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Implementation of a safety program initiative for monitoring infusion disease modifying therapies for multiple sclerosis

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Abstract

Objective: To determine the efficacy of a safety program designed for monitoring infusion disease-modifying therapies (DMTs) prescribed for multiple sclerosis (MS).

Background: Infusion-based high-efficacy DMTs represent a major advance in the treatment of MS. However, safe administration requires close monitoring. Non-adherence to safety monitoring can lead to DMT-related complications.

Methods: A safety nurse navigator reviewed charts for infusion DMT patients from November 2020 to December 2022, and contacted them to address incomplete safety monitoring. Patients were screened for the primary outcome of incomplete safe infusion, including outdated safety labs, imaging, and/or recent follow-up with their neurologist. Logistic regression was performed for predictors of incomplete safety monitoring and of successful safety intervention.

Results: Three hundred and forty-three patients were on infusible DMTs over the study time period: 75 natalizumab, 31 rituximab, and 237 ocrelizumab. Two hundred and eighty-six (83%) patients did not meet the criteria for safe infusion; 64% lacked safety labs, 47% prescriber follow-up, and 26% an MRI. The nurse succeeded in 82% of interactions. B-cell depletion was linked to outdated lab monitoring, whereas natalizumab use was associated with outdated appointments and imaging.

Conclusions: This safety initiative identified gaps for managing infusion-based MS DMTs. Our safety nurse navigator successfully identified incomplete safety monitoring and intervened to avoid drug-related complications.

Keywords: Natalizumab, outcome measurement, disease-modifying therapies, multiple sclerosis, implementation science

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Introduction

Infusion-based high-efficacy disease-modifying therapies (DMTs) such as natalizumab and ocrelizumab represent a major advance in the treatment of multiple sclerosis (MS), particularly for patients with highly active MS who carry a greater risk for the development of disability. These medications are increasingly prescribed, not only as second-line drugs for patients who have subtherapeutic response to 'first-line' therapies but also as initial therapy for those with rapidly evolving or aggressive disease.[1,2] However, while these medications generally demonstrate greater efficacy in preventing new inflammatory activity in MS, they also are associated with more concerning safety profiles. In the OPTIMISE:MS pharmacovigilance study, natalizumab and ocrelizumab were associated with the highest rate of incident adverse events amongst the MS DMTs.[3] Natalizumab is associated with higher risks of developing progressive multifocal leukoencephalopathy (PML) in patients previously exposed to the John Cunningham virus (JCV).[4] Established risk factors that increase risk of PML include the level of anti-JCV antibodies in serum as assessed by

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anti-JCV antibody index, the use of immunosuppressant therapy before natalizumab initiation, and the duration of natalizumab treatment, all of which require close contact with the health system. In addition, anti-CD20 therapies such as rituximab and ocrelizumab can increase the risk of serious infections, including severe coronavirus disease 2019 (COVID-19).[5,6]

Safety monitoring practices for infusion therapies in MS can vary around the globe based on treatment availability, healthcare infrastructure, funding mechanisms, staffing, and beyond. In resource-rich practices, electronic health records and automated systems may play a role in greater adherence to safety protocols, with additional programs such as Biogen's Tysabri Outreach: Unified Commitment to Health (TOUCH) prescribing program providing an added layer of oversight. In contrast, lower-resource settings may face challenges such as limited access to or coordination of imaging and laboratory facilities, which can lead to inconsistent safety practices and heightened risks. Additionally, variations between providers attitudes can lead to inconsistent safety practices, such as the frequency of obtaining safety labs and imaging, choice of labs, timing of labs relative to infusion date, and beyond.

These associated risks highlight the importance of appropriate safety monitoring for patients with MS: regular laboratory monitoring, surveillance imaging, and routine follow-up with their MS provider. The COVID-19 pandemic has further disrupted care, especially 'non-urgent' care across health systems.[7] In a survey conducted during the pandemic, 2722 people with MS with aggressive disease were most likely to report disruptions in their care. Moreover, 50% of these same patients reported difficulty in obtaining their pharmaceutical care. Notably, disruptions in safety monitoring can also lead to infusions not being authorized, resulting in further delays in treatment. Another survey of over 1000 patients with MS performed early in the pandemic (April 2020) found that 22% of patients had cancelled a visit with their MS provider, 21% had cancelled laboratory tests, 11% cancelled an MRI, and 10% altered how they received their DMT in some way.[8] Furthermore, missed healthcare appointments can be a significant avoidable cost and health system inefficiency that leads to longer clinic wait times, and a further barrier to care for patients with MS.[9]

Given these challenges, the Johns Hopkins Multiple Sclerosis Precision Medicine Center of Excellence established a safety monitoring program for patients with MS on infusion-based therapy, to ensure patients would have their safety monitoring up to date at the time of infusion. Our goals were to (a) identify and quantify incomplete safety monitoring to care for patients on intravenously administered DMTs, (b) reduce the number of patients who received an infusion with incomplete safety monitoring, and (c) clarify any differences in safety monitoring and report on the outcome of our safety program intervention.

Methods

Participants

Patients eligible for the safety monitoring program had to meet specific criteria: a confirmed diagnosis of MS from the Johns Hopkins Multiple Sclerosis Precision Medicine Center of Excellence, regular follow-ups with an MS clinician at Johns Hopkins, prescription of certain therapies (ocrelizumab, rituximab, or natalizumab), and receiving infusions at the Johns Hopkins Infusion Center. Other MS patients following at Johns Hopkins without meeting all four criteria were excluded from the study.

Planning the intervention

Before the COVID-19 pandemic, questions arose about infection risks for patients on immunomodulatory therapies, especially due to the absence of COVID-19 vaccines. With more patients receiving infusion-based therapies, the MS Precision Medicine Center team reassessed safety monitoring. Previously, individual providers handled patient monitoring, but we planned a program to centralize safety checks before infusions at Johns Hopkins. This program includes monitoring lab tests, imaging, and appointments, aiming to prevent complications. We established a safety nurse navigator role to improve safety outcomes for infusion-based treatments.

Intervention

Between November 2020 and December 2022, a safety nurse navigator supervised safety checks for patients receiving ocrelizumab, rituximab, or natalizumab at Johns Hopkins Infusion center. They continuously tracked patient safety using real-time data in a spreadsheet. The data involved three key aspects: recent provider visits, annual brain MRIs (completed within the year prior to the infusion), and specific lab tests based on the medication. For natalizumab, this included a JCV antibody test every 6 months, while B-cell therapies required a range of annual tests (complete blood count, CD19

counts, serum immunoglobulins). For B-cell monitoring, annual labs were chosen with the understanding that there may be variations in the specific labs and frequency by provider. These labs were chosen as they were felt to be most likely to ordered at least yearly, while ensuring that patients were not considered to have incomplete safety monitoring due to variations in provider practice. If any data were missing, the nurse contacted patients via electronic medical record (EMR) messages or phone calls, arranging necessary tests or appointments. See Figure 1 for the nurse navigator's workflow.

Variables

The primary outcome was to determine the proportion of patients with incomplete safety monitoring. The other primary outcome was whether the nurse navigator's involvement successfully resolved the monitoring issue. Secondary outcomes included incomplete monitoring in specific categories (labs, imaging, appointments, or combinations) and identifying predictors of incomplete monitoring and successful interventions. We analyzed data over two periods: retrospectively the year before the COVID-19 pandemic (pre-intervention) from February 2019 to February 2020 and prospectively for the 2 years after implementing the safety program from November 2020 to December 2022. The post-intervention period was followed over 2 years rather than 1 year due to concerns about the degree of confounding that may have been present immediately at the start of the pandemic due to unforeseen changes in healthcare utilization. Patients were considered to have incomplete monitoring if identified at least once during either period. A successful intervention meant completing monitoring each time the patient was contacted.

Data sources/measurement

Between November 2020 and March 2022, 343 patients received B-cell depleting therapy or natalizumab at Johns Hopkins Infusion Center. Among these, 235 had infusions before the intervention period, while 108 started afterwards. We retrospectively reviewed patient data, including safety monitoring, demographics, and clinical details during the pre-intervention phase. Due to a combination of factors including some patients being lost to follow-up, complicating factors of imaging or lab monitoring being completed externally but not documented, not all safety monitoring components add up to the 343 total patients. We then did the same prospectively for the intervention period. We also noted travel distance to the center and whether the nurse navigator contacted and resolved safety concerns before subsequent infusions.

Statistical methods

We described the demographic, geographic, and clinical characteristics of the pre-pandemic and post-pandemic populations in terms of percentages for categorical variables and median for continuous variables. We also tabulated these characteristics by the presence/absence of outdated monitoring and each of the intervention outcomes, comparing differences in groups by nonparametric rank sum tests for continuous variables and chi-square tests for categorical variables. We also presented these associations in terms of unadjusted odds ratios. We further performed multiple logistic regression to determine if any factors were independently associated with incomplete safety monitoring. We defined statistical significance a priori as $p < 0.05$.

Results

Patient population

Over the course of the initiative, 343 patients were identified as receiving a B-cell depleting or natalizumab infusion at a Johns Hopkins Infusion Center between November 2020 and March 2022 (Table 1). Of these patients, 250 (72%) were female, and the average age was 43.6 years ($\pm$10.8). The majority of patients had relapsing remitting MS ($n = 293$, 85%) followed by secondary progressive MS ($n = 35$, 10%) and primary progressive MS ($n = 15$, 4%). Of the DMTs, 265 (77%) patients were on B-cell depleting therapies (either ocrelizumab or rituximab), and 78 (22%) were on natalizumab. The median Expanded Disability Status Scale (EDSS) was 2 (IQR 1–3). The median distance traveled to the infusion center was 19 miles (IQR 9–38).

When assessing for correlations between demographic variables, patients on B-cell depleting therapies were older (44 vs. 41, $p = 0.036$), and lived further from the infusion center (20.6 miles vs. 13.7 miles, $p = 0.004$).

Process measures and outcomes

From November 2020 to December 2022, the safety nurse navigator contacted patients with incomplete safety monitoring before their infusions. In the pre-intervention period, 122 of 235 eligible patients (51.9%) had incomplete safety monitoring, primarily due to incomplete lab tests (50.0%), followed by provider appointments (32.2%), then imaging (23.8%). Throughout the intervention period, 286 of 343 total

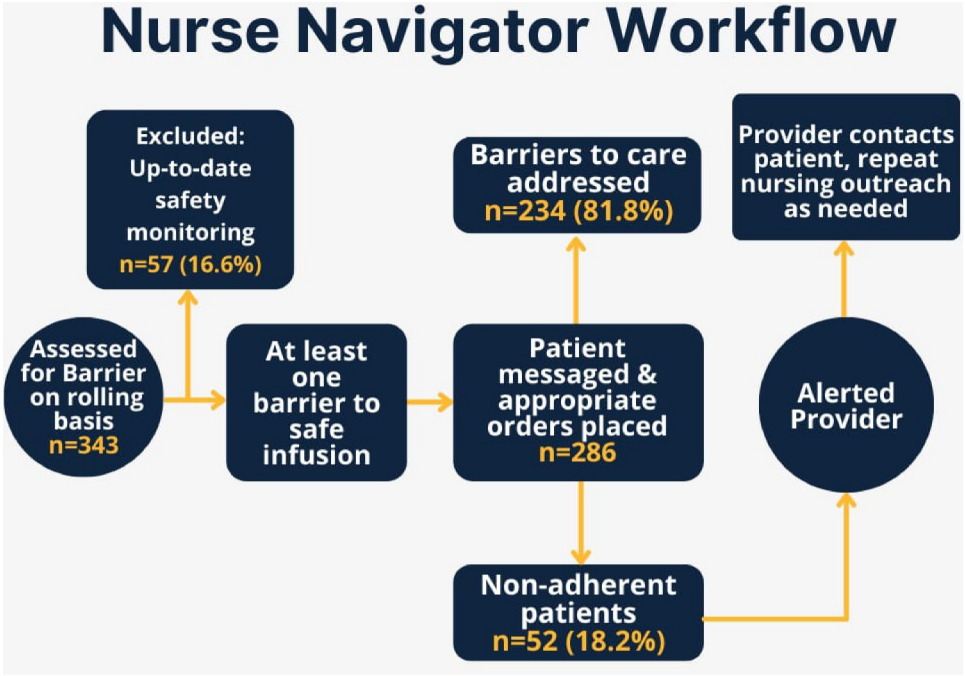

Figure 1. Nurse navigator workflow for safety monitoring.

Table 1. Patient demographics.

Clinical characteristics	Pre-pandemic (*n*% or median IQR)	Post-pandemic (*n*% or median IQR)
Total population	235 (100%)	343 (100%)
Age, median (IQR)	44 (36, 52)	43 (35, 53)
Distance from Greenspring Station, median (IQR)	18.92 (9.15, 37.21)	18.92 (9.15, 38.11)
EDSS, median (IQR)[a]	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)
Race, *n* (%)		
White	161 (68.5%)	237 (69.1%)
Black	58 (24.7%)	86 (25.1%)
Other	6 (6.8%)	20 (5.8%)
Sex, *n* (%)		
Female	169 (71.8%)	252 (73.5%)
Male	66 (28.2%)	90 (26.2%)
Therapy, *n* (%)		
Natalizumab	24 (16.9%)	75 (21.9%)
B-cell depletion[b]	117 (83.1%)	268 (78.1%)

[a]Estimated Disability Step Score.
[b]Ocrelizumab or Rituximab.

patients (83.3%) were contacted by the navigator due to safety concerns, leading to 81.8% successful interventions in completing monitoring before infusions. The comparison between pre- and post-intervention showed a significant reduction in incomplete safety monitoring (83.3% vs 16.6%, Z-statistic −17.5, $p < 0.0001$, Figure 2). Regarding the individual safety concerns, 184 (64.3%) patients were found to have incomplete safety monitoring, 136 (47.6%) had outdated provider appointments, and 75 (26.2%) had outdated imaging (Figure 3). A total of 106 (30.9%) patients were identified as having multiple

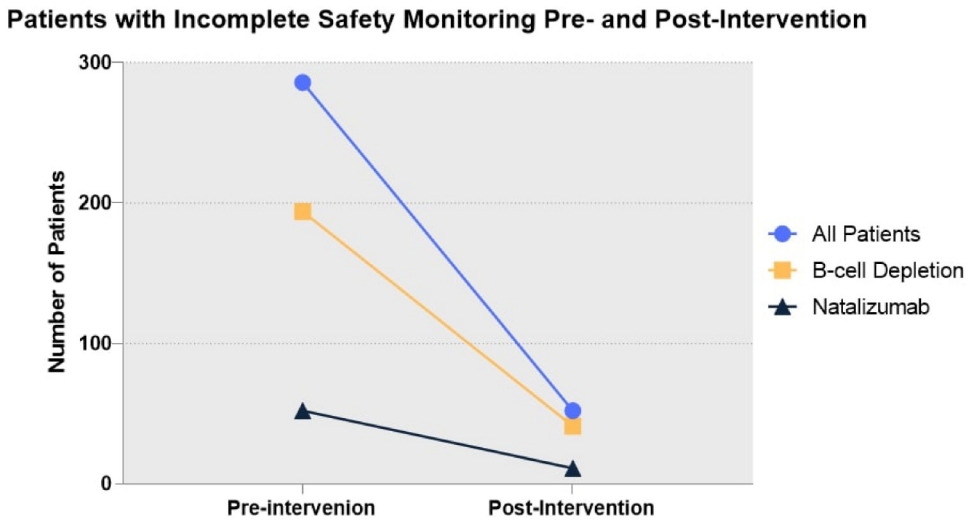

Figure 2. Incomplete safety monitoring pre-intervention and post-intervention across all patients, patients treated with B-cell depletion, and patients treated with natalizumab.

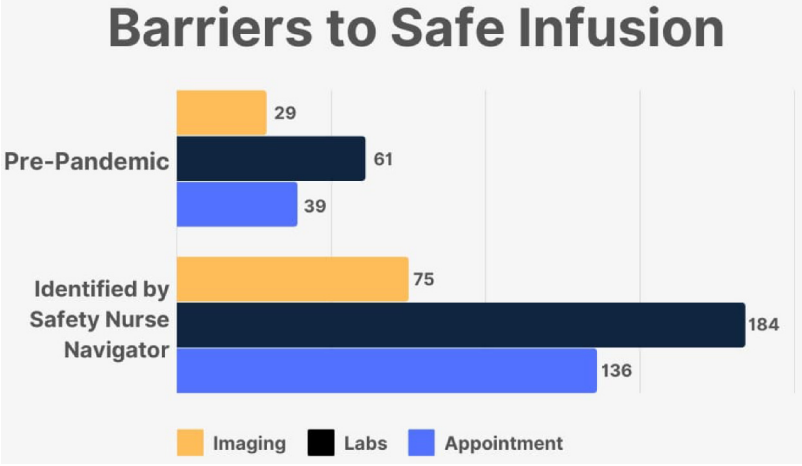

Figure 3. Safety concerns organized by category.

safety concerns, with 14 having outdated laboratory monitoring, appointments, and imaging. Forty-two patients had both outdated appointments and lab monitoring, 31 had both outdated appointments and imaging, and 30 had both outdated lab monitoring and imaging.

Observed associations of predictor variables with incomplete safety monitoring

In univariate analysis (Table 2), B-cell therapies were more likely associated with incomplete monitoring than natalizumab (82.2% vs. 17.8%, $p < 0.001$). B-cell therapies correlated with lower risk of outdated imaging ($p = 0.003$) and appointments ($p < 0.001$) but higher risk of incomplete lab monitoring (95.7% vs. 4.3% for natalizumab). Patients living farther from the center had more outdated lab tests (median 22.6 miles vs. 14.6, $p = 0.006$), while closer patients had more outdated appointments (median 16.1 miles vs. 22.6 miles, $p = 0.04$). No associations were found between incomplete safety monitoring and age, race, gender, or disability level. Among the 286 patients contacted, no specific characteristics predicted successful intervention in univariate analysis.

In multivariable analysis (Table 3), B-cell therapy was linked to more safety concerns (adjusted OR 3.19, 95% CI 1.61–6.31) and outdated lab testing (adjusted OR 17.0, 95% CI 7.21–40.3), but with fewer outdated appointments (adjusted OR 0.35, 95% CI 0.18–0.68)

Table 2. Safety concerns and intervention outcomes by univariate analysis.

Variable (*n*% or median IQR)	Safety concern = Yes	Safety concern = No	*p*-Value	Provider out of date = Yes	Provider out of date = No	*p*-Value	Lab monitoring out of date = Yes	Lab monitoring out of date = No	*p*-Value	Image out of date = Yes	Image out of date = No	*p*-Value	Successful Intervention = Yes	Successful Intervention = No	*p*-Value
N	286	57		136	171		184	122		75	230		234	52	
Age, median (IQR)	44 (35–52)	42 (35–54)	0.71	42.5 (35–51)	43 (35–54)	0.27	43 (35–52)	44 (36–52)	0.86	44 (37–51)	43 (35–53)	0.77	43 (35–52)	46 (36–53)	0.63
Distance to infusion center in miles, median (IQR)	19.0(9.2–37.8)	18.6 (8.9–41.4)	0.80	16.2 (9.0–36.7)	22.6 (10.0–41.9)	**0.043**	22.6 (10.2–42.4)	14.6 (8.7–34.4)	**0.006**	18.8 (9.0–36.2)	19.0 (9.2–40.1)	0.56	19.0 (9.0–40.1)	19.4 (10.3–34.1)	0.96
EDSS (IQR)	2.0 (1.0–3.0)	1.5 (1.0–3.0)	0.87	2.0 (1.0–3.0)	1.5 (1.0–3.0)	0.54	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.84	1.5 (1.0–3.5)	2.0 (1.0–3.0)	0.98	2.0 (1.0–3.0)	1.5 (1.0–2.5)	0.09
Race, *n* (%)			0.12			0.65			0.20			0.88			0.48
Black	77 (26.9)	9 (15.8)		38 (27.9)	42 (24.6)		53 (28.8)	27 (22.1)		19 (25.3)	59 (25.7)		60 (25.6)	17 (32.7)	
White	191 (66.8)	46 (80.7)		88 (64.7)	119 (69.6)		122 (66.3)	84 (68.9)		52 (69.3)	155 (67.4)		160 (68.4)	31 (59.6)	
Other	18 (6.3)	2 (3.5)		10 (7.4)	10 (7.4)					4 (5.3)	16 (7.0)		14 (6.0)	4 (7.7)	
Sex, *n* (%)			0.73			0.39			0.66			0.21			0.85
Female	208 (72.7)	44 (77.2)		101 (74.3)	121 (70.8)		9 (4.9)	11 (9.0)		54 (72.0)	166 (72.2)		171 (73.1)	37 (71.2)	
Male	77 (26.9)	13 (22.8)		35 (25.0)	50 (29.2)		52 (28.3)	32 (26.2)		20 (26.7)	64 (27.8)		62 (26.5)	15 (28.8)	
Therapy, *n* (%)			**<0.001**			**<0.001**			**<0.001**			**0.003**			0.49
Tysabri	51 (17.8)	24 (42.1)		37 (27.2)	21 (12.3)		8 (4.3)	50 (41.0)		23 (30.7)	35 (15.2)		40 (17.1)	11 (21.2)	
B-cell	235 (82.2)	33 (57.9)		99 (72.8)	150 (87.7)		176 (95.7)	72 (59.0)		52 (69.3)	195 (84.8)		194 (82.9)	41 (78.8)	

Due to variation in the combination of safety concerns (provider appointment, lab monitoring, imaging) missingness, and some patients who were lost to follow-up prior to intervention, each column of safety factors may not add up directly to the total of the 343 patients assessed. Bold values are significant associations

Table 3. Predictors of safety concerns and successful intervention.

Predictor variable	Identified safety concern = Yes (OR, 95% CI)	*p*-Value	Provider out of date = Yes (OR, 95% CI)	*p*-Value	Laboratory monitoring out of date = Yes (OR, 95% CI)	*p*-Value	Imaging out of date = Yes (OR, 95% CI)	*p*-Value	Successful intervention = Yes (OR, 95% CI)	*p*-Value
Age	1.01 (0.97–1.04)	0.74	0.98 (0.96–1.01)	0.21	0.98 (0.95–1.02)	0.31	1.00 (0.97–1.03)	0.84	0.98 (0.942–1.014)	0.22
Distance from infusion center	1.00 (0.99–1.01)	0.98	1.000 (0.99–1.00)	0.86	1.00 (0.99–1.01)	0.56	1.00 (0.99–1.01)	0.65	1.003 (0.995–1.012)	0.45
EDSS	0.95 (0.79–1.15)	0.60	1.077 (0.93–1.25)	0.34	0.96 (0.81–1.14)	0.64	1.07 (0.90–1.28)	0.42	1.259 (0.990–1.601)	0.06
Race										
Black	Reference		Reference		Reference		Reference		Reference	
White	0.36 (0.14–0.90)	**0.030**	0.887 (0.48–1.63)	0.699	0.67 (0.33–1.38)	0.281	0.76 (0.28–1.53)	0.44	2.325 (1.057–5.111)	**0.036**
Other	0.54 (0.10–3.12)	0.50	1.040 (0.33–3.26)	0.947	0.27 (0.08–0.95)	0.041	0.44 (0.09–2.23)	0.32	1.215 (0.287–5.143)	0.79
Sex										
Female	Reference		Reference		Reference		Reference		Reference	
Male	1.35 (0.61–2.97)	0.46	0.82 (0.44–1.49)	0.510	1.23 (0.62–2.43)	0.561	1.10 (0.55–2.21)	0.780	1.246 (0.499–3.115)	0.64
Therapy										
Natalizumab	Reference		Reference		Reference		Reference		Reference	
B-cell depletion	3.19 (1.61–6.31)	**0.001**	0.35 (0.18–0.68)	**0.002**	17.05 (7.21–40.32)	**<0.001**	0.31 (0.15–0.61)	**0.001**	1.826 (0.779–4.280)	0.17

Bold values are significant associations

and imaging (adjusted OR 0.31, 95% CI 0.15–0.61). White race correlated with lower risk of incomplete monitoring (adjusted OR 0.36) and higher likelihood of successful intervention (adjusted OR 2.33, 95% CI 1.06–5.11).

Discussion

Our study examined the reach, effectiveness, implementation, and maintenance of a safety monitoring program for MS patients on infusion therapies. Key findings include: (a) a majority of patients had incomplete safety monitoring; (b) this issue increased after the COVID-19 pandemic began; (c) implementing a safety nurse navigator program significantly and durably improved adherence to safety monitoring.

With increased utilization of high-efficacy therapies in MS, standardized safety monitoring programs are crucial. Our program for MS patients on IV therapies proved both feasible and sustainable. Over 2 years, most patients experienced incomplete safety monitoring before an infusion at least once, with a higher proportion in the intervention period. This increase might be due to a longer observation period and additional patients being newly diagnosed or switching therapies. Specific safety concerns remained similar between periods, except for more outdated lab monitoring. Clinicians prescribing natalizumab or B-cell therapies should note potential lapses in monitoring, emphasizing the importance of safety programs to mitigate adverse events and alleviate provider pressure in monitoring patient care. While not a specific outcome that was measured, it was notable that this safety monitoring program captured a variety of different events that needed clinical intervention or treatment modification, such as latent tuberculosis infections, hepatitis B reactivation, hypogammaglobulinemia, JCV seroconversion, pregnancy, and beyond. For patients with high-risk seroconversion of index level > 1.5 as an example, this would prompt transition to another treatment. For patients with hypogammaglobulinemia, this may have warranted treatment with intravenous immunoglobulin (IVIg) or transitioning to extended interval dosing.

During the pandemic, outpatient care access declined due to various stressors: psychological (apathy, fear), financial (income loss, work constraints), and technological shifts to telemedicine.[10,11] To address gaps in chronic condition management, especially for high-risk MS patients on potent therapies like natalizumab and ocrelizumab, creating outreach and patient education programs is crucial. Our outreach program notably improved adherence to MS care guidelines. Similar work in evaluating the efficacy of an oral chemotherapy monitoring clinic demonstrated a reduction in hospitalization rate, and subsequently, healthcare costs by an average of $1374 per patient, suggesting another potential benefit of such programs.[12]

While specific factors were linked to incomplete monitoring risk, success with the nurse navigator showed no clear correlation with demographics. This is especially important as prior work has demonstrated that certain demographic variables such as lower income, physical disability, and living in rural areas, are associated with unequal access to a neurologist amongst patients with MS.[13]

Previous studies suggested that patient portals reduce appointment no-shows by 50%.[14] Despite potential demographic factors impacting adherence, the nurse navigator's outreach proved highly effective. Further investigations at the Veterans Health Administration demonstrated that the further out an appointment is scheduled, the less likely the appointment was to be honored, with 45–60% attendance rate for appointments made >90 days from the appointment itself.[15] Given the scarcity of MS providers nationwide and the scheduling often done 6 to 12 months in advance, implementing a reminder system might help address this issue, although we did not evaluate the no-show rate in this study. In this case, funding was available for a nurse navigator program through the Neurology department, though generalizability of this model will depend on individual resources available at different institutions. Other institutions have worked to develop automated clinical decision support systems and reminders via the EMR for medications such as alemtuzumab, and in other fields such as primary care and oncology, though these have been in small cohorts.[16–19] However, this also demands resources and the infrastructure to build said clinical decision support tools. Further study into long-term cost–benefit effects and appointment attendance rates is warranted in future research.

Adjusted models revealed that white race was predictive of both a lower likelihood of identified safety concerns and a higher likelihood of successful program intervention. These findings may reflect disparities in safety monitoring or communication methods, consistent with prior research showing lower healthcare engagement among ethnic minorities, such as appointment-keeping and visit rates.[13,20] Racial differences in neurological healthcare, including MS

care, are likely multifactorial, encompassing social, economic, and environmental factors as well as broader social determinants of health. While Black Americans are now recognized as having a higher prevalence of MS and the highest MS mortality rates among racial groups, their underrepresentation in this study's cohort (25% Black compared to Baltimore's 58% Black population) suggests disparities in treatment practices or healthcare access.[21,22] Future research should explore the intersection of race and social determinants to enhance equity in patient safety monitoring and healthcare engagement.

Another contribution of this study is in identifying possible factors that could help identify patients who may be at greater risk of incomplete safety monitoring. Interestingly despite more frequent safety lab monitoring (JCV antibody titer every 6 months vs. yearly B-cell monitoring labs), and infusions, patients treated with natalizumab were less likely to have incomplete safety monitoring than those treated with B-cell depletion. This is likely driven by the overwhelming majority of incomplete laboratory monitoring occurring in patients on B-cell therapy, while otherwise incomplete imaging and provider follow-up were associated with natalizumab treatment. Notably, in addition to this safety monitoring program, Biogen, the manufacturer of natalizumab, runs the TOUCH monitoring program, created to minimize the risk of PML in patients on natalizumab. Through this program, only sites approved by the TOUCH program can prescribe and dispense the medication. As a result, for the infusion itself to be completed, providers must provide a JCV index value from within the last 6 months. Biogen covers the cost of the JCV index lab itself for patients being treated with natalizumab, while the same is not true for B-cell monitoring labs and any of the corresponding manufacturers for anti-CD20 medications. This is an additional layer of protection which is not the case with B-cell therapies. As our understanding of the risks associated with high-efficacy therapy grows, this could argue for the use of similar programs for B-cell depleting therapies to ensure patients are safely receiving their medications.

Paradoxically, while patients who lived further from the infusion center were less likely to complete their lab monitoring, patients who lived closer to the infusion center were less likely to schedule their provider appointments. This may be present a unique phenomenon relative to Baltimore, as the use of this safety monitoring program was primarily driven through contact via the EMR, which requires access to both reliable internet as well as technological devices, and notably only 78.0% of Baltimore households subscribed to Broadband internet, in comparison to 88.5% across the rest of Maryland.[23]

Study limitations include primarily using technology for patient contact, potentially causing inequities and selection bias. Patients using a patient portal might more readily respond, though efforts were made to reach non-responders via phone. The lack of prior knowledge about the study likely enhanced the validity of the observed outcomes by minimizing potential biases. For instance, knowing about the study might have influenced neurologists and patients to alter their usual behavior, such as increasing adherence to safety protocols independent of the intervention. However, it is possible that awareness of the safety monitoring program over time led to secondary improvements in compliance, though this effect was not formally assessed. Counting patients with any incomplete monitoring at any time could overstate the problem, while defining success as completed monitoring with each contact might underestimate the nurse navigator program's effectiveness. Most patients lived close to the infusion center, possibly affecting access to labs and imaging. The study's focus on English-speaking patients might not apply universally, particularly in areas with diverse language demographics. Being a single-center study may restrict generalizability to other institutions, influencing the program's applicability elsewhere. Due to limitations in data reporting in the EMR, we were unable to compare results between patients receiving their infusions in the JHU system versus those receiving their infusions elsewhere.

Future directions assessing the cost-effectiveness and expanding the safety program to oral MS treatments. We plan to work with our Neurology patient safety teams to better quantify rates of treatment-related adverse events in the pre- and post-implementation periods. We also hope to obtain patient and provider satisfaction data regarding the implementation and ongoing execution of this program. While collecting such data was beyond the scope of this program, it was notable that the number of patients in the pre-intervention era was approximately 70% of the cohort after the implementation of the safety monitoring program. In theory, establishing such a safety monitoring program reduces the clinical workload of clinicians. Examining variations in new patient numbers and clinicians' EMR time before and after

implementation will help understand the program's impact on clinical volume and workflow.

Conclusions

Establishing a safety monitoring program for MS patients on infusion therapies revealed prevalent safety concerns and boosted monitoring adherence over 2 years. Future studies aim to evaluate the program's impact through a cost analysis. While conducted in a single center, these initial findings might aid providers and administrators in enhancing safety monitoring for MS patients in the post-pandemic healthcare setting.

Authors' contributions

Study conception and design were performed by Shuvro Roy, Janelle Haughton, and Scott Newsome. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by Shuvro Roy and all authors commented on subsequent versions of the manuscript. All authors read and approved the final manuscript.

Data availability

The data that support the findings of this study are available from the corresponding author, SDN, upon reasonable request.

Declaration of conflicting interests

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Ethics approval

This is a quality improvement study. The Johns Hopkins Institutional Review Board has confirmed that this study does not meet the definition of human subjects' research.

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