Presenting author: Abhijit Gadkari | abhijit.gadkari@novartis.com

Travel Burden for Patients With Multiple **Sclerosis Treated** With Infusion Disease-**Modifying Therapies**

Ming-Hui Tai,¹ Swetha R. Palli,¹ Qiujun Shao,¹ Brandon Brown, 1 Cheng Shi, 1 John Arsenault, 2

¹Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; ²Humbi Analytics, Indian Creek, IL, USA

KEY FINDINGS & CONCLUSIONS

- Medicare beneficiaries with multiple sclerosis receiving infusion therapies traveled 83 miles per infusion visit, on average. The mean travel time per visit was 89 minutes
- Travel burden was higher in rural residents, with 32-33% of rural residents travelling >120 miles roundtrip per infusion visit compared with 17% of urban residents
- Commuting distance and time required for infusion therapies may therefore pose a significant burden for patients compared with therapies given at home
- Future research should assess the impact of travel burden on outcomes such as treatment adherence

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INTRODUCTION

- Among the disease-modifying therapies (DMTs) that are US Food and Drug Administration approved for the treatment of multiple sclerosis (MS), ofatumumab, ocrelizumab, natalizumab, alemtuzumab, and ublituximab are generally considered to be high-efficacy therapies (HETs)^{1,2}
- Except for ofatumumab, all other HETs are intravenous infusion therapies that need to be administered by health care providers (HCPs) at a hospital or infusion center or at an HCP's office.³⁻⁷ This could be a major access barrier for patients with MS due to limited mobility, time needed off work travel inconveniences, and disruption to daily activities

OBJECTIVE

To assess the travel burden for people with MS treated with

METHODS

Study Design

- This was a retrospective cohort design using 100% Medicare Fee-for-Service data from January 1, 2017 to December 31, 2023 (study period)
- Patients with MS who received ≥1 infusion DMT in clinical practice between January 1, 2017 and December 31, 2023 were included in the study. The infusion DMTs of interest included ocrelizumab, ublituximab, natalizumab, and alemtuzumab
- The index date was defined as the first observed DMT infusion during the study period. The following inclusion criteria were also applied for eligibility:
- ≥1 claim with a diagnosis of MS (International Classification of Diseases 10th Revision: G35) in any position any time during the study period
- ≥18 years of age as of the index date
- Eligible patients were also classified into specific, individual, non-mutually exclusive infusion DMT cohorts based on the receipt of infusion DMT during the study period
- The index date for each of the treatment-specific cohorts was defined as the date of the first observed claim of the respective infusion DMT under consideration
- The post-index period was defined as the period from the index date (inclusive) until the end of continuous enrollment or the end of the study period, whichever came first. Outcomes were measured during the post-index periods

Study Outcomes

- The travel (ie, commuting) distance and travel time calculations were based on the 5-digit residential zip codes of the patient (from their enrollment file) and the facility where the infusion was administered (from the infusion claim). One-way travel distance between all possible unique zip code pair combinations were calculated using the Openrouteservice time-distance matrix service (OSM)8
- For the travel distance calculation, OSM employs graph-based algorithms to find the most efficient routes on the road network. Then, the cumulative of individual road segment lengths making the most efficient route was used to calculate the 1-way driving distance
- Patients with total travel distance >250 miles were considered as outliers and excluded
- The average estimated weekday travel time between the patient's and infusion facility's 5-digit zip codes was used to calculate the travel times. It was the cumulative of the time obtained by dividing each road segment length by the corresponding maximum speed limit
- The speed calculations were based on a base speed (ie, ideal speed for an automobile under optimal conditions) that was then adjusted for road/way type, surface type, track type (grade 1-5 for indicating firmness), slope or incline, turns/intersections/roundabouts delays, and other region-specific factors (eg, traffic signals and congestions, regulations, etc.). Default OSM routing preferences were used
- Categorization of urban/rural residence was based on rural-urban commuting area codes9

Statistical Analyses

- Patient characteristics at index and study outcomes were described either as:
- Mean, SD, median, and 25th and 75th percentiles for continuous
- Frequency and percentage for categorical variables
- Total driving distance burden (computed as 2*one-way travel distance) was summarized in miles per-patient-visit (PPV) and per-patient-year (PPY)
- PPV distance was reported continuously and categorically (0-10, 11-20, 21-30, 31-60, 61-120, 121-240, and 241-500 miles)
- PPY distance was reported continuously
- Total travel time burden (computed as 2*one-way travel time) was summarized in minutes at PPV and PPY
- PPV time was reported continuously and categorically (0-30, 31-60, 61-90, 91-120, 121-180, 181-240, and >240 minutes).
- PPY times were reported continuously
- As this was a descriptive analysis, no statistical testing was performed

RESULTS

- Among 36,810 included patients receiving infusion DMTs in clinical practice, mean (SD) age was 54 (12) years, 69% were female, 78% were White, and 73% resided in urban areas. 65% received ocrelizumab at index (**Table 1**)
- Patient demographics and clinical characteristics were similar between treatment cohorts (ocrelizumab [n=26,984], natalizumab [n=11,646], alemtuzumab [n=1323], and ublituximab [n=146]), except alemtuzumab users who appear to be younger (mean [SD] age: 49 [12] years) than all other infusion DMT users

Table 1. Patient Demographic and Clinical Characteristics

| | All | Ocrelizumab | Natalizumab | Alemtuzumab | Ublituximab |
|---------------------------|-------------|-------------|---------------|-------------|-------------|
| - | (N=36,810) | (n=26,984) | (n=11,646) | (n=1323) | (n=146) |
| Age, years | | | , , , , _ , | | |
| Mean (SD) | 53.6 (12.3) | 56.4 (12.1) | 52.4 (12.2) | 49.4 (11.7) | 56.5 (11.8) |
| 18-44 | 21.5% | 19.1% | 27.7% | 37.0% | 13.7% |
| 45-64 | 47.6% | 46.6% | 50.5% | 51.3% | 50.7% |
| ≥65 | 30.8% | 34.3% | 21.7% | 11.7% | 35.6% |
| Sex | | | | | |
| Female | 69.3% | 66.8% | 75.2% | 70.4% | 71.9% |
| Male | 30.7% | 33.2% | 24.8% | 29.6% | 28.1% |
| Race | | | | | |
| Asian | 0.4% | 0.5% | 0.3% | <11 (NA) | <11 (NA) |
| Black or African American | 14.6% | 13.7% | 17.0% | 16.0% | 11.6% |
| Hispanic | 2.8% | 2.8% | 2.8% | 4.3% | <11 (NA) |
| Other | 1.1% | 1.1% | 1.1% | 1.1% | <11 (NA) |
| Unknown | 3.0% | 3.1% | 2.5% | 2.9% | <11 (NA) |
| White | 78.1% | 78.8% | 76.3% | 75.3% | 78.8% |
| Rural/urban residence | | | | | |
| Large rural | 10.9% | 10.6% | 11.1% | 13.4% | 8.2% |
| Small town/rural | 8.6% | 8.7% | 7.9% | 9.4% | <11 (NA) |
| Suburban | 10.0% | 9.9% | 10.0% | 10.4% | 9.6% |
| Unknown | <11 (NA) | <11 (NA) | 0% | 0% | 0% |
| Urban | 73.1% | 72.9% | 73.7% | 67.6% | 78.8% |
| Region | | | | | |
| Midwest | 25.4% | 26.5% | 22.2% | 24.6% | 27.4% |
| Northeast | 22.1% | 22.5% | 22.0% | 9.3% | 27.4% |
| South | 34.5% | 33.1% | 37.0% | 49.7% | 33.6% |
| Unknown | 0.2% | 0.3% | 0.1% | <11 (NA) | 0% |
| West | 17.9% | 17.6% | 18.6% | 16.3% | 11.6% |
| Year of the index date | | | | | |
| 2017 | 25.6% | 14.4% | 60.8% | 62.5% | 11.6% |
| 2018 | 24.3% | 28.4% | 11.8% | 19.3% | 8.2% |
| 2019 | 14.3% | 15.8% | 9.2% | 10.3% | <11 (NA) |
| 2020 | 10.7% | 12.1% | 6.2% | 4.2% | 7.5% |
| 2021 | 9.6% | 11.0% | 5.3% | 1.9% | <11 (NA) |
| 2022 | 8.6% | 10.1% | 4.0% | 1.0% | <11 (NA) |
| 2023 | 7.1% | 8.2% | 2.7% | <11 (NA) | 55.5% |
| Medicare entitlement | 7.170 | J.2 /0 | 2.1 /0 | -11 (14/1) | 30.070 |
| Age | 28.9% | 32.1% | 20.2% | 10.7% | 34.2% |
| Disability | 71.1% | 67.8% | 79.8% | 89.3% | 65.8% |
| Disability and ESRD | <11 (NA) | <11 (NA) | <11 (NA) | 0% | 0% |
| ESRD | <11 (NA) | <11 (NA) | <11 (NA) | 0% | 0% |
| | >11 (INA) | >11 (IVA) | >11 (IVA) | U 70 | U 70 |
| CCI category | 88.6% | 87.9% | 01.00/ | 90.60/ | 83.6% |
| Mild | | | 91.0% | 89.6% | |
| Moderate | 8.4% | 9.0% | 6.5% | 8.3% | 13.0% |
| Severe | 3.0% | 3.1% | 2.4% | 2.1% | <11 (NA) |

9. United States Department of Agriculture. Rural-urban commuting area codes. Accessed May 2, 2024. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes/

CCI, Charlson Comorbidity Index; CMS, Centers for Medicare and Medicaid Services; ESRD, end-stage renal disease; NA, not available CMS requires categories with patient numbers below 11 to be reported as <11; therefore, percentages are not available

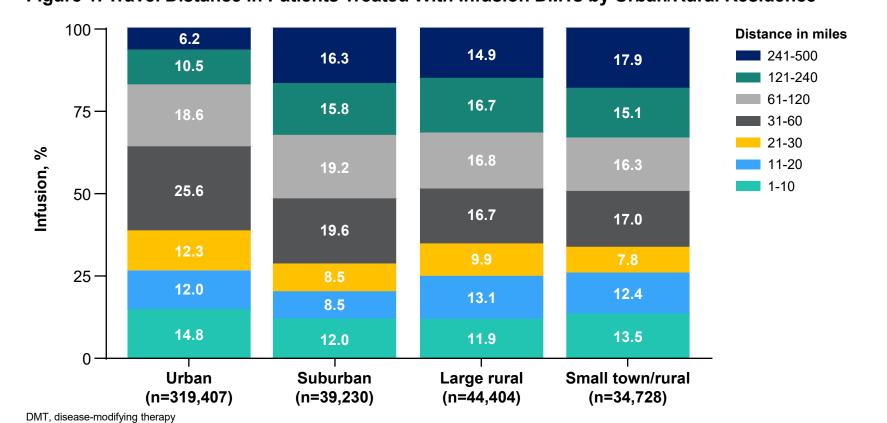
- The mean (SD) and median total distance travelled PPV for all DMTs was 83 (96) miles and 46 miles respectively. The PPV mean (SD) and median travel time was 89 (84) and 63 minutes, respectively (**Table 2**)
- Across each treatment cohort, the mean (SD) and median total distance travelled per visit ranged from 78 (96) miles and 44 miles, respectively, for ublituximab to 90 (105) miles and 46 miles, respectively for alemtuzumab. Mean (SD) and median observed travel time per visit ranged from 80 (74) and 59 minutes, respectively, for natalizumab to 123 (107) and 89 minutes, respectively, for alemtuzumab

Table 2. Summary of Travel Distance and Travel Time for Patients Treated With Infusion DMTs

| | All | Ocrelizumab | Natalizumab | Alemtuzumab | Ublituximab |
|--------------------------------------|--------------------|-------------------|---------------------|--------------------|-------------------|
| | (N=36,810) | (n=26,984) | (n=11,646) | (n=1323) | (n=146) |
| Travel distance (roundtrip in miles) | | | | | |
| PPV | | | | | |
| Mean (SD) | 82.6 (96.0) | 82.7 (97.0) | 81.4 (93.6) | 89.5 (104.5) | 78.2 (95.6) |
| Median (IQR) | 45.9 (21.0-103.0) | 45.8 (20.1-103.8) | 45.8 (21.9-100.0) | 46.1 (20.8-120.9) | 44.4 (21.1-86.5) |
| PPY | | | | | |
| Mean (SD) | 271.5 (504.4) | 140.1 (186.6) | 504.8 (775.9) | 241.4 (371.7) | 94.7 (165.0) |
| Median (IQR) | 106.6 (39.6-285.2) | 70.6 (27.9-169.1) | 223.7 (74.8-563.6) | 91.2 (35.0-266.6) | 37.5 (11.6-115.6) |
| Travel time (roundtrip in minutes) | | | | | |
| PPV | | | | | |
| Mean (SD) | 88.6 (84.1) | 90.7 (86.9) | 79.9 (74.0) | 122.6 (106.7) | 99.9 (80.1) |
| Median (IQR) | 63.1 (36.2-111.0) | 64.0 (36.4-113.5) | 59.4 (34.0-100.4) | 88.5 (47.1-162.8) | 71.2 (44.6-146.5) |
| PPY | | | | | |
| Mean (SD) | 281.2 (443.0) | 153.6 (181.0) | 492.8 (660.1) | 337.9 (440.8) | 127.3 (169.8) |
| Median (IQR) | 139.5 (64.5-316.9) | 97.6 (49.7-187.7) | 286.8 (105.6-613.2) | 179.3 (67.2-416.1) | 60.6 (25.3-170.9) |
| | | | | | |

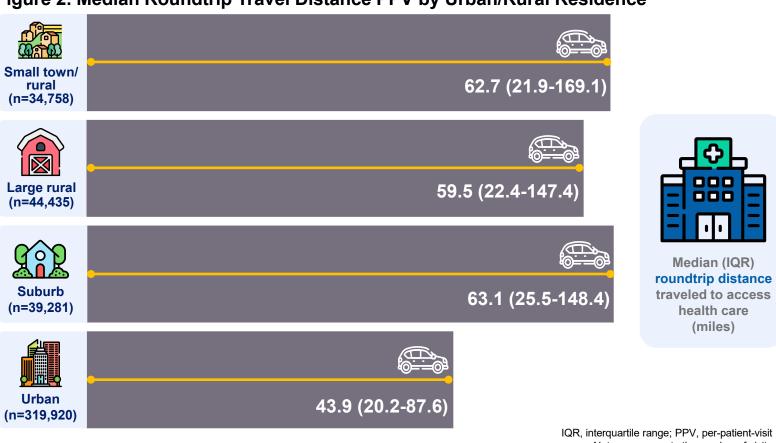
DMT, disease-modifying therapy; IQR, interquartile range; PPV, per-patient-visit; PPY, per-patient-year

- Substantial variation across urban vs rural geographic areas was observed. Approximately 32% of patients living in large rural areas traveled >120 miles per visit vs 17% of urban residents (**Figure 1**)
- Figure 1. Travel Distance in Patients Treated With Infusion DMTs by Urban/Rural Residence

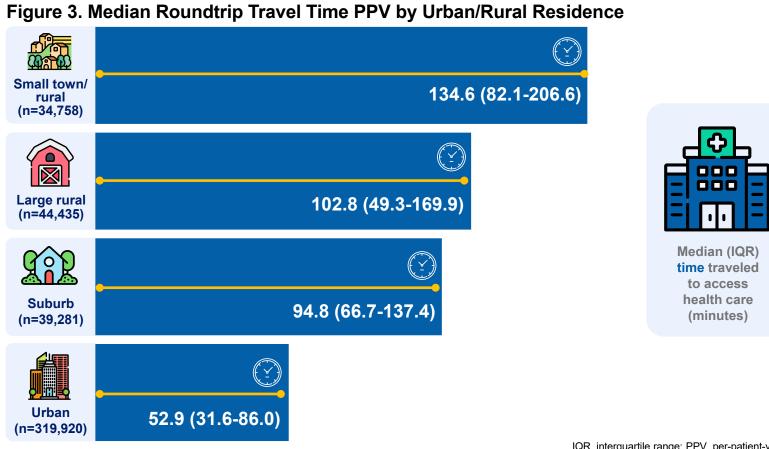


• Urban residents experienced the shortest travel distance compared with all other residence types (**Figure 2**) and much shorter travel times (PPV, 73 minutes) compared with rural residents (PPV, 122 minutes) (Figure 3)

Figure 2. Median Roundtrip Travel Distance PPV by Urban/Rural Residence



Note: n represents the number of visits



IQR, interquartile range; PPV, per-patient-visit Note: n represents the number of visits

1. Samjoo I et al. J Comp Eff Res. 2021;10(6):495-507. 2. Samjoo I et al. J Comp Eff Res. 2023;12(7):e230016. 3. Novartis Pharmaceuticals Corporation. Prescribing information. Kesimpta® 2022. Accessed April 10, 2024. https://www.novartis.com/us-en/sites/novartis_us/files/kesimpta.pdf; 4. Genentech. Prescribing information. Ocrevus® 2024. Accessed April 10, 2024. https://www.tysabri.com/content/dam/commercial/tysabri/pat/en_us/ pdf/tysabri_prescribing_information.pdf; 6. Sanofi SA. Prescribing Information. Lemtrada® 2024. Accessed April 10, 2024. https://products.sanofi.us/lemtrada.pdf; 7. TG Therapeutics, Inc. Prescribing Information. Briumvi® 2022. Accessed April 10, 2024. https://www.tgtherapeutics.com/label-prescribing-info/uspi-briumvi.pdf; 8. Openrouteservices. Routing speed limits for car. Accessed May 6, 2024. https://github.com/GIScience/openrouteservice/blob/master/ors-engine/src/main/resources/re

Note: n represents the number of visits

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Disclosures

Ming-Hui Tai, Swetha R. Palli, Brandon Brown, Cheng Shi, and Abhijit Gadkari are employees of Novartis Pharmaceuticals Corporation. Quijun Shao is a previous employee of Novartis Pharmaceuticals Corporation. John Arsenault is a consultant from Humbi Analytics LLC and provided additional analytic support for this poster