributor to substandard care for migraine.

In the United States, migraine prevalence is inversely related to household income.6,12 Migraines may lead to lower socioeconomic status by impairing school and work performance. Some data suggest that the converse explanation is more likely, namely, that low income increases the risk of migraine.20 Our findings suggest that inadequate insurance magnifies the already high burden of migraine on low-income families.

Our study has limitations. The treating clinician made the diagnosis of migraine; we had no independent verification of diagnosis. While the misdiagnosis of migraine is important clinically, it would not invalidate our study findings because we are studying the effect of insurance status on prescribing behavior at visits where the prescriber diagnoses migraine. We were also unable to assess migraine severity. However, given that most migraine is moderate to severe, with 91% of migraineurs reporting functional impairment, our assumption that rates of moderate to severe migraine are similar among groups seems reasonable.2 We also had no data on the duration of individual migraines; some patients seen in the ED may have had intractable headaches for which triptans are less effective and thus less likely to be prescribed.

Another limitation of our study is that our definition of prophylactic medication was, by necessity, broad; some of the individuals receiving these medications may have done so for indications other than migraine. It is also possible that some individuals were receiving standard migraine therapy, but that it was not administered or prescribed during the sampled visit. However, there is no a priori reason to expect that either of these issues would preferentially affect one group more than another.

Using the prescription of a triptan or DHE or the prescription of a prophylactic agent as proxies for standard care of migraine headache, we have found that the uninsured are twice as likely as the privately insured to receive substandard migraine care. Migraineurs insured by Medicaid are also more likely to receive substandard care. This effect appears to be mediated in large part by the fact that the uninsured and Medicaid-insured receive more of their migraine care in the ED. Given the economic and humanitarian costs of undertreated migraine, neurologists should advocate for comprehensive coverage of physician care and standard medications to minimize migraine’s toll.

**AUTHOR CONTRIBUTIONS**

Statistical analysis was conducted by Dr. A. Wilper.

**DISCLOSURE**

Dr. Wilper has received honoraria for lectures not funded by industry and receives research support from the Mountain States Tumor and Research Institute. Dr. Woolhandler receives research support from the Robert Wood Johnson Foundation. Dr. Himmelstein has received honoraria for lectures not funded by industry; serves on the editorial board of the International Journal of Health Services; and receives research support from the Robert Wood Johnson Foundation. Dr. Nardell has received honoraria...
for lectures not funded by industry; serves on the editorial board of Muscle & Nerve and has received royalties from publications in UpToDate.

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REFERENCES