

A Claims-Based Analysis of Secondary Progressive Multiple Sclerosis (SPMS): Prevalence, Demographics, and Costs

Considerations for Commercial and Medicare Advantage Payers

Commissioned by Novartis Pharmaceuticals Corporation

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Secondary progressive multiple sclerosis (SPMS) is a disabling multiple sclerosis (MS) phenotype marked by relentlessly progressing neurologic disability.¹ While treatment with disease-modifying therapies (DMTs) may delay the time from diagnosis with relapsing remitting MS (RRMS) to secondary progression, at the time of this analysis there were no therapies approved by the U.S. Food and Drug Administration (FDA) for SPMS with a manageable risk-benefit ratio.^{2,3} The different types of MS are not distinguishable by International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. However, medical combined with pharmacy administrative claims data can be used to reasonably identify patients with different MS phenotypes. This paper examines the prevalence, demographics, and healthcare cost of SPMS patients.

The SPMS analysis of the commercial market was based on the years 2013-2017 in the Truven Health Analytics MarketScan Commercial Claims Database (MarketScan) that contains all paid claims generated by more than 28 million commercially insured lives. For the Medicare market, we analyzed years 2014-2016 of Milliman's Consolidated Health Cost Guidelines Source Database (CHSD).

Key Findings

Our SPMS analysis of commercial and Medicare Advantage Prescription Drug (MA-PD) claims data suggests that:

- Distinguishing SPMS from other phenotypes of MS can be challenging in several contexts.⁴ There is no relevant biomarker and the transition from RRMS is evident only retrospectively. Identification of patients with transitioning or early SPMS in administrative claims is challenging as claims-based disability markers may not be observed until neurologic progression or disability is advanced.
- We estimate that in 2016 there were approximately 44,000 and 23,000 SPMS patients in the commercial and MA-PD markets, respectively, constituting 15% and 29% of the total MS population in these markets.
- The majority of RRMS patients are in the commercial population, while the majority of SPMS patients are in Medicare.
 - More than half of MA-PD SPMS patients are disabled individuals under 65 years of age, with an SPMS prevalence more than seven times the prevalence in the MA-PD-aged population.
- RRMS and SPMS patients are treated with DMTs at similar rates within commercial and within MA-PD, with higher treatment rates for both phenotypes in the commercial versus MA-PD populations.
 - While the percentage of MS patients with SPMS in the MA-PD-disabled and -aged populations is similar, disabled beneficiaries are more likely to be treated with DMTs.
 - Older MS patients are generally less likely to be treated with DMTs, regardless of MS phenotype.
- SPMS patients incur higher total healthcare costs than RRMS patients, with the greatest differences observed for younger patients in both the commercial and MA-PD-disabled populations.
 - In the MA-PD-aged population, SPMS patients have higher non-DMT medical spending (\$2,097 versus \$713 per patient per month in 2016 dollars) and RRMS patients have higher DMT medical and pharmacy spending (\$1,624

versus \$1,231 per patient per month). These differences largely offset one another and the two phenotypes have similar total expenditures.

Background

MS is a chronic inflammatory demyelinating disorder affecting the central nervous system (CNS).³ The median age at disease presentation is 28–31 years, which contributes to the high social and economic costs associated with the disease. Women are affected more than three times as frequently as men, and Caucasians are affected more than other racial groups.^{5,6} Recent observations of increased MS prevalence may be related to factors such as increasing incidence of MS, earlier diagnosis by advanced imaging, and greater longevity of MS patients, although survival still remains lower than in a population matched for age, sex, and socioeconomic status.^{7,8}

Most people with MS experience relapses and remissions in neurological symptoms, especially in the early stages of the disease, and clinical symptoms are commonly associated with evidence of CNS inflammation.⁴ MS is differentiated into phenotypes based on how patient symptoms change over time. Approximately 85% to 90% of all new cases present as RRMS, in which patients experience periodic increases in neurologic symptoms from exacerbations of disease activity (relapses) that are primarily inflammatory in nature, separated by remission periods of various durations during which symptoms completely or partially remit.³ There is no progression of disease disability during remission; if full recovery does not occur after a relapse, patients experience a step-wise accumulation of disability. The other 10% to 15% of newly diagnosed MS patients present with primary progressive MS (PPMS), where patients do not experience significant relapses but experience steady, rapid progression of neurologic disability.⁹

There have been significant advances in the treatment of RRMS over the past 20 years with the development of DMTs that decrease the risk of relapse and CNS lesion formation by targeting inflammation from immune-mediated processes.¹⁰ Recent studies suggest that early therapy with some DMTs may have a favorable impact on long-term disability and death due to MS, though additional long-term studies are needed for confirmation.^{10,11} However, DMT efficacy in reducing brain atrophy in clinical trials has been modest at best, and brain atrophy and brain lesion load predict future level of disability in MS.^{12,13}

THE TRANSITION TO SPMS

When individuals with RRMS experience worsening neurologic disability independent of relapses, the disease is re-classified as SPMS.⁴ The majority of RRMS patients eventually develop SPMS, although it is possible that long-term treatment with DMTs might reduce the number of patients who develop SPMS or delay their transition.^{14–17} Historically, this transition has occurred 11 to 19 years after diagnosis among patients without DMT treatment.^{18,19} While one study of active management of MS with DMTs showed that only 11.3% of patients with RRMS transitioned to SPMS during a 10-year period, the evidence about whether modern DMT treatment alters the rate of conversion to SPMS, time to conversion, age of transition, and subsequent cumulative disability after transition is limited, and longer term follow up studies are needed to answer these questions.^{2,16,20} Conversion from RRMS to SPMS is a critical event, both because it signals progression of disability and because treatments available to date have shown no efficacy in modifying the course of SPMS. Notably, several DMTs approved for treating RRMS have failed to show clinical benefits for patients with SPMS in a controlled, clinical trial setting.²¹ However, DMTs may slow progression in the minority of SPMS patients who experience ongoing relapses.^{20,22–25} At the time of this analysis, there were no FDA-approved therapies for SPMS to specifically slow progression and that have a manageable risk-benefit ratio, so SPMS management primarily has involved alleviation of symptoms, optimization of residual functions, and prevention of complications.³

Distinguishing between RRMS and SPMS phenotypes can be challenging in several contexts.⁴ There is no relevant biomarker and the transition is evident only retrospectively. The mean duration of the period of diagnostic uncertainty about the transition to SPMS is three years, due to the subtle nature of early progressive disease and physicians' caution in applying a progressive label in the context of the lack of evidence-based treatments and concerns about insurance coverage for certain DMTs.²⁶ Moreover, identifying patients with transitioning or early SPMS in administrative claims data is challenging because claims-based disability markers may not be observed until neurologic progression or disability is advanced.

SPMS PREVALENCE AND MORBIDITY

A systematic literature review estimated the prevalence of SPMS in the United States at 371/1,000,000 (270/1,000,000–450/1,000,000), with wide variation across individual studies.²⁷ Sources of information on MS phenotypes as a percentage of MS patients include registry and population survey data. SPMS patients make up about 25%, 26%, and 19% of all MS patients included in the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry, in the New York State Multiple Sclerosis Consortium (NYSMSC) database, and as respondents to the U.S. National Health and Wellness Survey (NHWS), respectively.^{9,28,29} Note that MS phenotypes are self-reported in the NARCOMS Registry and the NHWS.

A significantly greater proportion of patients with SPMS than RRMS report multiple neurological symptoms, including difficulty balancing or walking and bladder dysfunction, along with lower employment rates and greater disruption to their working lives and everyday life activities.²⁹ Other studies have shown that the later stages of MS represent a significant socioeconomic burden, due principally to patients' reduced work capacity and the costs associated with increased activity impairment and the need for personal care.^{30–33}

Researchers have estimated annual healthcare costs for people with MS at more than \$24,000, greater than the general population, with medications as the main cost drivers for MS patients with low disease severity, and loss of income combined with informal care needs as the largest costs for those with more advanced disease.^{34–36} A systematic review of studies estimating the cost-of-illness of MS found that while the total cost per patient and year varied greatly between studies, mainly due to differences in which costs were included and how severity of disease was handled, the total costs increased with higher levels of disease severity, demonstrating a typical cost ratio of 3:1 for the most severe group compared to the mildest severity categorization.³⁴

DISEASE-MODIFYING THERAPY USE IN SPMS

At the time of this analysis, there were no FDA-approved therapies for SPMS aside from mitoxantrone, although use of the latter has been limited because of its poor benefit-risk profile.^{37,38} In responses to the NHWS, a higher proportion of patients with SPMS than RRMS reported not using a DMT (50.0% versus 26.5%).²⁹ In the absence of approved treatments, the majority of treated SPMS patients use the same medications as RRMS patients, suggesting that conversion to the SPMS phenotype is not associated with therapy switch.²⁹ SPMS patients in the NARCOMS Registry similarly reported higher rates of no DMT use compared to RRMS patients (49.7% versus 20.7%).⁹ For the minority of SPMS patients with superimposed relapses, DMT use has been found to be associated with a lower rate of disability progression.^{25,39}

Findings

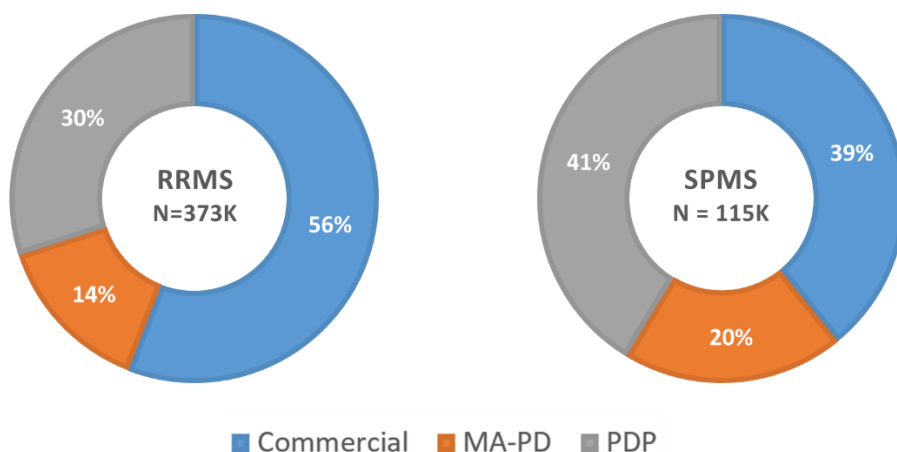
We analyzed the size, payer mix, and healthcare spending characteristics of the commercial and MA-PD MS populations with different phenotypes in commercial (2013-2017) and MA-PD (2014-2016) claims data. We divided MS patients into four categories based on their reported neurological and disability progression levels as of 2016: recently diagnosed MS, RRMS, early SPMS, and established SPMS. Recently diagnosed patients were defined as those patients with MS first identified in 2015 or 2016 (commercial) or 2016 (MA-PD). SPMS patients were defined as those MS patients identified by the end of 2016 by one or more of the six claims-based criteria for progression described in the Data Sources and Methodology section of this paper below. Established SPMS patients reported their earliest progression date prior to October 2015, while early SPMS patients reported their earliest progression date on or after October 2015 and prior to October 2016. For purposes of this analysis, all patients not identified as SPMS were defined as RRMS, although both the SPMS and RRMS categories may include some PPMS patients.

SPMS PREVALENCE BY MARKET

The estimated 2016 SPMS prevalence rates in the U.S. commercial and MA-PD populations are 336 per 1,000,000 members age 18 and older and 1,223 per 1,000,000 members, respectively, as displayed in Figure 8. The commercial and MA-PD SPMS populations constitute 15% (approximately 44,000 patients) and 29% (approximately 23,000 patients) of the total MS population in these markets, respectively, compared to 25% in the NARCOMS Registry, 26% in the NYSMSC database, and 19% of MS respondents to the NHWS.^{9,28,29} Although we used multiple progression criteria to identify SPMS, we likely identified commercial SPMS patients with more advanced disability compared to self-reported registry or survey data phenotype designation, potentially underestimating SPMS in this younger population. This is because subtle early progression would not be reflected in claims data. Although we used the same progression criteria for the MA-PD population, we expect that our SPMS estimates are relatively complete for this group given the median age of MS presentation of 28 to 31 years and typical timeframes for transitioning from RRMS to SPMS, as well as the fact that beneficiaries may enroll in Medicare on the basis of significant, permanent disability.^{3,40}

We compared the contributions of the MS phenotypes to the total MS RRMS and SPMS populations in the commercial, MA-PD, and Medicare Prescription Drug Plan (PDP) markets. To estimate the PDP population, we applied the derived MA-PD MS phenotype prevalence rates to PDP national estimates, adjusted for differences in disability rates and low income subsidy (LIS) eligibility in the MA-PD and PDP markets. We found that the majority of RRMS patients are in the commercial population, while the majority of SPMS patients are in the MA-PD and PDP populations. The resulting distributions from this analysis are displayed in Figure 1. In addition, we observed that the SPMS prevalence rate for members with the LIS is about three times the rate for non-LIS members.

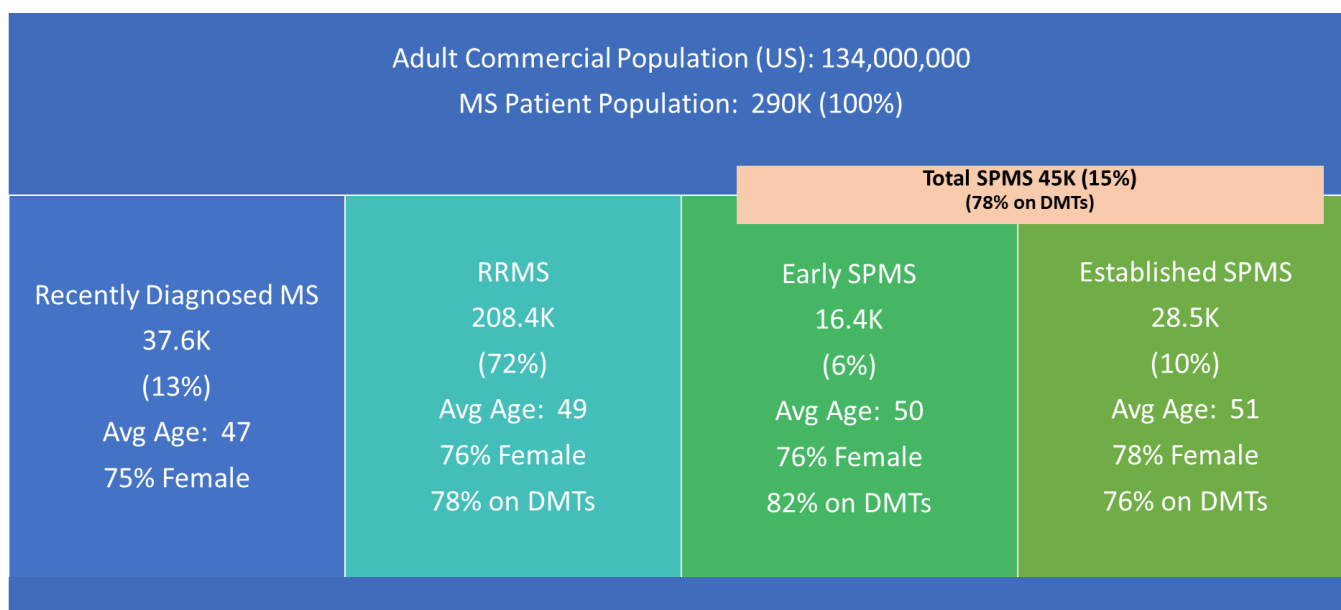
FIGURE 1: PERCENTAGE OF RRMS AND SPMS THAT ARE COMMERCIAL, MA-PD, OR PDP



DEMOGRAPHICS AND DMT USE

We found similar rates of DMT treatment in SPMS and RRMS within each market as displayed in Figures 2A and 2B. We did not observe the substantially higher rate of DMT use for RRMS compared to SPMS that has been found in registry and survey studies of MS patients (adults of all ages) who self-report these phenotypes.^{9,29} As shown in Figure 2A, the DMT use rate in commercial RRMS of 78% in our analysis is similar to the DMT use rates in those studies of 79.3% and 73.5%. However, the survey and registry studies also found DMT use rates in RRMS to be about 50% greater than the DMT use rates for SPMS, while we found a commercial SPMS DMT use rate of 78% which is the same as the RRMS rate.^{9,29} The average age of commercial established SPMS patients in our study is 51 years, younger than the average age of SPMS participants in the other studies (56 and 62 years), and that may contribute to our higher observed DMT use rate if older patients are less likely to be treated with DMTs.

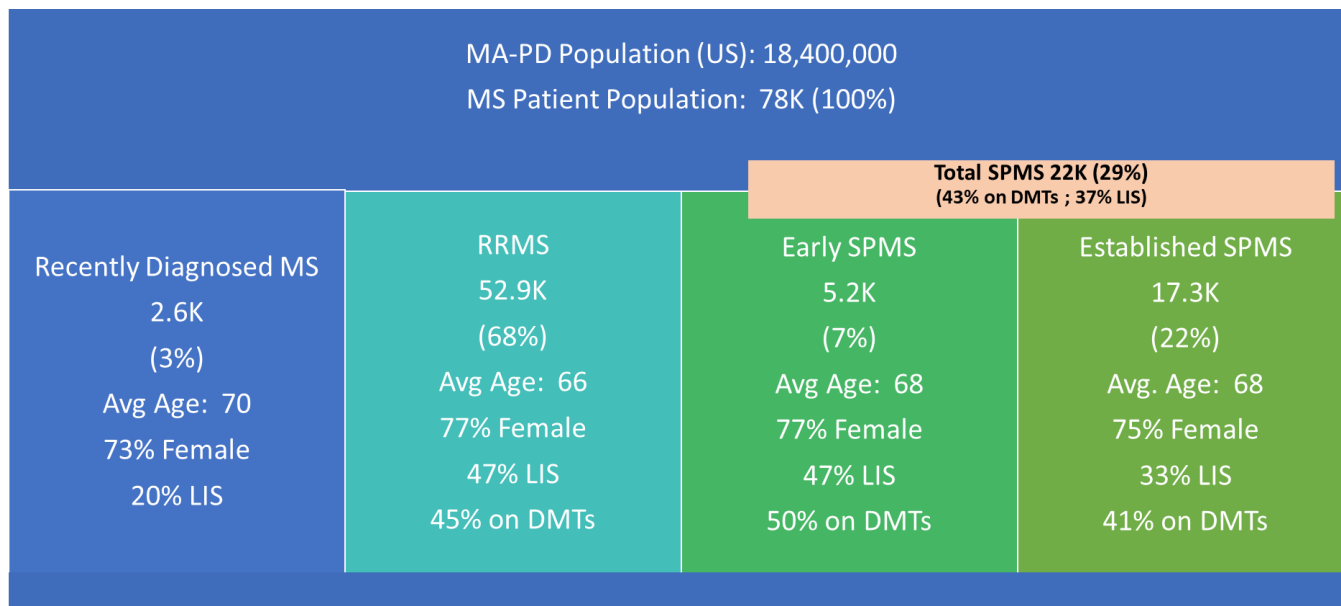
FIGURE 2A: NATIONAL COMMERCIAL ESTIMATES



In the MA-PD population, we found a substantially lower RRMS DMT use rate of 45% compared to the registry and survey studies, while our overall MA-PD SPMS DMT use rate of 43% was similar to the rates of 50.3% and 50% from those studies.^{9,29} We

expected to observe lower rates of DMT use in established SPMS compared to RRMS, especially in the MA-PD-aged population where the literature suggests that DMTs may be stopped after a period of no relapses and the probability of relapse decreases with age.^{39,41,42} However, the rate of DMT use in the established SPMS MA-PD population is only slightly lower than early SPMS and RRMS patients, 41% versus 50% and 45%. For SPMS patients under age 75, the DMT use rate is 60% across the commercial, MA-PD, and PDP populations.

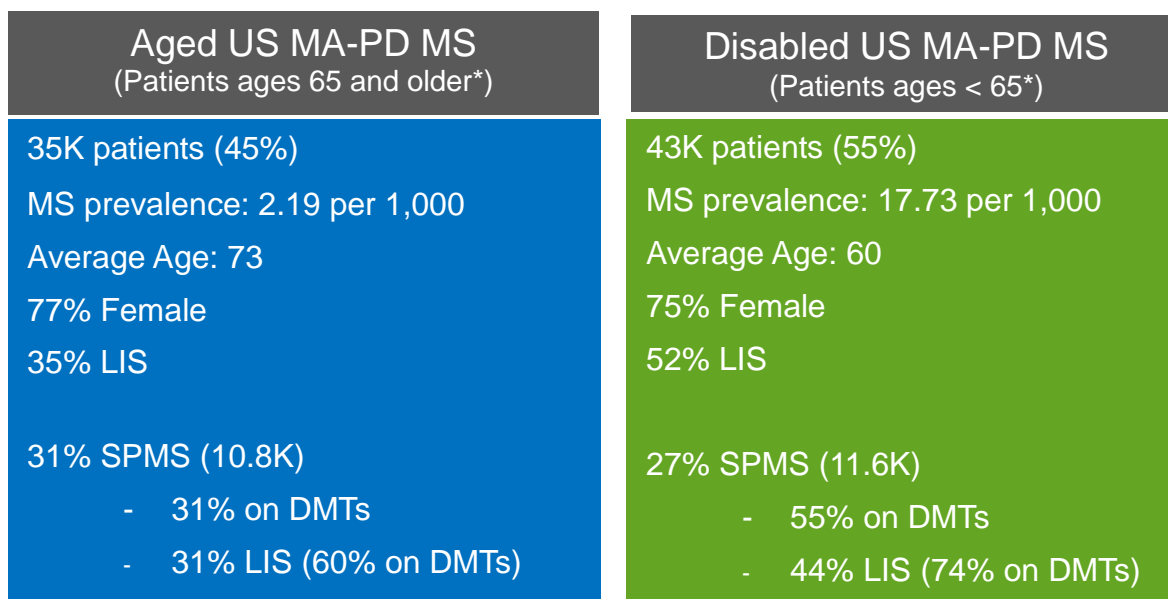
FIGURE 2B: NATIONAL MEDICARE ADVANTAGE ESTIMATES



MEDICARE DRILL DOWN: AGED VS DISABLED

As displayed in Figure 3, the disabled/under age 65 MS population comprises 55% of the total MA-PD MS population. This compares to the 15% of all Medicare beneficiaries under age 65 and disabled.⁴³ This high representation of disabled individuals with MS in MA-PD is likely due to the serious morbidity associated with MS. MS has a high prevalence among disabled MA-PD beneficiaries, approximately eight times the aged MA-PD population, although the percentage of MS who are SPMS in the aged and disabled MA-PD populations is similar. This suggests that disabled beneficiaries have substantial MS-related disability that may allow them to qualify for Medicare coverage, even prior to experiencing secondary progression that would identify them as SPMS in our analysis. While both populations have a similar percentage of SPMS patients, MA-PD-disabled MS patients are substantially younger than MA-PD-aged beneficiaries and a higher proportion receive the LIS. The MA-PD-disabled SPMS patient population reports a higher DMT use rate of 55% than the rate observed for the MA-PD-aged SPMS population. This suggests that DMT use rates may be negatively correlated with age and use may be more prevalent among the disabled because they more often receive the LIS with lower cost-sharing. We see a similar pattern in the SPMS MA-PD-aged patient population where DMT use rates decrease as patients age as indicated in Figure 4.

FIGURE 3: COMPARISON OF AGED TO DISABLED MS PATIENTS IN MA-PD



* Age for distinguishing Aged vs Disabled calculated as of 1/1/2014.

FIGURE 4: MA-PD-AGED SPMS DMT USE RATES BY AGE GROUP

Age Group	65-69 Years	70-74 Years	75+ Years	Total
Percent of MA-PD-Aged SPMS Population	54%	33%	13%	100%
DMT Use Rate	42%	30%	16%	31%

SPMS patients incur higher total healthcare costs than RRMS patients, with the greatest differences observed for younger patients, both in the commercial and MA-PD-disabled populations as displayed in Figure 5. In the commercial MS population, SPMS patients have substantially greater medical and non-DMT prescription drug spending than RRMS patients, while prescription DMT costs are similar to RRMS. In the MA-PD aged population, medical spending is considerably higher for SPMS than RRMS, while DMT spending is higher for RRMS. These differences partially offset one another in the total spending. For the MA-PD-disabled population, medical spending is substantially higher for SPMS but DMT spending is similar for RRMS and SPMS.

FIGURE 5: MS PHENOTYPES PER PATIENT PER MONTH (PPPM) ANNUAL SPEND (2016 ALLOWED AMOUNTS)

COMMERCIAL						
	% of Market	Medical	Rx	Med DMT	Rx DMT	Total
RRMS	72%	\$825	\$310	\$414	\$3,628	\$5,178
SPMS	15%	\$3,036	\$757	\$963	\$3,067	\$7,824
Recently Diagnosed	13%	\$1,680	\$305	\$222	\$2,228	\$4,434
MS Total	100%	\$1,279	\$379	\$474	\$3,360	\$5,491
MA-PD Aged						
	% of Market	Medical	Rx	Med DMT	Rx DMT	Total
RRMS	65%	\$713	\$321	\$59	\$1,565	\$2,657
SPMS	31%	\$2,097	\$458	\$44	\$1,187	\$3,786
Recently Diagnosed	4%	\$2,388	\$392	\$0	\$90	\$2,870
MS Total	100%	\$1,210	\$366	\$52	\$1,383	\$3,010
MA-PD Disabled						
	% of Market	Medical	Rx	Med DMT	Rx DMT	Total
RRMS	71%	\$712	\$421	\$189	\$2,278	\$3,600
SPMS	27%	\$1,921	\$653	\$166	\$2,198	\$4,939
Recently Diagnosed	2%	\$1,496	\$405	\$205	\$217	\$2,322
MS Total	100%	\$1,054	\$483	\$183	\$2,208	\$3,928
MA-PD Combined						
	% of Market	Medical	Rx	Med DMT	Rx DMT	Total
RRMS	68%	\$712	\$372	\$125	\$1,926	\$3,134
SPMS	29%	\$2,018	\$547	\$99	\$1,644	\$4,307
Recently Diagnosed	3%	\$2,093	\$396	\$68	\$132	\$2,689
MS Total	100%	\$1,134	\$423	\$115	\$1,783	\$3,455

Considerations for payers

SPMS is a disabling condition affecting approximately 44,000 and 70,000 patients in the commercial and Medicare markets, respectively. Until 2019, available treatments had not shown efficacy once an MS patient reached a level of significant disability that signaled the patient's transition to SPMS. While it is unknown whether treatment with current DMTs delays the time from diagnosis with RRMS to SPMS transition, our analysis indicates that SPMS patients use DMTs at a similar rate to RRMS patients in both the commercial and Medicare markets. However, medical costs for SPMS patients tend to be about two to three times higher than for RRMS patients, and that difference is not explained by higher use of DMTs covered through the medical benefit (therapies with intravenous administration).

Payers should expect a higher prevalence of SPMS patients in their Medicare business (MA-PD and PDP products) than in commercial business. By contrast, the majority of RRMS patients are covered by commercial insurance. Within the Medicare population, the prevalence of SPMS among the disabled population is about seven times that of the aged population. The high correlation between disability and eligibility for the LIS means that SPMS is likely to be more important for MA-PDs and PDPs with high proportions of LIS members.

Data sources and methodology

ADMINISTRATIVE CLAIMS DATA AND ELIGIBLE MEMBER POPULATIONS

Our analysis of the commercial market was based on the years 2013-2017 from Truven Health Analytics MarketScan Commercial Claims Database (MarketScan) that contains all paid claims generated by more than 28 million commercially insured lives. Members were further required to be 18 or older by the end of 2015 and under the age of 65 as of the end of 2016. The selected 19 million members represent approximately 15% of the 2016 national commercially insured adult population. To be eligible for the study, members were additionally required to report continuous medical and pharmacy coverage as an active employee, early retiree, or COBRA enrollee (or a dependent of one) in a non-capitated health plan from January 2013 through January 2016 for a final study eligible population of 6.5 million members.

For the Medicare market, we analyzed years 2014 to 2016 from Milliman's Consolidated Health Cost Guidelines Source Database™ (CHSD). The CHSD contains proprietary historical claims experience from several of Milliman's Health Cost Guideline (HCG) data contributors. The database contains annual enrollment and paid medical and pharmacy claims for over 2.4 million Medicare beneficiaries enrolled in MA-PD health plans nationwide, representing approximately 13% of the 2016 national MA-PD population. To be included in our study, members were required to report continuous medical and pharmacy coverage from January 2014 through January 2016. Among those with continuous coverage, disabled beneficiaries were identified as those reporting ages less than 65 prior to 2016. The selected 756,308 beneficiaries represent a population that is 88.3% aged (versus disabled), and 17.4% are enrolled with the LIS.

STUDY POPULATION

Patients were flagged as diagnosed with MS if they reported three or more qualifying events of any (or multiple) of the following: inpatient, outpatient, and DMT encounters within a consecutive 12-month period, where the first of the three occurred by the end of 2016. This methodology is the preferred algorithm of investigators working on behalf of the United States Multiple Sclerosis Prevalence Workgroup.⁴⁴ We reviewed all claims incurred in the 2013-2017 (for commercial) or 2014-2016 (for MA-PD) for qualifying events, which are defined below. Inpatient and outpatient encounters required an MS ICD-9-CM or ICD-10-CM diagnosis code {*ICD-9-CM 340* or *ICD-10-CM G35*} in any position to qualify:

- Inpatient (IP) encounters were defined as an inpatient admission (acute or non-acute) for which a MS diagnosis code is recorded in any diagnosis code position on the inpatient claim. To account for transfers between institutions and avoid double-counting, multiple overlapping hospital admission and discharge records were counted as one IP encounter. If an IP encounter occurred with an admission date within 24 hours of discharge from the prior IP encounter, the second IP encounter was not considered a separate IP encounter.
- Outpatient (OP) encounters were defined as all non-inpatient services including outpatient facility (i.e. emergency department, observation), evaluation and management, lab, pathology, radiology, DME, etc. – no exclusions) for which MS is recorded in any diagnosis code position on the outpatient claim. Multiple outpatient encounters by one patient on the same day are treated as one OP encounter. Additionally, OP service claims for dates within an IP encounter (admission to discharge date) are not counted as an OP encounter.
- DMT encounters were defined as physician administered or prescription drug claims for DMTs including daclizumab, dimethyl fumarate, fingolimod, glatiramer acetate, interferon beta 1a, interferon beta 1b, natalizumab (in the absence of a diagnosis code for inflammatory bowel disease on the same claim), ocrelizumab, pegylated interferon beta 1a, and terflunomide.
- We assigned the date of service of the earliest qualified identifying claim (those followed by the required two or more qualifying events within 12 months) across all available data as each patient's MS index date.

We identified 16,594 commercial and 2,871 MA-PD patients with MS using the above methodology.

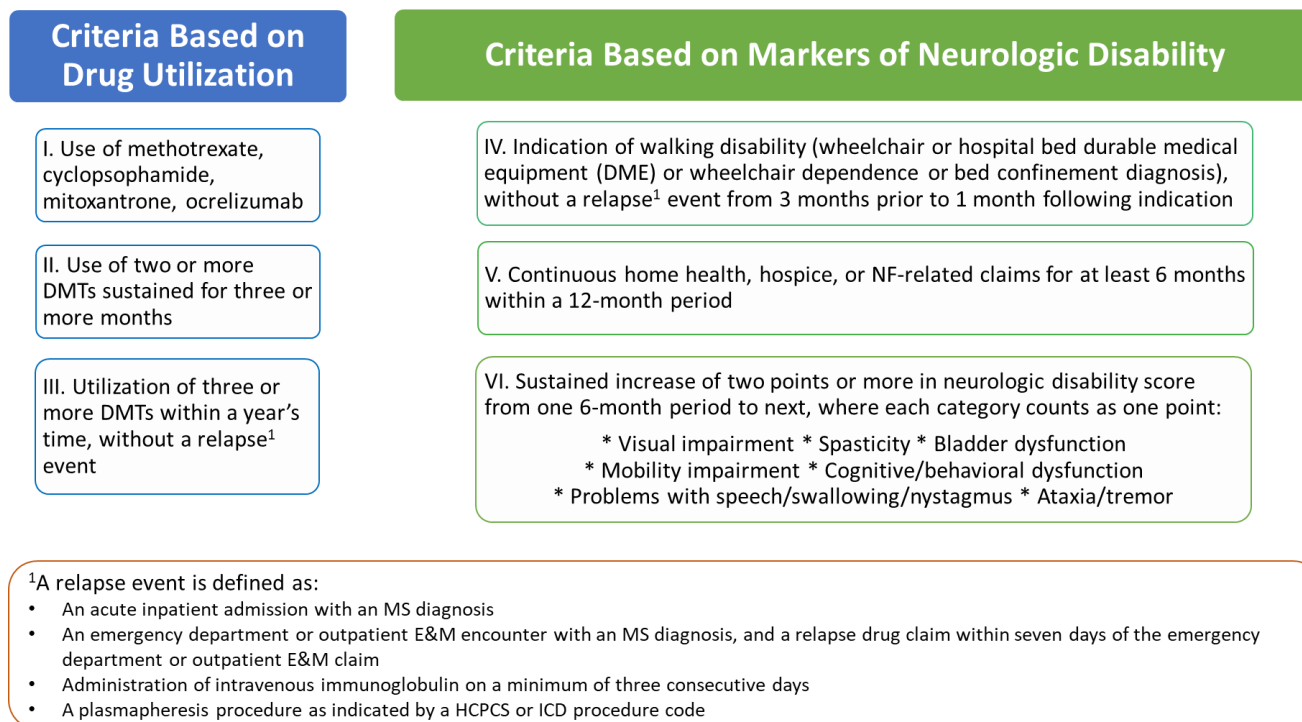
PHENOTYPE IDENTIFICATION

We divided the MS patients into four meaningful categories based on reported progression levels as of index year 2016: recently diagnosed MS, RRMS, early SPMS, and established SPMS. Recently diagnosed patients were defined as those patients with MS index dates in 2015 or 2016 (commercial) or 2016 (MA-PD). These patients reported a minimum of two full years of continuous coverage where they did not meet our MS identification criteria, leading up to their first MS encounter, which is the time of initial MS diagnosis. Only patients with MS index dates in the earliest two years of the available data were flagged as RRMS or SPMS.

We followed these patients for indications of progression from the MS index date through the end of the study period. SPMS patients were defined as those MS patients who reported progression in one or more of six claims-based criteria in Figure 6 by the end of 2016. Established SPMS patients were those who reported their earliest progression date prior to October 2015. Early

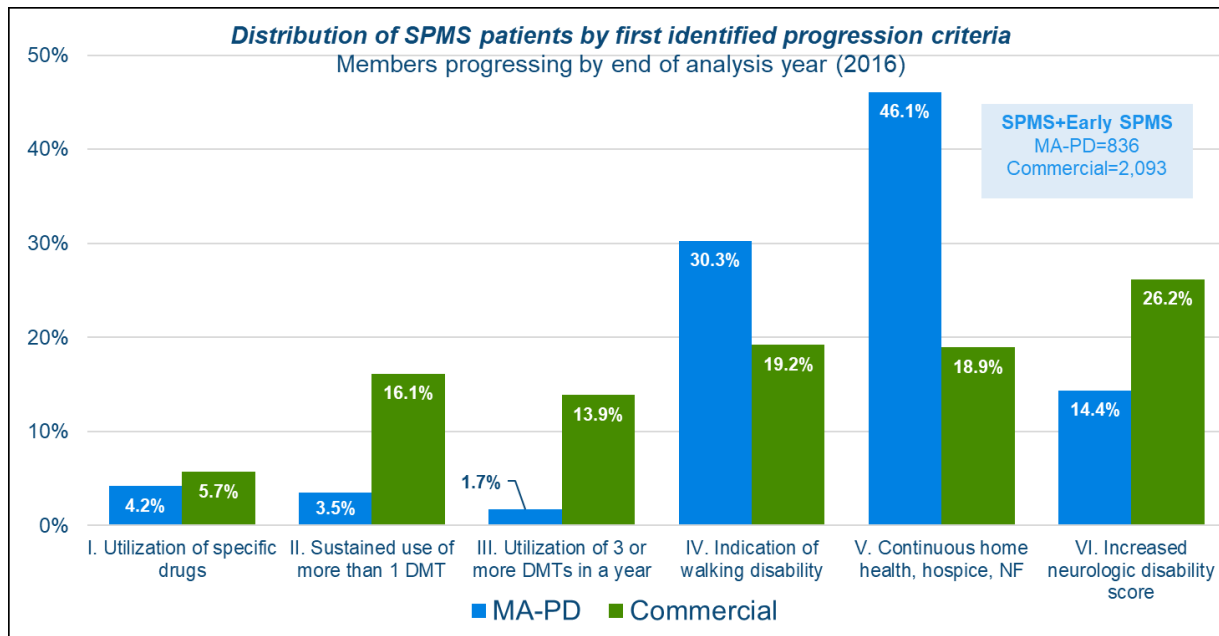
SPMS patients were those who reported their earliest progression date on or after October 2015 and prior to October 2016. All patients not identified as SPMS were defined as RRMS. The criterion involving the utilization of specific drugs and all criteria based on markers of neurologic disability were adapted from a publication that excluded such patients exhibiting progression from the RRMS phenotype.⁴⁵ MS drug claims were identified using Healthcare Common Procedure Coding System (HCPCS) codes and National Drug Codes (NDCs).

FIGURE 6: CLAIMS-BASED PROGRESSION CRITERIA TO IDENTIFY SPMS PATIENTS: ONE OR MORE OF THE FOLLOWING SIX CRITERIA INDICATE SPMS



The results of these progression criteria are summarized in Figure 7. Increased neurologic disability score was the most common first identifying progression indication for SPMS patients in the commercial MS population. In contrast, continuous home health, hospice, or NF utilization was the most common first identifying progression indication for SPMS in the MA-PD MS population.

FIGURE 7: SPMS MEMBERS BY MARKET AND FIRST IDENTIFIED PROGRESSION CRITERION

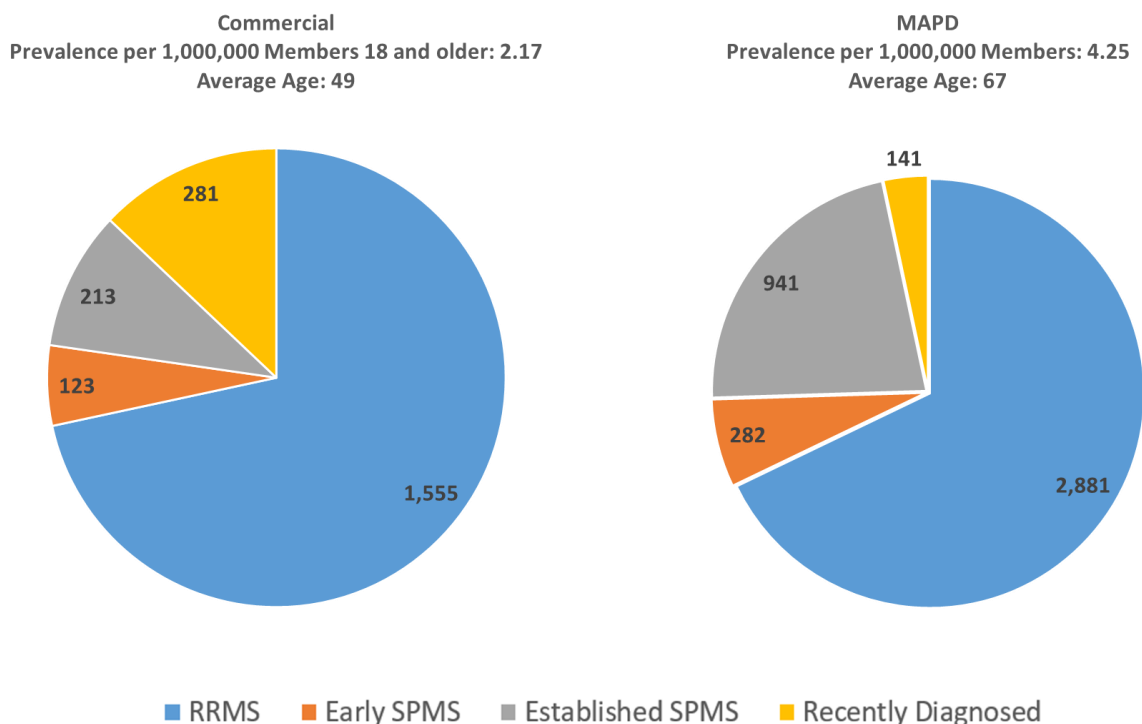


Because we imposed a three-year look-back period restriction for commercial patients to be included in our analysis, we believe our identification logic initially underestimated the rate of progression for early SPMS, because 15% to 20% of the commercial population leaves the database from one year to the next. Our early SPMS patients showed signs of progression in 2016, but they were identified as MS with no progression in years 2013 and 2014. To compensate for the likely underestimation of early SPMS patients in this database, we doubled the rate of these early SPMS patients in 2016.

We developed prevalence rates for the various MS phenotypes separately for commercial, MA-PD-aged, and MA-PD-disabled populations and applied them to national enrollment figures. For PDP, we applied MA-PD prevalence rates by disability and LIS status, and assumed a 30% selection factor for non-LIS beneficiaries based on Milliman research.

Prevalence rates for both commercial and MA-PD populations are provided in Figure 8 below.

FIGURE 8: PREVALENCE RATES OF MS BY PHENOTYPE, COMMERCIAL VERSUS MA-PD



National patient populations used were obtained from available literature. The national commercial population estimate used the number of enrollees as reported by the Kaiser Family Foundation for the 2016 US population for ages over 18, enrolled with either employer and non-group coverage.⁴⁶ The national MA-PD and PDP populations were both provided by the Centers for Medicare & Medicaid Services (CMS). We summarized the number of 2016 Medicare Advantage enrollees with both Part A and B for both aged and disabled populations for MA-PD and the number of PDP enrollees using the *2018 Low Income Subsidy Enrollment by Plan* report.^{47,48}

Costs in this report represent allowed amounts, defined as amounts paid for medical services by both payer and patient combined.

Limitations

The figures in this report were produced based on an analysis of national databases. Results for any particular health plan may vary substantially from those presented here due to demographics, enrollment mix, local practice patterns, contractual terms, and other factors.

The use of claims data to identify neurologic progression in MS patients that occurs in the transition from RRMS to SPMS is unlikely to identify earlier stages of progression that could mark this transition in clinical data. This limitation is expected to have more impact on identification of SPMS in the commercial population, who would be expected to have less advanced progression based on their younger average age compared to the MA-PD population. In addition, Ocrelizumab (used in one of the progression criteria) was not available before 2017 and as such was not available in the MA-PD data used for the analysis.

Our methodology likely includes some PPMS patients who progress immediately after diagnosis in the RRMS and SPMS populations, especially in the commercial population where newly diagnosed patients are most likely to be observed due to their younger age. For patients for whom we cannot determine initial diagnosis (the RRMS, early SPMS, and established SPMS categories), our default assumption is RRMS or SPMS. For MA-PD, we believe it is unlikely that the reported SPMS beneficiaries are incident PPMS since MS patients are typically diagnosed prior to Medicare age (65) or are enrolled in Medicare at a younger age most likely due to MS-related disability. However, as with commercial SPMS patients, some portion of the SPMS MD-PD beneficiary population will, in reality, be established PPMS patients. The difficulty in identifying PPMS patients may cause an overestimation of RRMS and SPMS patient counts to some extent, but it is challenging to know by how much of each phenotype.

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