The Economic Burden of Multiple Sclerosis in the United States

Estimate of Direct and Indirect Costs

Bruce Bebo, PhD, Inna Cintina, MPA, MA, Nicholas LaRocca, PhD, Leslie Ritter, BS, MA, Bari Talente, BA, JD, Daniel Hartung, PharmD, MPH, Surachat Ngorsuraches, PhD, Mitchell Wallin, MD, MPH, and Grace Yang, PhD

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Abstract

Background and Objectives
A recent report estimated that approximately 1 million adults were living with multiple sclerosis (MS) in the United States. Although MS is rarely the direct cause of death, its debilitating effects on normal body functions can result in considerable disruption to daily living and life roles including work, physical independence, mobility, social interaction, and participation in leisure activities. This study estimated the total economic burden of MS in the United States in 2019.

Methods
This study used a prevalence-based approach to estimate the national economic burden of MS. Claims from 3 sources (Medicare Current Beneficiary Survey, Medicare Standard Analytical File, and Optum de-identified Normative Health Information System) were used to obtain direct costs and a survey was developed to collect indirect costs (e.g., labor market productivity losses, costs of paid and unpaid caregivers, home modification) from 946 patients with MS (PwMS). Direct medical costs reflected the difference in the total average annual amount paid for PwMS vs matched controls without MS. Future earnings loss due to premature death attributable to MS was calculated using Centers for Disease Control and Prevention mortality data and Medicare claims data.

Results
The estimated total economic burden was $85.4 billion, with a direct medical cost of $63.3 billion and indirect and nonmedical costs of $22.1 billion. Retail prescription medication (54%); clinic-administered drugs, medication, and administration (12%); and outpatient care (9%) were the 3 largest components of the direct costs. The average excess per-person annual medical costs for PwMS was $65,612; at $35,154 per person, disease-modifying therapies (DMTs) accounted for the largest proportion of this cost. The cost per DMT user ranged from $57,202 to $92,719, depending on sex–age strata. The average indirect and nonmedical costs were $18,542 per PwMS and $22,875 per PwMS if caregivers’ costs were included. Lost earnings due to premature death, presenteeism, and absenteeism losses were the largest indirect cost components.

Discussion
MS is a costly chronic disease, with direct costs of prescription drugs and indirect productivity loss being important cost drivers. Our findings suggested that the burden of MS in the United States has been underestimated.
In 2017, approximately 1 million US adults were living with multiple sclerosis (MS). MS disease onset usually occurs between ages 20 and 40 years and often leads to disability. It affects nearly 3 times as many women as men; prevalent in White people with northern European ancestry, it has become increasingly common among Black people. MS manifests with a multitude of symptoms that may intensify and subside over time, creating relapsing-remitting and progressive patterns of disease. People with MS (PwMS) experience higher rates of comorbidities than the general population.

MS is the leading progressive neurologic condition of young working-age adults. Nearly 30% of working-age individuals with MS across the United States rely on Social Security Disability Insurance (SSDI). MS has caused significant economic burden in the United States. PwMS have higher health care utilization compared to controls without MS. Although MS is rarely the direct cause of death, its debilitating effects result in considerable disruption to daily living and life roles, including physical independence, mobility, social interaction, and participation in leisure activities. Neurologic disability can prevent PwMS from working or limit employment opportunities and reduce earnings. In addition, many family members need to leave their employment to become caregivers.

Prior studies examining the economic burden of MS in the United States are outdated due to recent changes in the prevalence estimates of MS and the development of new treatments in the past 2 decades. The objective of this study was to provide an estimate of the economic burden of MS in the United States in 2019.

Methods

We used a prevalence-based approach in estimating the economic burden of MS. The direct and indirect costs of MS were estimated based on the disease-attributable cost approach and human capital approach, respectively.

Data Sources

We relied on a variety of primary and secondary data sources to estimate different components of the costs of MS, including existing national survey data, public and private claims data, national death records, and a self-administered survey (Figure 1). We relied on MS prevalence estimates for 2010 that were published in the literature in 2019. To obtain the 2019 MS estimates, we used the strategy described by the MS Prevalence Workgroup and applied an annual growth rate of 2.3% to the 2010 estimates.

To estimate the direct medical costs of MS, we used the 2017–2019 Medicare Standard Analytical File (Medicare 5%) and the 2017–2019 Optum de-identified Normative Health Information (dNHI) System. The 2018 Medicare Current Beneficiary Survey (MCBS) was used for the estimation of prescription drugs and long-term care costs for the Medicare population, as these costs were not reported in the Medicare 5%. Future earnings loss due to premature deaths attributable to MS was estimated using death certificates from the Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER) Detailed Mortality Database for 2015–2017, 2018 Medicare 5% sample claims data, Bureau of Labor Statistics earnings data, and CDC National Vital Statistics Report. Finally, we implemented a web-based survey to estimate the caregiver burden utilizing a set of comprehensive measures of labor market consequences for PwMS and their caregivers. It also included cost of medical treatments that were not typically covered by insurance and were paid out-of-pocket. For indirect cost estimates, we also utilized data from the American Community Survey (ACS) public use micro-data, Current Population Survey (CPS) Volunteer Supplement, and data published by the Independent Sector.

Study Samples

For the dNHI and the Medicare files, PwMS were identified if they had continuous coverage for both medical and pharmacy benefits in the study year and MS diagnostic code (ICD-9 code 340 or ICD-10 code G35) at any time during the year at either the primary or the secondary diagnosis positions. Also, for the dNHI claims, they must have had ≥3 MS-related inpatient visits, outpatient visits, or prescription claims for an MS disease-modifying therapy (DMT) in any combination within a 1-year period. For Medicare 5% claims that did not include Medicare Part D drug claims, we required ≥2 MS-related inpatient or outpatient visits in any combination. For the 2018 MCBS file, we required ≥2 MS-related medical claims, any drug claim for a DMT, or 1 answer in the MCBS survey file indicating that the person had MS. For the questionnaire (see Supplementary materials, links.lww.com/WNL/B879), a total of 946 PwMS completed the survey. eTables 1–5 show the characteristics of our survey respondents.

A comparison of the characteristics of the total MS population as calculated from the prevalence estimates and that of the
survey respondents found that the survey sample is slightly younger than the prevalent MS population and has slightly more female participants. Therefore, we stratified the survey sample and the MS population into both age group and sex strata and applied weights for each survey respondent to represent the underlying population.

**Estimation of Direct Costs**
We used dNHI, Medicare claims, and the MCBS to estimate medical costs related to MS. Per-person medical costs included primary payer paid amount, out-of-pocket expenses, and third party paid amounts. We calculated the per-person direct medical costs for 2017, 2018, and 2019 as well as a 3-year average cost. The direct excess medical costs were calculated as the difference in the annual per-person costs between the MS samples and matched controls by age, sex, race/ethnicity, and insurance (10:1 control-to-case ratio). We also estimated the direct medical costs of MS by insurance types, age, sex, and types of health care services, including cost of hospital inpatient stays, physician office visits, prescription medications, administration of prescription medication in the outpatient setting, durable medical equipment, outpatient services, and nonacute institutional care (e.g., skilled nursing facility, nursing home, or hospice). The prescription medication costs, identified from the pharmacy claims, included DMT costs. The administration of medication in the clinic setting was identified from outpatient/physician claims. All costs were expressed in 2019 dollars.

**Estimations of Indirect and Nonmedical Costs**
Indirect costs included future earnings loss due to premature mortality, reduced labor market participation because of early retirement, productivity loss for those in the labor force, productivity loss from reduced participation in social activities, and nonmedical costs of MS. To estimate the loss in future earnings, we first estimated the number of premature deaths associated with MS and then multiplied that number by an estimate of average current value of future earnings (by

### Table 1 MS Prevalence by Population Characteristics

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<thead>
<tr>
<th>Age, y</th>
<th>Number of persons estimated to have MS</th>
<th>Percent of total MS population</th>
<th>Population</th>
<th>Prevalence, %</th>
<th>Prevalence per 100,000 people</th>
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<tbody>
<tr>
<td>18–44</td>
<td>255,841</td>
<td>26.5</td>
<td>117,818,671</td>
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<td>45–64</td>
<td>483,596</td>
<td>50.1</td>
<td>83,323,439</td>
<td>0.58</td>
<td>580</td>
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<td>65–74</td>
<td>177,359</td>
<td>18.4</td>
<td>31,483,433</td>
<td>0.56</td>
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<td>≥75</td>
<td>48,389</td>
<td>5.0</td>
<td>22,574,830</td>
<td>0.21</td>
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<table>
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<th>Sex</th>
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<th>Percent of total MS population</th>
<th>Population</th>
<th>Prevalence, %</th>
<th>Prevalence per 100,000 people</th>
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<tr>
<td>Male</td>
<td>246,990</td>
<td>25.6</td>
<td>124,348,656</td>
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<td>Female</td>
<td>718,195</td>
<td>74.4</td>
<td>130,851,717</td>
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<tr>
<td>Total</td>
<td>965,185</td>
<td>100</td>
<td>255,200,373</td>
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</table>

Abbreviation: MS = multiple sclerosis.
Source: Wallin et al. We applied the annual growth factor of 2.3% to the 2010 estimates to calculate prevalence in 2019.
We computed the net current value of future earnings for men and women by age group to estimate the national productivity loss of early mortality associated with MS. We assumed 0 loss in earnings from MS for those aged 75 and older. This approach incorporated information on average annual earnings, labor force participation rates, and mortality rates for men and women in the United States and assumed a productivity growth rate of 1% and a discount rate of 3%, a rate often used in public health studies.22,23,24

All other indirect and nonmedical cost categories were estimated from the survey. Among working age (18–64 years) PwMS, 58.7% were in the labor market, compared to the US labor force participation rate of 63.1%. The labor market employment-related earnings loss due to MS was calculated as the counts of PwMS who had retired or stopped working in the past 12 months and indicated that MS played a major role in their early retirement decision, multiplied with the median annual earnings by age, sex, and job status obtained from the 2019 ACS public use microdata.19 Because the job status of PwMS before retirement was unknown, we used the allocation of full-time to part-time job status among currently working PwMS.

Based on the number of days in an average working month during 2019 that the PwMS and the caregivers missed work or felt less productive while at work because of MS and the average daily earnings calculated from the self-reported annual earnings, we calculated the annualized productivity loss due to absenteeism and presenteeism (with an adjustment factor applied to each day felt unproductive).

We evaluated the plausibility of reported hours by comparing the reported volunteering hours with the average national annual volunteering hours obtained from the CPS Volunteer Supplement (2017).20 We took a conservative approach by calculating the percentage of people volunteered and average hours volunteered from CPS and multiplied it with the estimated percentage productivity loss from our survey (calculated as the difference between before and after hours divided by before hours). Productivity loss due to forgone volunteering activities was calculated as volunteering hours affected per year times $27.20, the estimated dollar value per hour volunteering according to the Independent Sector.21

Nonmedical costs included expenses for purchasing formal daily care, modification to homes, purchases of special motor vehicles, food, or dietary supplements, and increased travel costs for medical visits, as well as medical tourism. We estimated the costs of nonmedical components and medical out-of-pocket costs by multiplying the weighted percentage of families who responded as having incurred such expenses and the median expense per family per year with the total MS population in 2019 by age and sex.

We also asked whether the PwMS had received Supplemental Security Income, SSDI, or other types of disability income (e.g., income from state disability insurance, VA benefits, long-term disability benefits) in 2019.

Finally, we projected the number of people with MS and the economic burden over the next 20 years assuming current population growth and mortality trends. Specifically, we applied the estimated age- and sex-specific MS prevalence rate to US Census population projections for 2020–2039.25 We assumed that MS incidence increased 2.3% annually and mortality rates and per-person burden remained constant during this period.

**Standard Protocol Approvals, Registrations, and Patient Consents**

The study was reviewed and exempted by the New England Institutional Review Board. Standard contracts and data use agreements were obtained for the analysis of all datasets.
Types of service

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<th>Types of service</th>
<th>Total excess medical cost due to MS</th>
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<tr>
<td></td>
<td>In million $</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital inpatient</td>
<td>$3,910</td>
</tr>
<tr>
<td>Nonacute institutional care</td>
<td>$1,568</td>
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<tr>
<td>Outpatient medication and administration</td>
<td>$7,768</td>
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<td>Outpatient facilities</td>
<td>$5,537</td>
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<tr>
<td>Physician office</td>
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<td>Durable medical equipment</td>
<td>$252</td>
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<tr>
<td>Other ancillary</td>
<td>$1,728</td>
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<tr>
<td>Prescription medication without DMT</td>
<td>$3,999</td>
</tr>
<tr>
<td>Prescription medication, DMT</td>
<td>$33,930</td>
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<tr>
<td>Overall</td>
<td>$63,328</td>
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</tbody>
</table>

Abbreviations: DMT = disease-modifying therapy; MS = multiple sclerosis. Source: Lewin Group analyses of MS prevalence using published prevalence rates and Census population projection for 2017–2019 combined with direct medical cost estimates using 2017–2019 Optum claims;13 2019 Medicare Standard Analytical File 5% sample claims;13 and 2018 Medicare Current Beneficiary Survey.15 Estimates for people with MS <65 years of age are based on commercial claims; for those ≥65, on Medicare claims.

Results

Table 1 presents the estimated prevalence of MS by population characteristics for this study. Approximately 1 million individuals in the United States had MS in 2019. The prevalence of MS increased with age. The 45–64 age group represented the largest share (50%) of the MS population. Whereas the prevalence among those younger than 45 years was low (0.22%), this age group represented the second largest group in the MS population (nearly 30%). Women had a higher prevalence than men (0.55% and 0.20%, respectively; 549 women and 199 men per 100,000 people); women also represent 74% of the total MS population in 2019.

Economic Burden

Figure 2 shows the cost components of the burden. The estimated total economic burden of MS in 2019 was $85.4 billion, including direct medical costs of $63.3 billion and an additional nearly $21.0 billion in indirect costs and $1.1 billion in nonmedical costs and cost of health care services not covered by insurance.

Excess medical costs represent 74% of overall economic burden of MS. Table 2 presents the direct medical costs of MS by age, sex, and types of service. Overall, the average excess per-person medical cost was $65,612. When compared to a matched comparison group, the direct costs for PwMS differed by age, sex, and insurance coverage. Per-person cost was slightly higher for PwMS <65 years of age ($66,356) than for those ≥65 ($63,175). Men, although incurring slightly higher per-person costs than women with MS ($63,896 vs $70,603 per person), had a lower overall direct medical cost, due to the lower prevalence of MS among men.

Outpatient retail prescription medications (including DMT and non-DMT) were the largest cost component ($37.9 billion or about 60% of the direct medical costs) when compared to other components. DMT costs accounted for 89% of the total outpatient medication expenditure. As a consequence, per-person costs were lower if DMT costs were excluded: $29,258 for those <65 years and $34,392 for those ≥65. The usage of DMT varied substantially by age group, with about 50% of adults with MS age 18–64 regardless of sex and 21% of men and 40% of women aged ≥65 treated with DMT (eTable 6, links.lww.com/WNL/B879). Therefore, the cost per PwMS who used DMT was high and ranged from $57,202 to $92,719, depending on sex or age strata.

Clinic-administered medications (including infused DMTs) and outpatient facilities were the next 2 largest direct medical cost categories ($6.7 billion and $5.5 billion, respectively).

Table 3 shows the estimated indirect and nonmedical costs of MS. The estimated total indirect costs of MS were $21.0 billion in 2019 (or 25% of the total burden) with nearly $16.8 billion to PwMS and $4.2 billion to unpaid caregivers. Premature death accounted for the largest share ($8.0 billion; 38%) of indirect costs, followed by presenteeism ($5.9 billion; 28%) and absenteeism ($5.6 billion; 26%). The costs of absenteeism and presenteeism for the caregivers were about half of those for PwMS. The average indirect per capita cost was $17,407 for PwMS only and $21,741 for PwMS and caregivers. The total nonmedical costs were $752 million, with paid nonmedical daily care being the largest share ($247 million [33%]), followed by purchase of special equipment for
home or vehicle ($202 million [27%]). The average nonmedical cost per capita was $780. Finally, the medical costs associated with experimental, alternative, and nontraditional treatments that were not covered by insurance represented $342 million. The average per capita cost for health care not covered by insurance was $355.

The overall burden was higher when the government supplemental income programs based on disability eligibility were considered. Transfer payments to PwMS represented an additional $6.7 billion, which we did not include in the total burden as transfer payments are often used to pay for both medical and nonmedical services, which would double count costs.

**Discussion**

To determine the total economic burden associated with MS in the United States, this study used large claims databases to estimate the direct medical cost of MS by types of health care services and used a survey to collect indirect and nonmedical costs for PwMS, caregivers, and families. We found that, in 2019, MS was associated with an overall cost of $85.4 billion. We estimated that by 2039, there will be nearly 1.2 million PwMS in the United States and the economic burden will increase to $108.1 billion. The main driver of the burden was direct medical costs, especially prescription drugs, such as DMT (54% of the total medical costs per PwMS), which became available in the past several decades.

Although DMTs were found to make up more than 50% of the total medical costs per PwMS, these therapies provide value to patients. Studies have shown DMTs to reduce relapses, decrease disability, and improve health-related quality of life. In addition, when patients are treated early, DMTs can delay the progression of disease and reduce the number of new lesions and could lead to lower treatment costs, reduced health care utilization, fewer days of work loss, and lower direct and indirect costs. It is important to note that as the cost of DMTs rises and the affordability decreases, patients may be deterred from starting DMTs or be forced to interrupt their therapy.

The total economic burden of MS estimated in this study was higher than estimates in prior United States–based studies. For example, based on data from 1994, the total annual cost of MS was estimated at $34,103 per person. A more recent study in 2006 based on a survey estimated that the average total cost of MS was about $47,215 per patient per year (2004 dollars). Our direct medical cost of PwMS of $65,612 was substantially higher than in these previous studies even when those cost estimates were inflated to 2019 dollars. The largest cost component within our medical costs was DMT that were...
not included in other recent cost estimates. If the average DMT cost was added to the per person direct cost estimated by Whetten-Goldstein et al., it would be >$60,000. A more recent study from the United States estimated medical costs of MS to be $13.9 billion in 2016 dollars, substantially smaller than our estimate ($63.3 billion). However, these studies had very different data sources and methods, and included different cost components, and are therefore not directly comparable to our estimates.

The total per person cost estimate from our study is similar to those of some other chronic, disabling diseases in the United States. For example, a per-person cost estimate (including direct medical, indirect, and nonmedical costs) for amyotrophic lateral sclerosis is $63,693, and $50,952 for Duchenne muscular dystrophy (in 2010 dollars). Whereas the per-person burden of Parkinson disease is smaller than our estimate for MS ($49,997 in 2017 dollars vs $88,132 in 2019 dollars), the indirect and nonmedical costs of Parkinson disease are comparable to those of MS ($20,969 vs $22,520).

This study has several limitations. First, we used MCBS data for long-term care costs and prescription drug costs for the Medicare population. Although we aggregated the analysis to larger subgroups when sample sizes were small, certain strata-specific estimates might still be subject to small sample size and outlier issues. Second, because MS is likely to affect overall health, we did not want to overcontrol in estimating the direct medical costs and therefore only included age, sex, race/ethnicity, and insurance in matching PwMS to people without MS. Third, due to lack of MS-specific mortality data for patients younger than 65, we relied on imputed rates. Fourth, the indirect and nonmedical costs were estimated using a self-administered survey, which may subject to nonrepresentativeness, nonresponse, or recall biases. We compared demographic characteristics of survey respondents to claims data and found the survey respondents to be slightly younger, although we applied weights to adjust for this. Lastly, we did not include the Medicaid and veteran populations in the cost estimates.

It is important to address why we used the human capital approach to estimate indirect costs and its implications. Although the human capital approach is frequently used in cost-of-illness analyses, it has limitations. It assumes a worker is irreplaceable and that the loss of productivity will not be made up. Using the friction cost method would account for this; however, this method is limited to the effects of a short-term period and has its own set of limitations. In addition, although the human capital approach may overestimate the economic burden of an illness, it is important to understand not only the cost due to loss of productivity but also the potential cost for employers to hire replacements.

The findings of this study help underscore the burden of MS in the United States and potential effects of policy or treatment interventions. The results suggest a possible role for additional policy initiatives to better support individuals and families affected by MS, in terms of providing treatment and long-term care, worksite support, employment, and occupational training. The findings will inform decision-making regarding MS-related health resource investment and prioritization. For example, high caregiver losses could be alleviated by support at the state and national levels; employment and productivity-related losses can be reduced by providing necessary accommodations and adding flexibility for PwMS in their current jobs such that they continue to be productive. These measures could reduce the economic burden of MS and help improve the lives of those living with MS and their family caregivers.

Acknowledgment
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Disclosure
B. Bebo, L. Ritter, and B. Talente are employees of the National Multiple Sclerosis Society. I. Cintina is an employee of The Lewin Group, which received funding from the National Multiple Sclerosis Society for the study. N. LaRocca and Daniel Hartung are paid consultants for the National Multiple Sclerosis Society. N. Ngorsuraches has served as a site investigator for a University of Utah project funded by Bristol Myers Squibb, received research support from the PhRMA Foundation, and has led a project funded by Eugene Washington Patient-Centered Outcomes Research Institute (PCORI) Engagement Awards. M. Wallin has nothing to disclose. Go to Neurology.org/N for full disclosures.

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Appendix
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<th>Name</th>
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<th>Contribution</th>
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<tr>
<td>Bruce Bebo, PhD</td>
<td>National Multiple Sclerosis Society, New York, NY</td>
<td>Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data</td>
</tr>
<tr>
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<td>Department of Health Outcomes Research and Policy, Harrison School of Pharmacy, Auburn University, AL</td>
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<td>Mitchell Wallin, MD, MPH</td>
<td>VA Multiple Sclerosis Center of Excellence-East, Washington, DC; George Washington University School of Medicine in Washington, DC</td>
<td>Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data</td>
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<td>Grace Yang, PhD</td>
<td>The Lewin Group, Falls Church, VA</td>
<td>Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data</td>
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References

# Indirect Costs

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