Healthcare resource utilization and costs of commercial and Medicare-enrolled adult patients with Multiple Sclerosis in Urban and Rural settings

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Abstract

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Background: Multiple-sclerosis (MS) is a chronic progressive neurological disease that affects almost 1 million people in the United States, with an economic burden of over $85 billion USD. Previous studies have demonstrated that rural MS patients have reduced access to a neurologist compared to urban MS patients, but how this disparity impacted these patients was not explored. However, healthcare resource utilization and cost in MS patients in rural and urban areas has not been previously studied.

Objective: The primary objective of this study was to describe the healthcare resource utilization (HCRU) and healthcare costs of commercial and Medicare enrolled patients with MS in rural and urban settings.

Methods: We conducted a retrospective cohort study using health insurance claims from the Merative MarketScan® Commercial and Medicare Supplemental Databases. MS cases were identified as having ≥2 MS outpatient (OP) claims, dated ≥30 days apart, within 1 year or ≥1 MS inpatient (IP) claim (ICD10: G35) during the index/case identification period. The index date was defined as the first occurrence of meeting case criteria during December 31st, 2017, to December 31st, 2022. We examined all-cause HCRU by summarizing the number of IP admissions, OP services, emergency department (ED) visits and OP pharmacy fills in the 6 months post-index. Additionally, we assessed all-cause health care costs, including IP, OP, ED and pharmacy, over 1 year following index using the Kaplan-Meier sample average estimator to account for censoring. We reported total healthcare costs as the sum of IP, OP, ED and OP

pharmacy costs. Analyses were conducted separately for the commercial and Medicare supplemental groups; all-cause HCRU and costs were summarized overall and by rural and urban status.

Results: Our cohort consisted of 47,636 commercially insured patients and 3,318 Medicare patients. During the 6 months following index date, rural commercial patients had a slightly elevated mean number of IP admissions (1.4) and length of stay (LOS) (4.4 days) than the urban patients (1.3, 4.4). This trend is not repeated in the Medicare Supplemental population. In that population, the rural cohort had a lower mean number of IP admissions (1.3), and LOS (5.00) compared to the urban cohort (1.4, 5.9). For ED visits, in both the commercial and Medicare cohorts, the rural patients had lower average ED visits than the urban patients (Commercial: 1.5 vs. 1.6 rural vs urban) (Medicare: 1.7 vs. 1.8). OP visits follow this trend with the rural cohort having fewer visits among those that did have OP visits 6 months post-index in both insurance cohorts (Commercial: 9.4 vs. 10.0 rural vs urban) (Medicare: 12.7 vs. 14.4). However, there is a difference seen in the OP pharmacy fills. For both commercial and Medicare insurance, the rural cohorts had higher mean and median OP pharmacy fills than the urban cohorts The commercial rural patients had a mean of 31.5 (SD 20.8) 30-day standardized pharmacy fills and a median of 27.3 (IQR 15.9 – 42.6) compared to the urban patients with a mean of 27.7 (SD 19.4) and median of 23.4 (IQR 13.4 – 37.3). The Medicare rural patients had a mean of 38.1 (SD 23.9) 30-day standardized pharmacy fills and a median of 35.9 (IQR 22.3 – 48.9) compared to the urban patients with a mean of 36.6 (SD 20.2) and a median of 34.2 (IQR 22.3 – 48.7).

Conclusion: Rural patients tended towards lower average healthcare resource utilization (HCRU), and thus lower costs than the urban patients with some notable exceptions. Rural patients had higher mean and median pharmacy fills and higher costs in both insurance categories. This may point to rural MS patients relying more on prescription drugs to compensate for reduced access to medical services. MS patients require complicated care and insight into their HCRU and costs, can aid healthcare decision-makers in optimizing care for these patients.

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Introduction

Multiple-sclerosis (MS) is a chronic progressive neurological disease that affects almost 1 million people in the United States[1,2]. Common symptoms include fatigue, spasticity, weakness, vision changes, pain and difficulty with cognitive function[4,5]. MS is most common in Caucasian females between the ages of 20 and 40, although it can affect any individual at any age[3]. The economic burden of MS is estimated to be over $85 billion USD in 2022, with approximately a quarter being indirect and nonmedical costs[6].

There is no cure for MS but treatment with disease-modifying treatments (DMTs) translate into reduced disease burden and better economic outcomes[7]. Another way to reduce disease burden and improve economic outcomes is to identify and remove barriers to accessing medical care and DMTs. Previous studies have identified barriers to accessing medical care and DMTs by characterizing the patterns of healthcare utilization and DMT usage from the perspective of specific patient populations. Many studies have examined health care resource utilization (HCRU), and costs associated with MS in those who are newly diagnosed or newly initiating first or second line treatment. However, studies analyzing outcomes by residential status, rural versus urban, are lacking.

Studies in other disease areas have shown conflicting results when looking at rural and urban HCRU and costs. Some studies have found that rural populations have lower HCRU in all categories measured, while other studies have shown that rural patients have higher HCRU in certain categories compared to urban patients[9-11]. Previous studies have demonstrated that rural MS patients have reduced access to a neurologist compared to urban MS patients, but how this disparity impacted these patients was not explored. To our knowledge, no studies have explored HCRU and healthcare expenditures by rural and urban status in MS patients.

The primary objective of this study is to describe the healthcare resource utilization (HCRU) and healthcare costs of commercial and Medicare enrolled patients with MS in rural and urban settings.

Methods

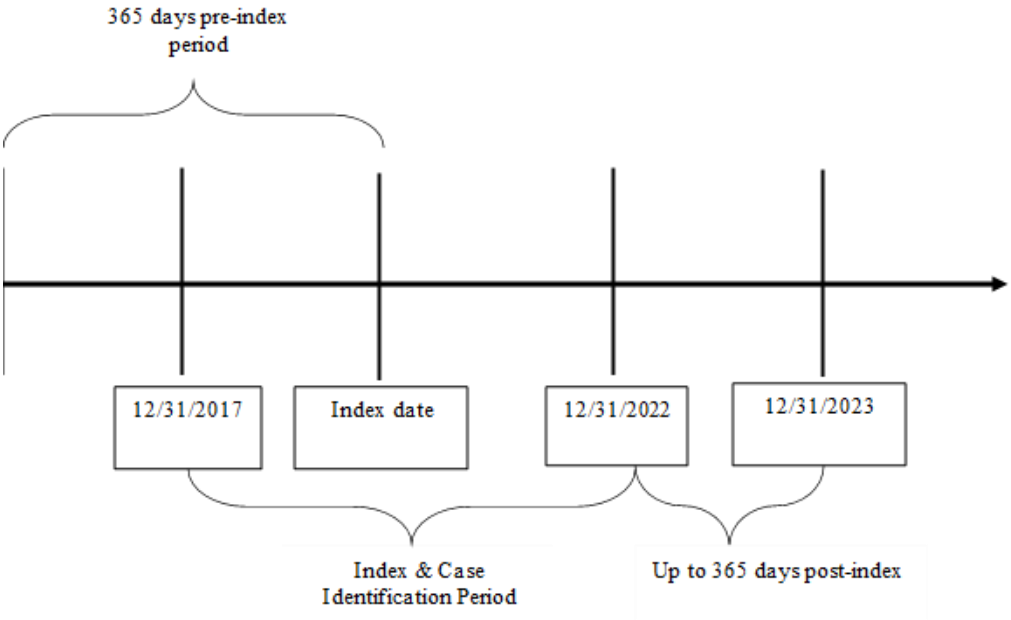
Study Design and Data Source

We conducted a retrospective cohort study using health insurance claims to describe the HCRU and costs among commercial and Medicare enrolled patients with MS in the United States.

Data from the Merative MarketScan® Commercial and Medicare Supplemental Databases was used to identify patients and capture HCRU and costs. The MarketScan Commercial and Medicare Supplemental Databases are created for patients enrolled in commercial insurance plans as well as Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans. It contains individual-level, de-identified health insurance claims data on more than 200 million lives and includes information on IP, OP, and OP pharmacy encounters, as well as enrollment data from large employers and health plans across the US[16].

The study period was December 31st, 2017, until December 31st, 2023. The index/case identification period was from December 31st, 2017 until December 31st, 2022, to allow for 5 years of identification time. This timeframe was chosen to include pre-Covid, during Covid and post-Covid HCRU and cost information.

Figure 1. Study Timeline



Sample Selection

The case definition for being defined as an MS case was having ≥2 MS OP claims, dated ≥30 days apart, within one year or ≥1 MS IP claim during the case identification period. An MS claim was defined as having and ICD10 code of G35 in any of the top four diagnostic positions for the claim. This algorithm has not been formally validated but has been used in previous literature[15]. We evaluated several different algorithms before selecting this approach. We rejected algorithms requiring patients to fill a DMT for MS as we were interested in all MS patients regardless of MS therapy. Instituting a 30-day separation between OP MS claims was more discerning (fewer patients qualified as cases) than requiring 3 OP MS visits with no separation. Considering those patients to be potentially misdiagnosed within the first month of their encounter, the stricter definition of 2 OP MS visits separated by 30 days minimum was adopted while maintaining the more lenient requirement of one IP MS encounter. The index date was defined as the first occurrence of meeting case criteria during December 31st, 2017, to December 31st, 2022.

Inclusion Criteria

In order to be included as a patient in the study, the patient had to meet the MS case definition of at least 2 MS OP claims at least 30 days apart within one calendar year (365 days) or at least one MS IP admission during the index period (December 31st, 2017, and December 31st, 2022). Patients had to be adults (at least 18 or older on index), not missing MSA or age on index and have at least one year of continuous pre-index enrollment (Figure 2).

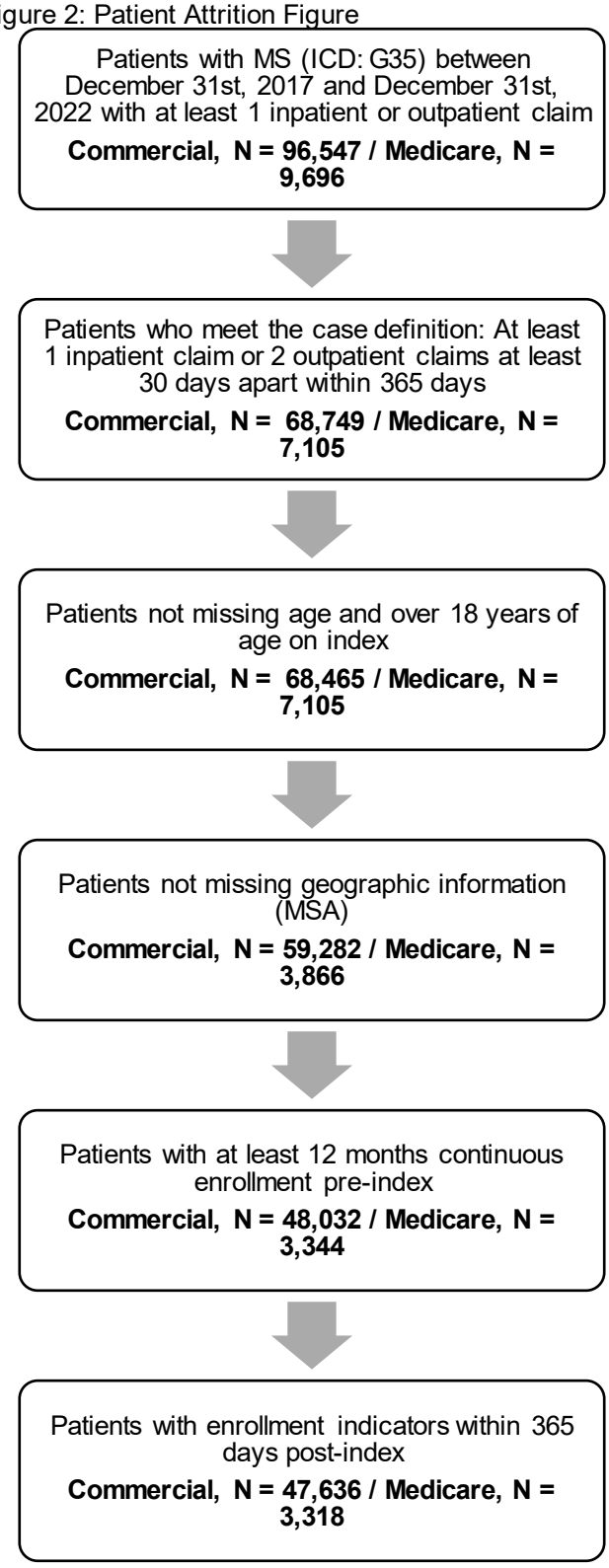
Exclusion Criteria

Those missing age or MSA upon index or who were below age 18 upon index were not included. Patients without one-year continuous pre-index were excluded from the analysis. Cohort selection is visualized in Figure 2.

Follow-Up Period

Patients were followed for up to a year following their index date. Patients were followed until they left the insurance plan, for 12 months post-index or until the end of the study period, December 31st, 2023, whichever came first.

Figure 2: Patient Attrition Figure



Study Measures and Outcomes

Baseline Patient Characteristics

We assessed baseline characteristics including patient age, MSA, gender, region, health plan type, Charlson Comorbidity Index (CCI) and employment classification. Among patients with non-missing MSA, an MSA of 0 indicated the patient was in a rural location and an MSA that is non-zero indicated an urban location(Figure 2).

Primary Outcomes

Our primary outcomes of interest were HCRU in the 6 months following patient index and healthcare costs. We chose a 6-month follow-up period for HCRU, as most patients (94%) had complete follow-up for at least six months. HCRU components analyzed include the number of IP visits, the number of ED visits, the number of OP services and the number of OP pharmacy fills. Definitions for the visits were adapted from previous literature and outlined in Supplementary Table S1.

We assessed total 1-year costs, as well as costs separately by care setting/service type (IP, ED, OP services, and pharmacy). For costs, we selected a one-year follow-up period and used the Kaplan-Meier sample average (KMSA) to account for censoring beyond 6 months. Total healthcare costs are the sum of IP, ER, OP, and pharmacy costs. Healthcare costs were measured from a payer's perspective (health plan payment plus the coordination of benefit excluding patient payments).

Statistical Analysis

We summarized baseline characteristics using descriptive characteristics. Continuous variables were characterized using mean and standard deviation (SD) and median and interquartile range (IQR) when appropriate. For categorical variables, counts are given with their corresponding percentages.

To summarize HCRU, we calculated the number of patients having ≥ 1 admission and the mean number of IP admissions, among those who had at least 1 IP admission. We also calculated the mean length of stay per admission for those that had an IP admission. For ED visits, we calculated the number of patients who had ≥ 1 admission, and among those that did have an ED admission, the average number of ED visits per patient. For OP services, we calculated the number of patients that had at least 1 service, and among those that did, the mean number of valid OP services and the same with OP pharmacy fills. This analysis was run in the overall commercial and Medicare cohorts but then also stratified by rural and urban status. We conducted a descriptive analysis in this study but future work can consider formally testing differences using comparative statistical testing.

To summarize costs, the mean 1-year cumulative cost following index date was estimated using the Kaplan Meier sample average (KMSA) to account for differential follow-up due to censoring. We censored patients at discontinuation of insurance coverage, after 12 months of follow-up or at the end of the study period, whichever occurred first. We estimated the cumulative mean costs during the 1-year post-index period by calculating the sum of the monthly mean costs among patients who remained in the health plan at the start of each month, weighted by the Kaplan-Meier estimate of the probability of remaining in the health plan at the start of each month. Nonparametric bootstrapping with 10,000 independent samples was used to generate percentile-based 95% CIs for the KMSA estimates. We reported costs as 1-year and monthly means. We performed cohort selection and statistical analyses using SAS version 9.4 (SAS Institute, Cary, NC) and R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline Characteristics

A total of 47,636 commercial-enrolled MS patients and 3,318 Medicare-enrolled MS patients met the study inclusion criteria. The mean age of each cohort was 47 years (SD 10.7) and 71 years (SD 6.9)

respectively. There were expected differences between the commercial and Medicare cohort in terms of Charlson Comorbidity Index (CCI) Score, employment status and geographical region.

In the commercial cohort, there were some differences between rural and urban patients. The average age in the rural cohort was slightly higher than the urban cohort, 48.1 years (SD 10.7) versus 47.2 years (SD 10.7). The majority of patients in both cohorts were active full-time employees (65.8% vs.75.5% for rural and urban respectively), had a preferred provider organization (PPO) health plan (56.9% vs. 47.4%), were female (77.2% vs. 75.6%), had a CCI score of 0 (83.2% vs. 84.8%) and had received MS Care during the baseline pre-index period (89.3% vs. 90.3%). However, for geographical region, the urban cohort is more evenly spread out across Northeast, North Central, South and West (22.4%, 22.1%, 38.3%, 17.1%) whereas the rural cohort is concentrated in the South and North Central areas (45.8%, 31.8%).

The Medicare rural and urban cohorts did not have any major difference. In the rural cohort the average age was 71.1 years (SD 6.8) and 71.5 years (SD 7.0) in the urban cohort. The majority of patients in both cohorts were Medicare Eligible Retirees for Employment Status (78.3% vs. 72.2% for rural and urban respectively), had a PPO health plan (71.8% vs. 58.6%), were female (76.4% vs. 75.6%), had a CCI score of 0 (73.2% vs. 74.2%) and received MS care during baseline (81.0% vs. 81.7%). Patients were more spread out across categories in terms of plan type and geographical region in the urban cohort than the rural cohort; however, in both cohorts, more patients were located in the north central geographical region (65.7% for rural, 46.0%% for urban) than any other region.

Table 1. Baseline Demographics for Commercial and Medicare Supplemental Cohorts

	Commercial Insurance			Medicare Supplemental		
Variable	Overall (N = 47,636)	Rural (N = 5,623)	Urban (N = 42,013)	Overall (N = 3,318)	Rural (N = 785)	Urban (N = 2,533)
Age (mean, SD)	47.3 (10.7)	48.1(10.7)	47.2(10.7)	71.4 (6.9)	71.1 (6.8)	71.5 (7.0)
Employment Status (N (%)						
Active Full Time	35,410 (74.3%)	3,701 (65.8%)	31, 709 (75.5%)	217 (6.5%)	44 (5.6%)	173 (6.8%)
Active Part-Time or Seasonal	565 (1.2%)	33 (0.6%)	532(1.3%)	15 (0.5%)	0 (0.0%)	15 (0.6%)
Early Retiree	2,637 (5.5%)	531 (9.4%)	2,106 (5%)	29 (0.9%)	9 (1.1%)	20 (0.8%)
Medicare Eligible Retiree	505 (1.1%)	112 (2.0%)	393 (0.9%)	2,444 (73.7%)	615 (78.3%)	1,829 (72.2%)
Retiree (Unknown)	29 (0.1%)	3 (0.1%)	26 (0.1%)	10 (0.3%)	0 (0.0%)	10 (0.4%)
COBRA Continuee	337 (0.7%)	33 (0.6%)	304 (0.7%)	1 (0%)	0 (0.0%)	1 (0.0%)
Long Term Disability	674 (1.4%)	80 (1.4%)	594 (1.4%)	22 (0.7%)	2 (0.3%)	20 (0.8%)
Surviving Spouse/Dependent	159 (0.3%)	30 (0.5%)	129 (0.3%)	324 (9.8%)	83 (10.6%)	241 (9.5%)
Other/Unknown	7,320 (15.4%)	1,100 (19.6%)	6,220 (14.8%)	256 (7.7%)	32 (4.1%)	224 (8.8%)
Type of Plan (N (%))						
Basic/Major Medical	1 (0%)	0 (0%)	1 (0%)	0 (0%)	0 (0%)	0 (0%)
Comprehensive	1,154 (2.4%)	138 (2.5%)	1,016 (2.4%)	660 (19.9%)	118 (15.0%)	542 (21.4%)
EPO	403 (0.8%)	33 (0.6%)	370 (0.9%)	20 (0.6%)	3 (0.4%)	17 (0.7%)
HMO	5,884 (12.4%)	416 (7.4%)	5,468 (13.0%)	496 (14.9%)	85 (10.8%)	411 (16.2%)

POS	5,032 (10.6%)	485 (8.6%)	4,547 (10.8%)	16 (0.5%)	3 (0.4%)	173 (0.5%)
PPO	23,104 (48.5%)	3,199 (56.9%)	19,905 (47.4%)	2,048 (61.7%)	564 (71.8%)	1,484 (58.6%)
POS with Capitation	374 (0.8%)	12 (0.2%)	362 (0.9%)	2 (0.1%)	0 (0.0%)	2 (0.1%)
CDHP	4,782 (10.0%)	698 (12.4%)	4,084 (9.7%)	15 (0.5%)	2 (0.3%)	13 (0.5%)
HDHP	5,471 (11.5%)	517 (9.2%)	4,954 (11.8%)	28 (0.8%)	5 (0.6%)	23 (0.9%)
Missing	1,431 (3.0%)	125 (2.2%)	1,306(3.1%)	33 (1.0%)	5 (0.6%)	28 (1.1%)
Gender (N (%))						
Female	36,088(75.8 %)	4,341 (77.2%)	31,747 (75.6%)	2,514 (75.8%)	600 (76.4%)	1,914 (75.6%)
Male	11,548 (24.2%)	1,282 (22.8%)	10,266 (24.4%)	804 (24.2%)	185 (23.6%)	619 (24.4%)
Geographical Region (N (%))						
Northeast	10,053 (21.1%)	624 (11.1%)	9,429 (22.4%)	570 (17.2%)	107 (13.6%)	463 (18.3%)
North Central	11,087 (23.3%)	1,788 (31.8%)	9,299 (22.1%)	1,682 (50.7%)	516 (65.7%)	1,166 (46.0%)
South	18,672 (39.2%)	2,575 (45.8%)	16,097 (38.3%)	669 (20.2%)	106 (13.5%)	563 (22.2%)
West	7,819 (16.4%)	631 (11.2%)	7,188(17.1%)	397 (12.0%)	56 (7.1%)	341 (13.5%)
Unknown	5 (0.0%)	5(0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Charlson Comorbidity Score Index (CCI) (N (%))						
0	40,304 (84.6%)	4,714 (83.2%)	35,638 (84.8%)	2,454 (74.0%)	575 (73.2%)	1,879 (74.2%)
1	3,920 (8.2%)	531 (9.4%)	3,397 (8.1%)	471 (14.2%)	124 (15.8%)	347 (13.7%)
2	2,174 (4.6%)	259 (4.6%)	1,921 (4.6%)	280 (8.4%)	66 (8.4%)	214 (8.4%)
3+	1,238 (2.6%)	162 (2.9%)	1,082 (2.6%)	113 (3.4%)	20 (2.5%)	93 (3.7%)
Recent MS Care during Baseline						
Yes	42,954 (90.2%)	5,021 (89.3%)	37,933 (90.3%)	2,705 (81.5%)	636 (81.0%)	2,069 (81.7%)
No	4,682 (9.8%)	602 (10.7%)	4,080 (9.7%)	613 (18.5%)	149 (19.0%)	464 (18.3%)

EPO = Exclusive Provider Organization Plan; HMO = Health Maintenance Organization Plan; POS = Point-of-Service Plan; PPO = Preferred Provider Organization Plan; CDHP = Consumer-Driven Health Plan; HDHP = High-Deductible Health plan

Primary Outcomes

Healthcare Resource Utilization

IP admissions. During the 6 months following the index date, among commercial patients, at least one IP admission was observed in 603 (10.7%) of the rural patients and in 4,893 (11.7%) of the urban patients. The rural cohort had an average of 1.34 (SD 0.8) IP admissions per patient and an average length of stay

(LOS) of 4.4 days (SD 4.9) among those that had an IP admission. The urban cohort had an average of 1.3 (SD 0.8) IP admissions and average LOS of 4.4 (SD 5.5) per patient. In the Medicare group, at least one IP admission was observed in 136 (17.3%) of the rural patients and 566 (22.3%) of the urban patients. The rural patients had an average of 1.3 (SD 0.7) IP admissions and a mean LOS of 4.98 (SD 3.75) days per patient. The urban patients had average 1.36 (SD 0.81) and a mean LOS of 5.9 (SD 6.6) days per patient. Rural commercial patients had a slightly elevated mean number of IP admissions and length of stay than the urban patients. This trend is not repeated in the Medicare Supplemental population. The rural cohort had a lower mean number of IP admissions and LOS compared to the urban cohort.

ED visits. For ED visits, 875 (15.6%) rural commercial patients and 6,086 (14.5%) of urban commercial patients had an ED visit. The rural patients had an average of 1.5 (SD 1.4) ED visits per patient and the urban patients had an average of 1.6 (SD 1.5) ED visits per patient among those that had an ED visit. In the Medicare group 155 (19.7%) of rural patients visit and 540 (21.3%) urban patients had an ED visit. Among those that had an ED visit, the rural patients had an average of 1.7 (SD 1.3) ED visits per patient and the urban patients had 1.8 (SD 1.8). For ED visits, in both the commercial and Medicare cohorts, the rural patients had lower average ED visits than the urban patients.

OP services. For OP services, 5,571 (99.1%) rural patients and 41,588 (98.9%) urban patients had an OP service . Among those, rural commercial patients had an average of 9.4 (SD 9.0) OP services per patient and urban commercial patients had 10.0 (SD 10.0). In the Medicare population, 764 (97.3%) rural patients and 2,454 (96.9%) urban patients had an OP service. Among those, rural Medicare patients had an average of 12.7 (SD 13.6) OP services while urban patients had an average of 14.4 (SD 14.3) per patient. The rural patients in both insurance cohorts had fewer OP services among those that did have OP services 6 months post-index compared to urban patients.

OP Pharmacy fills. The commercial cohort had 5,016 (89.2%) rural patients and 36,528 (86.9%) urban patients with an eligible OP pharmacy fill. Among those, rural patients had an average of 31.5 (SD 20.8) 30-day standardized fills while urban patients had an average of 27.7 (SD 19.4). In the Medicare group, 706 (89.9%) rural patients and 2,324 (91.7%) urban patients had an eligible OP pharmacy fill. Of those that had an eligible fill, the rural patients had an average 30-day standardized fill of 38.1 (SD 23.9) per patient and urban patients had 36.6 (SD 20.2). For both commercial and Medicare insurance, the rural cohorts had higher mean and median OP pharmacy fills than the urban cohorts.

Table 2: Healthcare Resource Utilization for commercially insured patients

	Commercial Insurance			Medicare Supplemental Insurance		
Characteristic	Total Study Population (N = 47, 636)			Total Study Population (N = 3,318)		
Medical HCRU	Overall (N = 47,636)	Rural (N = 5,623)	Urban (N = 42,013)	Overall (N = 3,318)	Rural (N = 785)	Urban (N = 2,533)
Inpatient (IP) Admissions						
Had >=1 admission (N, %)	5,496 (11.5%)	N = 603 (10.7%)	N = 4,893 (11.7%)	702 (21.2%)	136 (17.3%)	566 (22.3%)
Number of admissions among patients with >=1 admission, mean (SD)	1.3 (0.8)	1.4 (0.8)	1.3 (0.8)	1.3 (0.8)	1.3 (0.7)	1.4 (0.8)
Median (IQR)	1.0 (1.0-1.0)	1.0 (1.0 – 1.0)	1.0 (1.0- 1.0)	1.0 (1.0 - 1.0)	1.0 (1.0 - 1.0)	1.0 (1.0 - 1.0)

Range (Min – Max)	1.0 - 11.0	1.0 - 10.0	1.0 - 11.0	1.0 - 10.0	1.0 - 4.0	1.0 - 10.0
Length of stay per admission among patients with >=1 admission, mean (SD), days	4.4 (5.4)	4.4 (4.9)	4.4 (5.5)	5.7 (6.2)	5.0 (3.8)	5.9 (6.6)
Median (IQR)	3.0 (2.0 - 5.0)	3.0 (2.0 - 5.0)	3.0 (2.0 - 5.0)	4.0 (2.0 - 7.0)	4.0 (2.0 - 6.5)	4.0 (2.0 - 7.0)
Range (Min – Max)	1.0 - 152.0	1.0 - 45.0	1.0 - 152.0	0.0 - 77.0	1.0 - 22.0	0.0 - 77.0
Emergency Department (ED) Visits						
Had >=1 visit (N, %)	6,961 (14.6%)	875 (15.6%)	6,086 (14.5%)	695 (20.9%)	155 (19.7%)	540 (21.3%)
Number of visits among patients with >=1 visit, mean (SD)	1.6 (1.5)	1.5 (1.4)	1.6 (1.5)	1.7 (1.7)	1.7 (1.3)	1.8 (1.8)
Median (IQR)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	1.0 (1.0 - 2.0)	1.0 (1.0 - 2.0)	1.0 (1.0 - 2.0)
Range (Min – Max)	1.0 - 44.0	1.0 - 27.0	1.0 - 44.0	1.0 - 26.0	1.0 - 9.0	1.0 - 26.0
Outpatient (OP) Services						
Had >=1 visit (N, %)	47,159 (98.9%)	5,571 (99.1%)	41,588 (98.9%)	3,218 (96.9%)	764 (97.3%)	2,454 (96.9%)
Number of services among patients with >=1 service, mean (SD)	10.0 (9.9)	9.4 (9.0)	10.0 (10.0)	14.0 (14.2)	12.7 (13.6)	14.4 (14.3)
Median (IQR)	7.0 (4.0 - 13.0)	7.0 (4.0 - 12.0)	7.0 (4.0 - 13.0)	10.0 (5.0 - 18.0)	9.0 (5.0 - 16.0)	10.0 (5.0 - 19.0)
Range (Min – Max)	1.0 - 179.0	1.0 - 92.0	1.0 - 179.0	1.0 - 180.0	1.0 - 178.0	1.0 - 180.0
Pharmacy HCRU	Overall (N = 47,636)	Rural (N = 5,623)	Urban (N = 42,013)	Overall (N = 3,318)	Rural (N = 785)	Urban (N = 2,533)
OP Pharmacy Fills*						
Had >=1 fill (N, %)	41,544 (87.2%)	5,016 (89.2%)	36,528 (86.9%)	3,030 (91.3%)	706 (89.9%)	2,324 (91.7%)
Number of 30 day fills among patients with >=1 fill, mean (SD)	28.2 (19.6)	31.5 (20.8)	27.7 (19.4)	36.9 (21.1)	38.1 (23.9)	36.6 (20.2)
Median (IQR)	23.9 (13.7 - 38.2)	27.3 (15.9 - 42.6)	23.4 (13.4 - 37.3)	34.5 (22.3 - 48.7)	35.9 (22.3 - 48.9)	34.2 (22.3 - 48.7)

Range (Min – Max)	0.03 - 155.6	0.03 - 123.1	0.03 - 155.6	0.03 - 115.7	0.03 - 107.2	0.03 - 115.7

HCRU = Healthcare Resource Utilization

Health Care Costs

The mean cumulative 1-year healthcare costs for rural commercial patients were $49,398 (95% CI: $47,943 - $50,936) and $51,286 (95% CI: $50,709 - $51,873) for urban patients. Mean cumulative, 1-year healthcare costs for rural Medicare patients were $39,540 (95% CI: $36,106 - $43,246) and $39,103 (95% CI: $37,105 - $41,228) for urban Medicare patients. Cumulative costs were calculated as the sum of IP, OP, ED and pharmacy costs. Mean monthly and 1-year costs are presented in Table 2 for IP, OP, ED, pharmacy costs and cumulative costs for the overall commercial and Medicare cohorts and then separated by rural and urban status.

Table 2: Healthcare Costs for commercially insured patients

Outcome	Month											
	1	2	3	4	5	6	7	8	9	10	11	12
Inpatient (IP)												
Monthly Overall IP Admissions Costs, mean	$2,442	$501	$351	$295	$357	$260	$137	$138	$122	$85	$105	$49
1-year Overall IP Admissions Cost, mean (95% CI)	$4,841 ($4,588 - $5,114)											
Monthly Rural IP admissions costs, mean	$2,061	$477	$205	$223	$336	$174	$106	$144	$85	$48	$143	$49
1-year Rural IP Admissions Cost, mean (95% CI)	$4,093 ($3,587 - $4,701)											
Monthly Urban IP Admissions Costs	$2,537	$523	$363	$370	$413	$216	$142	$152	$126	$100	$77	$49
1-year Urban IP Admissions Cost, mean (95% CI)	$4,942 ($4,665 - $5,236)											
Emergency Department (ED)												
Monthly Overall ED Visits Costs, mean	$251	$86	$88	$84	$78	$66	$34	$38	$31	$25	$20	$10
1-year Overall ED costs, mean (95% CI)	$780 ($742 - $822)											
Monthly, Rural ED costs	$206	$82	$54	$58	$59	$55	$30	$35	$29	$33	$20	$5

1-year Rural ED costs, mean (95% CI)	$639 ($575 - $712)											
Monthly, Urban ED Costs	$227	$99	$90	$80	$71	$70	$32	$49	$30	$25	$21	$9
1-year Urban ED costs, mean (95% CI)	$798 ($756 - $844)											
Outpatient (OP) Services												
Monthly Overall OP Services Costs	$4,616	$2,305	$2,145	$2,054	$1,739	$1,525	$2,243	$1,791	$1,705	$1,447	$1,328	$312
1-year Overall OP Services Cost, mean (95% CI)	$23,317 ($22,893 - $23,737)											
Monthly Rural OP Services Costs	$4,052	$1,786	$1,834	$1,752	$1,561	$1,237	$2,089	$1,578	$1,543	$1,298	$1,244	$287
1-year Rural OP Services Cost, mean (95% CI)	$19,698 ($18,664 - $20,786)											
Monthly Urban OP Services Costs	$4,209	$2,083	$1,913	$1,879	$1,664	$1,376	$2,058	$1,624	$1,448	$1,322	$1,205	$288
1-year Urban OP Services Cost, mean (95% CI)	$20,920 ($20,523 - $21,314)											
Pharmacy Fills												
Monthly Overall Pharmacy Fills Costs	$2,855	$2,676	$2,624	$2,549	$2,348	$2,226	$2,190	$2,059	$1,897	$1,803	$1,775	$387
1-year Overall Pharmacy Fills Cost, mean (95% CI)	$25,365 ($25,074 - $25,658)											
Monthly Rural Pharmacy Fill Costs	$2,949	$2,627	$2,469	$2,627	$2,362	$2,144	$2,256	$2,059	$1,922	$1,972	$1,996	$408
1-year Rural Pharmacy Fills Cost, mean (95% CI)	$25,594 ($24,786 - $26,439)											
Monthly Urban Pharmacy Costs	$2,909	$2,671	$2,559	$2,559	$2,340	$2,280	$2,179	$2,024	$1,910	$1,784	$1,752	$376
1-year Urban Pharmacy Fills	$25,333 ($25,018 - $25,651)											

Cost, mean (95% CI)												
Cumulative Health Costs												
Monthly Cumulative Costs, Overall	$9,588	$5,196	$4,897	$4,649	$4,207	$3,835	$4,394	$3,806	$3,462	$3,148	$2,969	$675
1-year Total Cumulative Costs, mean (95% CI)	$51,059 ($50,517 – $51,596)											
Monthly Cumulative Costs, Rural	$9,397	$5,195	$4,501	$4,782	$4,201	$3,600	$4,287	$3,935	$3,244	$3,318	$3,349	$812
1-year Total Rural Cumulative Costs, mean (95% CI)	$49,398 ($47,943 - $50,936)											
Monthly Cumulative Costs, Urban	$9,838	$5,231	$4,970	$4,649	$4,414	$3,899	$4,326	$3,694	$3,495	$3,116	$3,009	$686
1-year Total Urban Cumulative Costs, mean (95% CI)	$51,286 ($50,709 - $51,873)											

Table 3: Healthcare costs for Medicare patients

Outcome	Month											
	1	2	3	4	5	6	7	8	9	10	11	12
Inpatient (IP)												
Monthly Overall IP Admissions Costs	$2,591	$962	$701	$525	$747	$952	$148	$253	$120	$100	$214	$173
1-year Overall IP Admissions Cost, mean (95% CI)	$7,045 ($6,312 - $7,866)											
Monthly Rural IP admissions costs	$1,461	$700	$417	$240	$375	$964	$229	$184	$37	$199	$126	$22
1-year Rural IP Admissions Cost, mean (95% CI)	$4,829 ($3,896 - $5,902)											
Monthly Urban IP Admissions Costs	$2,655	$692	$906	$506	$506	$752	$286	$400	$151	$69	$88	$439
1-year Urban IP Admissions Cost, mean (95% CI)	$7,724 ($6,787 - $8,762)											
Emergency Department (ED)												

Monthly Overall ED Visits Costs	$214	$116	$63	$108	$120	$95	$25	$30	$40	$26	$13	$5
1-year Overall ED costs, mean (95% CI)	$880 ($745 - $1,037)											
Monthly Rural ED costs	$307	$35	$41	$23	$34	$27	$2	$23	$66	$10	$9	$9
1-year Rural ED costs, mean (95% CI)	$664 ($499 – $858)											
Monthly Urban ED Costs	$205	$149	$121	$55	$80	$102	$46	$22	$58	$50	$32	$4
1-year Urban ED costs, mean (95% CI)	$948 ($776 - $1142)											
Outpatient (OP) Services												
Monthly Overall OP Services Costs	$2,448	$1,426	$1,111	$1,276	$1,144	$1,076	$1,183	$952	$911	$898	$773	$196
1-year Overall OP Services Cost, mean (95% CI)	$13,614 ($12,722 - $14,573)											
Monthly Rural OP Services Costs	$2,554	$1,637	$1,547	$1,329	$1,198	$938	$1,135	$1,181	$1,230	$950	$1,184	$213
1-year Rural OP Services Cost, mean (95% CI)	$15,173 ($12,861 - $17,802)											
Monthly Urban OP Services Costs	$2,599	$1,463	$1,140	$1,324	$1,007	$994	$1,141	$1,092	$788	$843	$824	$118
1-year Urban OP Services Cost, mean (95% CI)	$13,158 ($12,224 - $14,140)											
Pharmacy Fills												
Monthly Overall Pharmacy Fills Costs	$2,062	$1,906	$1,770	$1,635	$1,817	$1,551	$1,550	$1,381	$1,200	$1,171	$1,168	$176
1-year Overall Pharmacy Fills Cost, mean (95% CI)	$18,065 ($16,997 - $19,177)											
Monthly Rural DMT Fills Costs	$1,610	$1,836	$1,797	$1,585	$1,867	$1,632	$1,751	$1,480	$1,348	$1,213	$1.225	$209

1-year Rural DMT Fills Cost, mean (95% CI)	$19,237 ($17,121 - $21,385)											
Monthly Urban Fills Costs	$2,294	$1,978	$1,872	$1,766	$1,557	$1,614	$1,575	$1,256	$1,180	$1,148	$1,100	$167
1-year Urban Fills Cost, mean (95% CI)	$17,699 ($16,460 - $19,008)											
Cumulative Health Costs												
Monthly Cumulative Costs, Overall	$7,219	$4,076	$3,886	$3,678	$3,479	$3,596	$3,205	$2,699	$2,397	$2,419	$2,393	$386
1-year Total Cumulative Costs, mean (95% CI)	$39,203 ($37,438 - $40,989)											
Monthly Cumulative Costs, Rural	$6,476	$4,060	$3,079	$3,456	$3,755	$2,295	$3,074	$3,226	$2,567	$2,462	$2,675	$553
1-year Total Rural Cumulative Costs, mean (95% CI)	$39,540 ($36,106 - $43,246)											
Monthly Cumulative Costs, Urban	$7,481	$4,101	$4,138	$3,703	$3,431	$3,265	$3,035	$2,404	$2,091	$2,278	$2,009	$266
1-year Total Urban Cumulative Costs, mean (95% CI)	$39,103 ($37,105 - $41,228)											

Discussion

We conducted a retrospective cohort study on commercial and Medicare-enrolled patients with MS and described all-cause HCRU and healthcare cost by rural or urban status for all adult MS patients. In this study, rural commercial patients tended to have a higher mean number of IP admissions and a longer LOS than urban commercial patients. However, in the Medicare cohort, the rural patients had lower mean IP admissions, and a lower LOS than the urban cohort. For ED visits and OP services, for both the commercial and Medicare cohorts, the rural patients had lower average utilization than the urban patients. However, this is reversed when it comes to OP pharmacy fills. For both commercial and Medicare insurance, the rural cohorts have higher mean and median OP pharmacy fills than the urban cohorts. In general, the rural patient's lower utilization results in having lower costs when compared to the urban cohort. The categories in which rural patients had higher utilization, resulted in them having higher costs than the urban patients. An example is the IP admissions costs for the rural patients were higher than when compared to the urban patients for commercially insured patients. Another example was the pharmacy costs since the rural patients in both the commercial and Medicare cohort had higher utilization than urban patients in that category and thus higher costs. An interesting exception to this is in the Medicare outpatient services category where Medicare patients had lower utilization but higher costs. Rural commercial patients had lower cumulative, mean, 1-year costs compared to urban commercial patients. Medicare rural patients had slightly higher cumulative, mean, 1-year costs compared to commercial patients. For both the commercial and Medicare patients, the majority of the cumulative costs were from OP pharmacy fills and OP services.

In published literature, differential utilization and expenditure patterns emerge between rural and urban patients but have not been explored in MS patients. Studies looking at general trends of ED and acute preventable care have noted that rural patients have increased ED visits and hospitalizations compared to urban patients[12,13]. Higher IP admissions in the rural commercial cohort compared to urban, could support the theory that rural patients are presenting to the hospital in worse shape than urban patients due to lack of medical services. The lower IP costs for the rural commercial patients calls into question the quality of services these patients are receiving. A theory suggested by Jiang et al., suggests that rural patients rely more on prescription medications since they have reduced access to medical services[14]. This theory may support the observed trend in the rural MS patients in our study. This would also align with the trends seen throughout the HCRU categories with the rural cohorts having less medical service utilization. Another interesting result is the OP costs for rural patients in both cohorts, is higher than for urban patients, despite the rural patients have lower average numbers of OP visits. This could signify rural patients compensating for reduced access to healthcare by having several tests and procedures done in one doctor's visit compared urban patients spreading such things out. The 1-year, cumulative mean costs for the Medicare rural cohort is slightly more than the Medicare urban cohort. Finally, in both the Medicare and commercial cohort, the OP pharmacy fill costs for rural patients are much higher when compared to the urban patients, contributing to the higher cumulative cost, signifying that medication cost could be a disproportionate burden on rural MS patients.

These findings have several implications for researchers and policymakers. The results of this study showed some differences in HCRU and healthcare costs for rural versus urban MS patients. We conducted a descriptive analysis in this study but future work can consider formally testing differences using comparative statistical testing. In general, with the exception of rural commercial IP admission and LOS, rural patients had lower HCRU and costs than urban patients. Future steps for researchers would be to characterize whether these disparities between rural and urban are due to differential access to medical services, reduced quality of care or due to some other factors. An important question to answer is if rural patients have lower utilization and costs because their disease is better managed or if they are simply not utilizing the healthcare system when necessary. Conversely, it could be possible that urban MS patients are over-utilizing healthcare resources. The increased medication use of rural patients compared to urban patients my signify an increased reliance on prescription medications to substitute for lack of medical services. Future work would serve to investigate and characterize this difference. Medication use for rural Medicare patients was much higher than urban Medicare patients, which could be of interest to policymakers. The Inflation Reduction Act's Medicare benefit redesign and drug price negotiation could reduce the burden of medication cost on these patients and improve outcomes.

There are several limitations to this study, the first of which is potentially misclassifying patients as MS cases. There is no one algorithm used to identify MS cases in electronic health claims data and the algorithm used in this study is not validated but has been used in previous literature[15]. We tested several case identification algorithms before requiring patients to have 1 IP MS visit or 2 OP MS visits, at least 30 days apart, in one year. We rejected algorithms requiring patients to fill a DMT for MS, to include those not taking prescription therapy for MS. Instituting a 30-day separation between OP MS claims was more discerning, fewer patients qualified as cases, than requiring 3 OP MS visits with no separation. Considering those patients to be potentially misdiagnosed within the first month of their encounter, the stricter definition of 2 OP MS visits separated by 30 days minimum was adopted while maintaining the more lenient requirement of one IP MS encounter.

Another major limitation of this study is how rural versus urban status was determined. The MSA value upon the patient's index date was set as that patient's designation throughout the study. However, as can be seen from the descriptive characteristics, the two cohorts are very similar to each other. This may mean that this method of classification does not accurately represent residential status. Moreover, there was a large amount of censoring that occurred due to patients having a missing MSA upon index. Approximately 14% of the commercial cohort was lost and 46% of the Medicare cohort was lost at this attrition step. This large amount of censoring is a limitation to my study in that it restricts the generalizability of my results to patients who had MSA upon index. Moreover, due to potential differences between the patients missing MSA upon index date and those not missing, my patient population is

biased towards those that have this information on their claims data. Why so many patients in the Medicare cohort were missing MSA is unknown at this time. Additionally, the duration of follow-up differed among patients. To account for differential follow-up, outcomes were analyzed using the KMSA estimator. We assumed all censoring was noninformative and that patients whose costs were observed were representative of patients whose costs were not observed. This assumption may not be accurate due to the rolling case identification period over 5 years. This study was susceptible to other inherent issues with retrospective cohort studies using claims data, such as coding errors or differences in billing practices.

We conducted a retrospective cohort study on commercial and Medicare-enrolled patients with MS and described overall HCRU and healthcare cost by rural or urban status for all MS patients. For the most part, rural patients had lower average healthcare resource utilization, and thus lower costs, than the urban patients. However, this is not the case when it comes to OP pharmacy fills and costs. In this category, rural patients have higher mean and median pharmacy fills and have higher costs in both insurance categories. This may point to rural MS patients relying more on prescription drugs to compensate for reduced access to medical services. MS patients require complicated care and insight into their HCRU, and costs can aid healthcare decision-makers in optimizing care for these patients.

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Supplementary Information /Appendix

Table S1: Admissions Definition Criteria

Claim Type *Adapted from Qian et. Al	Definition
ED (ED) Visits	1. Distinct SVCDATE AND 2. STDPLAC = 23 (ED – hospital) OR 3. SVCSCAT ending with “20” (emergency services)
IP Admission	1. Distinct SVCDATE
OP Visits	1. Distinct OP claim AND 2. Not an ED Claim as defined above AND STDPLAC = 11 (office), 12 (patient home), 15 (mobile unit), 17 (walk-in retail clinic), 18 (place of employment), 19 (on-campus OP hospital), 20 (urgent care center), 22 (off-campus OP hospital), 24 (ambulatory surgery center), 41 (ambulance-land), 42 (ambulance-Air or water), 49 (independent clinic), 50 (federally qualified health center), 53 (community mental health center), 56 (psychiatric residential treatment center), 57 (non-residential substance abuse treatment facility), 62 (comprehensive OP rehabilitation facility), 65 (ESRD Treatment Facility), 71 (state or local public health clinic), 72 (rural health clinic), 95 (OP not elsewhere classified), 99 (other).
Pharmacy Fill	1. Distinct SVCDATE AND 2. Distinct NDCNUM

Table S2: Outpatient Pharmacy Fills (**NOT** standardized to 30 days)

	Commercial Insurance			Medicare Supplemental		
Pharmacy HCRU	Overall (N = 47,636)	Rural (N = 5,623)	Urban (N = 42,013)	Overall (N = 3,318)	Rural (N = 785)	Urban (N = 2,533)
OP Pharmacy Fills						
Had >=1 fill (N, %)	41,565 (87.3%)	5,023 (89.3%)	36,542 (86.9%)	3,146 (94.8%)	747 (95.2%)	2,399 (95.3%)
Number of fills among patients with >=1 admission, mean (SD)	27.1 (19.8)	30.9 (21.6)	26.5 (19.4)	35.5 (29.9)	37.1 (29.1)	34.9 (30.2)
Median (IQR)	22.00 (13-36)	25.00 (15.00 - 41.00)	21.00 (13.00 - 35.00)	27.00 (18.00 - 43.00)	28.00 (18.00 - 43.00)	27.00 (17.00 - 42.00)

Range (Min – Max)	1.00 - 162.00	1.00 - 138.00	1.00 - 162.00	1.00 - 265.00	1.00 - 153.00	1.00 - 265.00

Table S3: All Distinct Outpatient Services

	Commercial Insurance			Medicare Supplemental		
OP Visits						
Had >=1 visit (N, %)	47,536 (99.7%)	5,612 (99.8%)	41,924 (99.7%)	3,298 (99.3%)	782 (99.6%)	2,516 (99.3%)
Number of visits among patients with >=1 visit mean (SD)	11.08 (10.8)	10.28 (9.8)	11.19 (10.9)	17.03 (16.7)	15.22 (15.6)	17.59 (17.0)
Median (IQR)	8.00 (4.00-14.00)	8.00 (4.00 - 13.00)	8.00 (4.00 - 14.00)	12.00 (6.00 - 22.00)	11.00 (5.00 - 20.00)	12.00 (6.00 - 23.00)