Short Report

Assessing Patient Preference: Preferred Time and Location of Infusible Therapies in Multiple Sclerosis and Neuroimmunologic Disorders

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Running title: Time and Location Preferences for Infusions

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Practice Points

- Patients with MS and neuroimmunologic disorders are increasingly treated with infusible monoclonal antibodies.

- Health care services should engage with patients to understand their preferences for the timing and location of these treatments and should be agile and innovative in their delivery of infusion care.

- Future research should investigate possible factors that affect preferences, such as fatigue and the consequences of rigid infusion scheduling on employment and patient adherence.
Abstract

Background: People with multiple sclerosis and neuroimmunologic disorders (herein referred to as patients) are increasingly treated with infusible monoclonal antibodies. This rise in demand has placed increased loads on current infusion services and mandates careful strategic planning. This study examined patient preferences for the timing and location of infusions and their association with demographic and disease variables to facilitate patient-focused strategic planning.

Methods: Ninety-one patients receiving an infusible therapy at an infusion service during March 2019 were asked to complete a questionnaire exploring eight domains, including preferences for time of infusions and location of infusion centers. Potential access to home-based treatment was included as an option. Unstructured (free-text) feedback on current service was also obtained.

Results: Eighty-three patients completed the survey (mean age, 42 years; 75% women). Infusions were predominantly natalizumab (66%) and ocrelizumab (25%). Of these patients, 71% were engaged in some form of work or study, and 83% of this group had to arrange time off from work or study to attend treatment. Seventy percent of patients would prefer their infusion before noon, and 60% would consider home-based infusions. Most used a car as their transport to the infusion service.

Conclusions: These results suggest that patients are more likely to prefer infusible treatment in the morning and are open to home-based infusions. This study provides information for health services to target service delivery at peak preference times and consider alternate ways of delivering infusible treatments. Int J MS Care.
Multiple sclerosis (MS) is a demyelinating disease of the central nervous system. Highly efficacious disease-modifying therapies (DMTs), such as the intravenously delivered monoclonal antibodies ocrelizumab and natalizumab, have modified the course of the disease, with marked reductions in relapse rate and disability progression.\textsuperscript{1-3} Neuroimmunologic disorders are also increasingly treated with the anti-CD20 monoclonal antibody rituximab, with resultant improved outcomes.\textsuperscript{4} To continue to reap the benefits of these DMTs, patient adherence and flexible access to infusion services are crucial. Most tertiary hospitals administer these infusions in an ambulatory stand-alone setting that requires careful management. Resource needs include space, appointment scheduling, nursing and medical professionals, pharmacists, and special DMT preparation areas.

MS Brain Health consensus standards suggest that when a patient agrees to start an infusible therapy it should be offered in less than 4 weeks, with an aspirational goal of initiating treatment within 7 days.\textsuperscript{5} As demand and activity on infusion services grow, there is a need for careful strategic planning to ensure that treatments can be initiated quickly and delivered efficiently. Increasing the resources at existing sites and using alternative locations such as home-based services or satellite sites all need to be considered. However, health care now demands that consumers are engaged not only in their care but also in the design and process of the facilities that administer their care.\textsuperscript{6-8} Understanding patient preferences for location, acceptability of home infusion, and administration time of their DMTs is important and central to the delivery of quality and efficient care.\textsuperscript{9,10}

This study aimed to explore patient preferences in strategic planning for the provision of infusible therapies in health care services, specifically, time preference and acceptability of
home-based infusions. We explored factors that may influence preferences, such as the distance from the service, employment, level of disability, childcare requirements, and location preference.

**Methods**

This was a cross-sectional study of patients attending an academic tertiary referral hospital infusion service (Alfred Health, Melbourne, Australia) in one calendar month under the MS and Neuroimmunology Service. All the patients were offered the survey and an explanation sheet on admission. Survey responses were anonymous; however, postal codes and respondent age, in years, were recorded.

Infusions are administered per approved hospital guidelines based on individual product monographs. Maintenance ocrelizumab 600 mg is administered over 3.5 hours, with a postinfusion observational period of 1 hour. The patient time commitment is, however, substantially longer due to premedications and aseptic pharmacy preparation. Therefore, the average time spent in the infusion service for a patient receiving ocrelizumab 600 mg is approximately 5.5 hours.\(^1\) Natalizumab 300 mg is prepared by the infusion nursing staff and administered over 1 hour. The postinfusion observational time adds another 1 hour, and the total time commitment is, therefore, approximately 2.5 hours.\(^2\)

Rituximab 1 g is given initially over 4.5 hours, with the possibility of a rapid infusion for subsequent doses if tolerated. Methylprednisolone 1 g is given over 30 minutes, with no postinfusion observation required.
The survey and procedure were approved by the Alfred Health Research and Ethics Unit.

**Survey Development**

The survey (Appendix S1, which is published in the online version of this article at ijmse.org) was developed by a focus group consisting of an MS neurologist, an MS nurse consultant, and a neurology pharmacist. Eight domains (Appendix S2) were agreed on that the group felt were essential to assist with future strategic planning. The survey was piloted with three patients attending the infusion service who met the study inclusion criteria. The purpose of the pilot study was to identify issues with health literacy, instructions, and formatting. No issues were identified.

**Statistical Analysis**

Fisher exact tests were used to compare the proportions of patients in various groups with a particular preference. These comparisons were adjusted for sex and infusion type using logistic regression.

**Results**

Of the 91 patients attending the infusion service in March 2019, 83 (91%) completed the survey (75% women; mean ± SD age, 42.2 ± 11.5 years). Twenty-one patients (25%) received
Ocrelizumab and 55 patients (66%) received natalizumab. The remaining seven participants (8%) received either rituximab or methylprednisolone.

Table 1 and Table S1 provide an overview of the results, showing associations with domains (Appendix S2) that may affect preference decisions for time of infusion and acceptance of home infusion, respectively. Of the 83 patients, 64 (77%) reported their preference for hospital-based infusions to be completed in a stand-alone ambulatory center in contrast to an in-patient ward environment. Seventy-four patients (89%) preferred the main infusion center of our service over attending smaller satellite sites. Fifty patients (60%) reported that they would prefer a home infusion to hospital-based infusion.

The preference for 61 patients (73%) was for their infusion to be delivered between 8 AM and 4 PM (Table 2). The dominant 4-hour time slot was 8 AM to noon, with 48 patients (58%) requesting this slot. Age was a strong predictor of preference for infusion timing. For each 1-year increase in age, patients were more likely to prefer treatment before noon (odds ratio = 1.04 [95% confidence interval, 1.00-1.09], P = .07). Patients 50 years and older (n = 22) were the most likely (n = 5; 23%) to request pre-8 AM infusions (Table 2), whereas patients younger than 30 years (n = 13) were the least likely request treatment before 8 AM (n = 1; 8%). Influences on patient preference for time of infusion (Table 1) saw trends in earlier in the day infusions influenced by greater self-rated disability and childcare requirements. Patients who were unable to walk 100 m (n = 10) were more interested in treatment earlier in the day.

Patients with employment and study commitments were more likely to prefer receiving infusions after noon (36% vs 17%) (Table 1). Similarly, patients receiving natalizumab were more likely than those receiving ocrelizumab to consider infusions after noon.
We examined factors that were associated with patient preference for home infusion (Table S1). Patients younger than 30 years, women, those who had no work or study commitments, and patients who required childcare were more likely to consider home infusions. Increased disability (70%), greater distance to travel (67%), and a shorter infusion (natalizumab) also influenced preference for home infusion.

**Discussion**

This study reinforces that patients are extremely willing to share their information and contribute to strategic planning, with a 91% response rate to the survey. The positive findings of this small study suggest that patients prefer to receive infusion treatment between 8 AM and 4 PM, with 8 AM to noon being the most preferred time. Age (>30 years) is the strongest factor predicking preference for having infusions before noon, with patients older than 50 years having the strongest request for pre-8 AM infusions. Patients with working or studying commitments had a slight preference for afternoon/late afternoon infusion slots. Women and those with long travel distances had a strong preference for home infusions.

The age of the infusion service cohort is a key aspect to consider in strategic planning. Multiple sclerosis is predominantly diagnosed between ages 20 and 45 years, affecting most people during their peak employment years and childbearing years. Patients older than 30 years prefer treatment earlier in the day ($P = .06$). Patients older than 42 years, the mean age in this data set, again are more interested in treatment earlier in the day, supporting age as a key factor to consider in strategic planning. A possible explanation for this trend may be that older patients...
are more secure in their employment places and have more flexibility and autonomy to arrive later to work, in contrast to younger employees who might be more likely to work in customer-facing roles and in less secure employment.

Continued and long-term employment in patients with MS is associated with higher quality of life and potentially fewer social support requirements. Although some studies have shown that higher-efficacy treatments increased the odds of patients remaining employed, what has not been addressed is the impact that employment has on preferences for time and location of infusions. Seventy-one percent of our patients were employed or studying full-time, and in 83% of this group, employment or study was affected by the infusion, requiring some form of leave to be taken.

Health care services should consider the benefits of an agile infusion service that supports continued employment and the psychological impact of nonemployment. Thirty-six percent of the employed or studying respondents preferred infusion times after noon, in contrast to only 17% of those not working or studying. However, working and studying respondents are slightly less likely to prefer/consider home infusions. Importantly, in contrast to another study, we did not offer a response option for office-based infusions. The DMTs have increased the potential for continued employment; however, rigid infusion service delivery may be detrimental to this goal.

Most respondents were women (75%) and were of childbearing age. Those who required childcare to attend infusions were more likely to prefer home infusions (73%) and to request and prefer treatments earlier in the day. Understanding the priorities of parents with MS is important as MS and neuroimmunologic disorder services strive to improve pregnancy planning and
postdelivery infusion initiation. Geographic distance of patients’ residence from the infusion center was a major factor determining preference for home infusions, with 67% of patients living greater than 20 km from the site preferring this option. Of this group, 80% preferred treatment between 8 AM and 4 PM. Understanding the travel and traffic burdens for these patients may assist in strategic partnering with satellite/alternative infusion sites. As expected, length of infusion time influenced preference for home infusion. Patients may be unwilling to have infusion nursing care in their homes for the 5 hours required to complete an ocrelizumab infusion.

The existing literature on infusion preferences of people with MS and neuroimmunologic disorders is limited.\textsuperscript{18-20} Researchers have focused on patient preference to multispecialty units such as hematology-oncology and non–hematology-oncology patient combination in one unit or satisfaction with home- or community-based infusion in rheumatoid arthritis, gastroenterology, and primary immunodeficiency.\textsuperscript{21-23} To date, to our knowledge, no other study has focused consumer engagement on infusion time preference or infusion location for people with MS and neuroimmunologic disorders.

Involving patients receiving infusible treatments in service improvement and strategic planning is now the gold standard of any health care service. It is now accepted that improvement in processes and quality needs to be centered on patient preferences, and a service cannot be innovative and agile without measuring and responding to these preferences.\textsuperscript{24-26}

These study data can facilitate planning of operational priorities and help ensure that patients receiving infusions can adhere to dosing regimens and avoid surplus suffering\textsuperscript{27} due to rigid time frames and only one physical central location.
Early Outcomes

We have gained early valuable information from this study. We have adjusted infusion nurse rosters to increase patient flow and access before noon, when most patients preferred their treatment. Pharmacy special preparations for ocrelizumab supply also required staff ratio adjustment and a push for earlier open hours to ensure that flow before midday could be maintained. Innovative solutions such as hospital in the home infusions are commencing.

Study Limitations

This small study has several limitations. We did not explore reasons for rescheduling appointments or frequency and reasons for late cancellations or failure to attend. Assessing stress/burden of employment and study commitments to attending infusions would have added more granular data to the study. Obtaining employment classifications would also have been useful, in conjunction with preference for office-based infusions. The contribution of specific MS-related symptoms, such as fatigue and/or bowel and bladder problems, on preferences could have added valuable insights.

Future studies with larger sample sizes with more exploration of issues highlighted over several months and at different sites are warranted based on the present study trends.

Conclusions
Engaging and meeting patients’ expectations and preferences presents many challenges to a modern MS and neuroimmunologic disorder health care service as capacity is tested. Patients’ and their health care services’ shared key goal is to derive maximum benefit from DMTs through compliance. This goal requires health services to be efficient, responsive, flexible, and engaged with their patients’ preferences as increasing DMTs enter the health arena. Understanding the drive behind these preferences ensures that the health service care delivery is not at odds with patient health and social goals.

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Table 1. Demographics and contributing factors in patients who would prefer afternoon to morning infusions

| Factor                        | Participants, No. | Prefer treatment after midday, No. (%) | Unadjusted analysis | Adjusted analysis |
|-------------------------------|-------------------|----------------------------------------|---------------------|------------------|
|                               |                   |                                        | OR (95% CI)         | P value          |
|                               |                   |                                        | P value             |                  |
| Sex                           |                   |                                        |                     |                  |
| Male                          | 21                | 9 (43)                                 | 0.46 (0.16-1.32)    | .46              |
| Female                        | 62                | 16 (26)                                | 0.50 (0.16-1.59)    | .23              |
| Treatment                     |                   |                                        |                     |                  |
| Ocrelizumab                   | 21                | 4 (19)                                 | 2.43 (0.77-9.33)    | .18              |
| Natalizumab                   | 55                | 20 (36)                                | 2.04 (0.62-8.08)    | .27              |
| Work/study status             |                   |                                        |                     |                  |
| Not working or studying       | 24                | 4 (17)                                 | 2.76 (0.90-10.45)   | .11              |
| Working or studying           | 59                | 21 (36)                                | 1.92 (0.58-7.56)    | .31              |
| Distance from hospital        |                   |                                        |                     |                  |
| \(<=20 \text{ km}             | 46                | 12 (26)                                | 1.12 (0.42-2.91)    | .31              |
| \(>20 \text{ km}             | 36                | 11 (31)                                | 1.07 (0.38-2.94)    | .90              |
| Self-rated disability         |                   |                                        |                     |                  |
| Cannot walk 100 m             | 10                | 2 (20)                                 | 1.88 (0.43-13.10)   | .72              |
| Can walk 100 m                | 72                | 23 (32)                                | 1.11 (0.21-8.37)    | .91              |
| Childcare to attend infusion  |                   |                                        |                     |                  |
| Do not require                | 72                | 23 (32)                                |                       |                  |
| Require                       | 11                | 2 (18)                                 | 0.47 (0.07-2.02)    | .49              |
| Age, y\(^a\)                  |                   |                                        | 0.60 (0.08-2.82)    | .55              |

**Note:** Adjusted OR for sex and infusion type. Age was not recorded for two patients. Distance from hospital not recorded for one patient. Disability not recorded for one patient. Treatment other than ocrelizumab or natalizumab, seven patients.

Abbreviation: OR, odds ratio.

\(^a\)Mean age is 42 years in this data set.
Table 2. Preference of infusion time by age and distance from hospital

| Group            | Patients in group, No. | Preferred time for treatment |   |   |   |
|------------------|------------------------|------------------------------|---|---|---|
|                  |                        | Before 8 AM                  | 8 AM to Noon     | Noon to 4 PM | 4 PM to 8 PM |
| All patients     | 83                     | 10 (12)                      | 48 (58)          | 13 (16)      | 12 (14)      |
| Age <30 y        | 13                     | 1 (8)                        | 6 (46)           | 4 (31)       | 2 (15)       |
| Age 30-39 y      | 21                     | 2 (10)                       | 12 (57)          | 2 (10)       | 5 (24)       |
| Age 40-49 y      | 25                     | 2 (8)                        | 16 (64)          | 3 (12)       | 4 (16)       |
| Age ≥50 y        | 22                     | 5 (23)                       | 13 (59)          | 3 (14)       | 1 (5)        |
| Distance ≤20 km  | 46                     | 7 (15)                       | 26 (57)          | 6 (13)       | 7 (15)       |
| Distance >20 km  | 36                     | 3 (8)                        | 22 (61)          | 7 (19)       | 4 (11)       |

Note: Data are given as number (percentage). Age was not recorded for two patients. Distance from hospital was not recorded for one patient.
Table S1. Demographics and contributing factors in patients who would prefer infusible therapies at home (Adjusted OR for sex and infusion type)

|                          | N   | Would consider home treatment, No. (%) | Unadjusted analysis | Adjusted analysis |
|--------------------------|-----|----------------------------------------|---------------------|------------------|
|                          |     |                                        | OR (95% CI)         | P value          | OR (95% CI) | P value |
| **Sex**                  |     |                                        |                     |                  |             |         |
| Male                     | 21  | 11 (52%)                               | 1.54 (0.56-4.22)    | .44              | 1.54 (0.56-4.22) | .42 |
| Female                   | 62  | 39 (63%)                               |                     |                  |             |         |
| **Treatment**            |     |                                        |                     |                  |             |         |
| Ocrelizumab              | 21  | 9 (43%)                                | 1.21 (0.43-3.37)    | .79              | 1.38 (0.47-4.02) | .56 |
| Natalizumab              | 55  | 34 (62%)                               |                     |                  |             |         |
| **Not working or studying** |    |                                        |                     |                  |             |         |
| Working or studying      | 59  | 35 (59%)                               | 0.88 (0.32-2.30)    | 1.00            | 0.98(0.34-2.72) | .97 |
| **Distance from hospital** |    |                                        |                     |                  |             |         |
| ≤20 km                   | 46  | 26 (57%)                               | 1.54 (0.63-3.87)    | .37              | 1.67 (0.66-4.33) | .28 |
| >20 km                   | 36  | 24 (67%)                               |                     |                  |             |         |
| **Disability**           |     |                                        |                     |                  |             |         |
| Cannot walk 100 m        | 10  | 7 (70%)                                | 0.60 (0.12-2.35)    | .73              | 0.70 (0.13-3.08) | .65 |
| Can walk 100 m           | 72  | 42 (58%)                               |                     |                  |             |         |
| **Childcare to attend infusion** |       |                                        |                     |                  |             |         |
| Do not require childcare | 72  | 42 (58%)                               | 0.60 (0.12-2.35)    | .73              | 0.70 (0.13-3.08) | .65 |
| Require childcare to     | 11  | 8 (73%)                                | 1.90 (0.50-9.24)    | .73              | 1.72 (0.45-8.48) | .45 |
| **Age**                  |     |                                        |                     |                  |             |         |
| ≤30 y                    | 16  | 12 (75%)                               |                      |                  |             |         |
| >30 y                    | 65  | 36 (55%)                               | 0.41 (0.11-1.33)    | .42              | 0.42 (0.11-1.37) | .17 |
| ≤42 y^a                  | 42  | 25 (60%)                               |                      |                  |             |         |
| >42 y^a                  | 39  | 23 (59%)                               | 0.98 (0.40-2.38)    | .98              | 1.01 (0.41-2.52) | .98 |

Note: Age was not recorded for two patients. Distance from hospital was not recorded for one patient. Disability was not recorded for one patient. Treatment other than Ocrelizumab and Natalizumab seven patients.

Abbreviation: OR, odds ratio.

^a42 is the mean age in this dataset
Appendix S1. Quality Assurance Survey of Ambulatory Neuroimmunology Patient Preferences’ on Outpatient Infusion Therapy Services

DEMOGRAPHICS

What postcode do you currently live in? ______________________

How old are you? ______________________

Gender:

☐ Male
☐ Female
☐ Unspecified/Other

Are you currently employed:  

☐ Full time
☐ Part time
☐ Not applicable

Are you full-time student?  

☐ Yes
☐ No

Do you take time off from work or school to attend your infusion?  

☐ Yes
☐ No
☐ Not applicable

Do you require childcare to allow you to attend your infusion?  

☐ Yes
☐ No

Can you walk unaided more than 100 meters?  

☐ Yes
☐ No

How did you travel to the infusion center today?  

☐ Car (You drove)
☐ Ride from family or friend
☐ Public Transport
☐ Taxi/Uber
INFUSION INFORMATION:

How would you rate the current accessibility to infusion therapy at Alfred Health?
- Excellent, non-restrictive
- Good, but somewhat restrictive
- Fair, but restrictive
- Poor, extremely restrictive

What infusion are you currently receiving?
- Ocrelizumab (Ocrevus)
- Alemtuzumab (Lemtrada)
- Natalizumab (Tysabri)
- Rituximab (Mabthera)
- Methylprednisolone
- Other: ______________________

Infusion preferences:
If you had a choice, what times would you like to start receiving your infusion? (Please select one)
- Before 8am (if infusion allows)
- 8-10am
- 10-12am
- 12-2pm
- 2pm-4pm
- 4pm-6pm
- 6pm-8pm

If you had a choice, where would your preference be to receive your infusion? (Please select one)
- The Alfred Hospital (55 Commercial Road Melbourne 3004)
- Sandringham Hospital (193 Bluff Rd, Sandringham 3191)
- Caulfield Hospital (260 Kooyong Rd, Caulfield 3162)

If receiving an infusion in hospital, where would you prefer the infusion to take place? (Please select one)
- Medical Day Unit
Would you be interested in receiving your infusion at home?

☐ Yes
☐ No

Comment:

What could the current Infusion Medical Day unit infusion service do to improve the care it provides to better meet the needs of its patients?

Thank you for your participation.
Appendix S2. Domains

| Domain                                |
|---------------------------------------|
| Age/sex                               |
| Distance to service                   |
| Infusion type                         |
| Disability                            |
| Employment/study commitments          |
| Childcare requirements                |
| Transport                             |
| Infusion location preference          |