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Treatment access and satisfaction on disease-modifying therapies of neuromyelitis optica spectrum disorder patients in China: a cross-sectional survey

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Abstract

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare and debilitating disease that has become more widely recognized in China. Legislative measures have been implemented by the government to improve treatment access for rare diseases.

Objectives: To investigate the diagnostic journey, treatment status, treatment accessibility, and treatment satisfaction of the NMOSD patients on disease-modifying therapies (DMTs) in China.

Design: A patient online survey.

Methods: This cross-sectional online survey was conducted between November 2022 and January 2023. Patients over 18 years old and diagnosed with NMOSD were included. The questionnaire consisted of five sections covering demographics, diagnostic and treatment experiences, DMTs availability, cost and affordability, and treatment satisfaction using the Treatment Satisfaction Questionnaire for Medication (version II). Patient opinions and demands were also collected at the end of the survey.

Results: A total of 375 patients diagnosed with NMOSD were recruited, of which 321 patients used DMTs. It required 1.22 ± 3.22 years and 3.58 ± 4.24 hospital visits for a definitive diagnosis. One-third of the patients still needed to travel for over 2 h to access DMTs. The total treatment expenditure was estimated to be CNY 59,827.00 (USD 8315.95) a year. Drug expenses alone accounted for 52.22% of the average annual household income. The most common challenges perceived were the inability to afford treatment and a lack of effective options. No significant difference was found in treatment satisfaction among DMTs, except that rituximab scored lowest in convenience compared to other DMTs. Patients' age and travel time required to obtain medications were negatively associated with global treatment satisfaction.

Conclusion: In China, patients with NMOSD face challenges in obtaining proper treatment due to diagnostic difficulties, distant medication access, and high costs. Policies should prioritize improving disease education and alleviating financial burdens for the patients.

Keywords: affordability, availability, disease-modifying therapy, neuromyelitis optica spectrum disorder, patient survey, treatment access

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Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, immune-mediated demyelinating disease with a global prevalence of approximately 0.34–10/100,000 people and 1.57–4.9/100,000 in the Asian population.[1] Visual, motor, and sensory impairments caused by neurological dysfunctions may hugely impact

the patients' quality of life.[2,3] Each NMOSD relapse may lead to permanent neurological damage. Therefore, early diagnosis and treatment are critical to impede disease progression.

Currently there is no cure for NMOSD. Disease-modifying therapies (DMTs) is the mainstay of treatment, and life-long treatment is generally required.[4] However, many of the DMTs are innovative immunomodulating agents that are either unavailable or unaffordable to patients. Like all rare diseases, drug access stands as the primary obstacle to proper treatment for NMOSD patients worldwide.[5] Studies on orphan drug accessibility have primarily focused on market access, drug prices, and the perspectives of payers and providers[6–12] while patient opinions may have been under-evaluated.

China has a relatively large NMOSD population with an incidence rate from 0.278 to 0.41 per 100,000 person-years.[13,14] Lack of effective treatment and the high economic burden are considered the major barriers to treatment access.[15] Following the release of China's 'First List of Rare Diseases' in 2018, there has been increasing attention to rare diseases in the country. The growing number of new drug approvals and the expanded inclusion of orphan drugs in the National Reimbursement Drug List (NRDL) have significantly improved the treatment accessibility for Chinese rare disease patients.[6] In light of recent policy changes, this study constructed a patient survey to investigate the diagnostic experience, treatment status, treatment accessibility, and treatment satisfaction from the perspective of individuals with NMOSD in China.

Methods

Survey design and participants

A cross-sectional survey regarding the treatment status and drug accessibility of NMOSD patients in China was launched online (www.wenjuan.com) between November 2022 and January 2023. In collaboration with NMO Family Shanghai, the first and largest patient organization dedicated to NMOSD in China, the survey link was circulated among various patient groups. Patients were recruited if they were 18 years of age or older and clinically diagnosed with NMOSD. To reduce selection bias, only patients who were unable to comprehend the questionnaire were excluded. Confirmation of informed consent was required and signed by all participants at the beginning of the survey before they could continue. Recruitment information was shared among patient groups through snowball sampling.

Questionnaire construction

Based on literature review and World Health Organization/Health Action International (WHO) analytical framework of drug accessibility, the questionnaire was structured in Chinese into five main sections: demographics, diagnosis details (time of first symptoms, time of first medical visit, and time of initial confirmed diagnosis), treatment experiences (use of DMTs and therapy changes), treatment availability, treatment costs, as well as patient opinions and treatment satisfaction. Only patients who have used DMTs, past or current, were involved in the questions regarding treatment availability and costs.

The list of DMTs provided in the questionnaire (Supplemental File) included any treatment agent that is classified as a DMT for NMOSD according to treatment guidelines and literature evidence, irrespective of their labeled indications or approval status in mainland China.

The Treatment Satisfaction Questionnaire for Medication (TSQM version II)[16] was also included as part of the survey to measure treatment satisfaction across four dimensions (effectiveness, side effects, convenience, and global satisfaction) for DMT use of each participant. The linguistically validated version of the TSQM in Simplified Chinese was authorized and permitted for use in this study. Due to the nature of cross-sectional survey, satisfaction questions were asked based on the current DMT or the last one used before treatment discontinuation, and comparisons could not be made between therapy switches.

Statistical analysis

The appropriate sample size was determined using G*Power software v3.1.9.7. A total of 270 participants would be required for a statistical power of 80%, an effect size of 0.25, and an alpha level of 0.05 for the following proposed analyses. The presentation of results data is primarily descriptive. Continuous variables are reported as mean values ± standard deviations or median values. Categorical variables are reported as percentages.

The association between current/last DMTs and TSQM scores was assessed using one-way analysis of variance (ANOVA). Correlations between patient factors and TSQM scores were analyzed with multifactor ANOVA. A *post hoc* analysis was conducted on factors that showed statistical significance. The *p*-values from the ANOVA results were adjusted using the false discovery rate (FDR). A linear regression was then performed on factors with FDR values <0.30. All statistical analyses were performed in SPSS software v26.0 (IBM Corp. in Armonk, NY, USA) with $p<0.05$ for statistical significance.

Results

Demographic characteristics

A total of 386 questionnaires were collected, of which 375 were valid for enrollment. Eleven patients were excluded due to age (under 18 years). The study population (Table 1) primarily consists of middle-aged adults with a mean age of 40.93 ± 12.21 years (median 38 years) and a female-to-male ratio of 9.1:1. Around 70% of the participants were from Eastern China. Although more than half (58.40%) of them were capable of working for personal income, 38.13% of them had an annual household income of less than CNY 50,000 (USD 6950), and 70.93% of them earned up to CNY 100,000 (USD 13,900) a year. The majority were covered by various types of National Basic Medical Insurance (NBMI) ($n=363$, 96.80%), with only 10 patients lacking healthcare coverage. Among them, 20 patients had dual coverage with both a type of NBMI and a commercial insurance plan.

Diagnosis experiences and treatment status

Twelve patients were uncertain of their diagnostic details. Of the remaining 363 patients, 342 (94.21%) of them chose to seek medical attention within the same year of their first symptom appearance, with a mean time from onset to initial visit of 0.26 ± 2.31 years. The time to definitive diagnosis was 1.22 ± 3.22 years, and a total of 252 (69.42%) patients were confirmed with NMOSD within the first year of their initial visit. This number increased to 4.00 ± 4.79 years when those diagnosed within the first year were excluded. The mean duration of disease in the 363 patients was 4.59 ± 3.87 years, with a median of 4 years (range, 0–20). Thirty-eight patients (10.47%) were newly diagnosed within 1 year, whereas the largest proportion of patients ($n=50$, 13.77%) had a disease history of 2 years. An average of 3.58 ± 4.24 visits were required prior to a definitive diagnosis. Only 24.24% of the patients were diagnosed on their first visit. Over 86% of the patients were diagnosed within 5 visits, but 18 patients (4.96%) still required more than 10 visits.

Among all 375 patients, 366 (97.60%) of them are currently receiving treatment, whereas only 9 of them have discontinued or never started treatment. The majority of the patients (321/375, 85.60%) were using or had used DMTs, whereas 54 patients were only treated for acute attacks. The primary reason for not being on DMTs was the high economic burden.

Over half (51.4%) of the 321 patients who received DMTs started with mycophenolate mofetil (MMF) and 30.21% of them began with azathioprine (AZA). Most of the patients were on a single-drug regimen ($n=299$, 93.15%), and MMF was the current or last DMT for 167 (52.02%) patients, followed by rituximab for 70 patients (21.81%). Among the 113 patients who switched therapies during their treatment course, 86 patients switched only once, whereas one patient switched six times. The average number of switches was 1.32 ± 0.70 in the 113 patients who switched therapies and 0.46 ± 0.75 for all 321 patients. When considering each therapy switch individually, AZA was discontinued most frequently, whereas MMF and rituximab were the most common drugs to switch to (see Figure 1). Treatment failure was the primary reason for therapy change in 72.98% of cases, followed by intolerable adverse effects (20.58%) and high cost (6.44%).

Availability

Hospitals are the main source for obtaining DMTs (68.22%), followed by community pharmacies (24.30%). Approximately one-third (28.66%) of the patients were able to obtain medications within a 1-h commute, whereas 28.97% of them still required over 2 h of travel (Table 2). In those who preferred self-pickup over delivery, 40.19% of patients claimed to live within an 'acceptable' distance from their regular hospitals. Only 77 (23.99%) of the patients had their DMTs delivered.

Table 1. Demographic characteristics of the study population.

Characteristics	Category	*n* (%)
Age	18–30	82 (21.87)
	31–40	120 (32.00)
	41–50	79 (21.10)
	51–60	69 (18.40)
	>60	25 (6.67)
Gender	Male	37 (9.87)
	Female	338 (90.13)
Residence type	Urban	213 (56.80)
	Rural	162 (43.20)
Area in China	Eastern	260 (69.33)
	Middle	75 (20.00)
	Western	40 (10.67)
Highest level of education	Up to primary school	16 (4.27)
	Middle/high school	146 (38.93)
	College/university	195 (52.00)
	Advanced degree	18 (4.80)
Main source of income	Personal income	219 (58.40)
	Family support	139 (37.07)
	Social securities/charities	12 (3.20)
	Disease groups	1 (0.27)
	No income	4 (1.07)
Annual household income (CNY)	<50,000	143 (38.13)
	50,000–100,000	123 (32.80)
	100,000–150,000	43 (11.47)
	150,000–200,000	30 (8.00)
	200,000–250,000	11 (2.93)
	>250,000	25 (6.67)
Insurance coverage	UEBMI	212 (56.53)
	URBMI	54 (14.40)
	NRCMI	85 (22.67)
	NFMC	12 (3.20)
	Commercial insurance only	2 (0.53)
	No insurance	10 (2.67)

NFMC, The National Free Medical Services for government officials; NRCMI, The New Rural Cooperative Medical Insurance; UEBMI, The Urban Employee Basic Medical Insurance; URBMI, The Urban Resident Basic Medical Insurance.

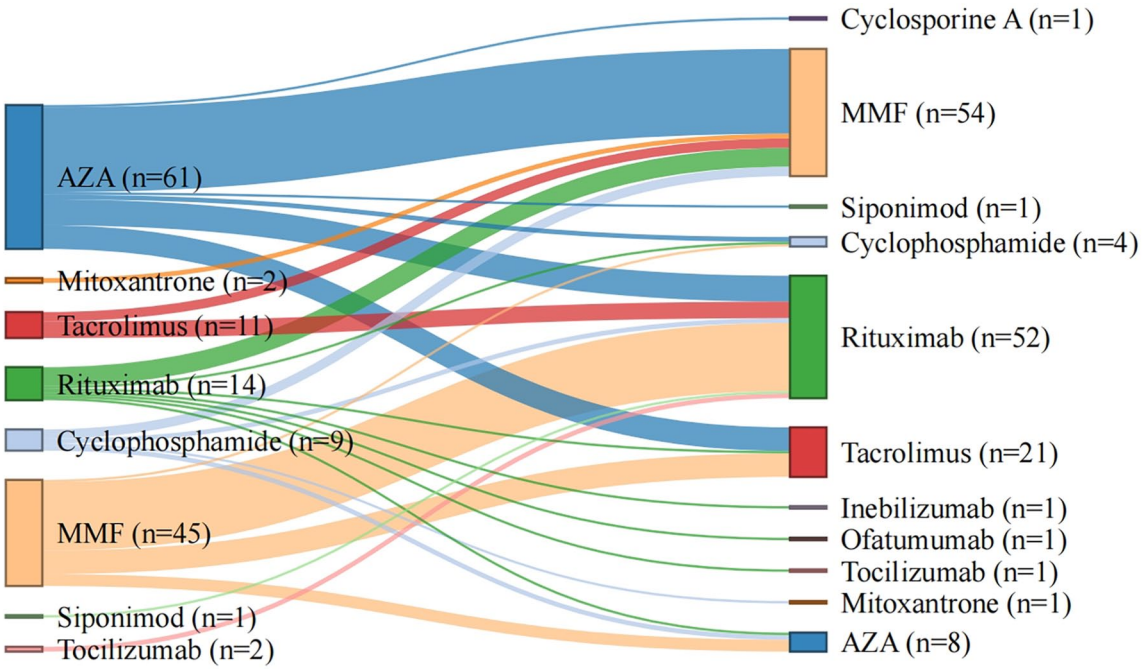

Figure 1. Therapy changes during NMOSD treatment.
The diagram illustrates the pattern of DMT switch, from left to right, in the 113 NMOSD patients who have changed their DMT of choice during treatment course.
AZA, azathioprine; DMT, disease-modifying therapy; MMF, mycophenolate mofetil; NMOSD, neuromyelitis optica spectrum disorder.

Cost and affordability

Over half of the 321 patients on DMTs visited hospitals more often than quarterly (Table 3). The mean and median costs per hospital visit (drug costs excluded) were CNY 3377.47 ± 559.19 and CNY 2500, respectively. The mean monthly out-of-pocket drug expenditure was CNY 3859.76 ± 1159.08 (median CNY 3000) which equals CNY 46,317.12 a year on average. Quarterly medical visits would result in a mean annual cost of around CNY 13,509.88 (USD 1877.87) and a total annual treatment expenditure (drugs included) CNY 59,827.00 (USD 8315.95). Based on their average annual household income of CNY 88,704.58, the patient families spent 52.22% and 67.45% of their annual income on drugs and total treatment expenses, respectively. Both percentages considerably exceeded the threshold of catastrophic healthcare expenditure of 40% household income defined by WHO. Moreover, cost of DMT was not reimbursed for the majority of patients.

Patient opinions

Medical professionals (245 votes), disease websites (200 votes), and patient organizations (195

Table 2. Drug access of NMOSD patients treated with DMTs.

Factors	*n* (%)
Main source to obtain DMTs	
Hospitals (including delivery)	219 (68.22)
Community pharmacies (including delivery)	78 (24.30)
Patient groups or disease organizations	17 (5.30)
Internet pharmacies	4 (1.25)
Pharmaceutical companies	3 (0.93)
Travel time required	
Home delivery or mail order	77 (23.99)
<30 min	41 (12.77)
30 min–1 h	51 (15.89)
1–2 h	48 (14.95)
>2 h	93 (28.97)
Other/unsure	11 (3.43)

DMT, disease-modifying therapy; NMOSD, neuromyelitis optica spectrum diseases.

Table 3. Costs and drug coverages of DMTs in surveyed NMOSD patients.

Factor	Category	*n* (%)
Frequency of follow-up visits	Every year or longer	65 (20.25)
	Every 6 months	87 (27.10)
	Every 3–4 months	100 (31.15)
	Every month	69 (21.50)
Cost per visit (excl. drugs) (CNY)	<200	33 (10.28)
	200–500	48 (14.95)
	500–1000	53 (16.51)
	1000–3000	80 (24.92)
	3000–5000	43 (13.40)
	5000–10,000	28 (8.72)
	>10,000	36 (11.21)
Out-of-pocket drug expenditure per month (CNY)	<200	22 (6.85)
	200–1000	77 (23.99)
	1000–5000	186 (57.94)
	5000–10,000	19 (5.92)
	10,000–30,000	14 (4.36)
	>30,000	3 (0.93)
NRDL drug coverages	100%	2 (0.62)
	80–100%	10 (3.12)
	60–80%	26 (8.10)
	40–60%	24 (7.48)
	20–40%	12 (3.74)
	<20%	10 (3.12)
	None	221 (68.85)
	Other/unsure	16 (4.98)

DMT, disease-modifying therapy; NMOSD, neuromyelitis optica spectrum diseases; NRDL, national reimbursement drug list.

votes) were the three most trusted sources of disease information, accounting for a total of 91.04% of all votes. Patient satisfaction was highest when medical professionals were the source of information, with a mean score of 3.81 ± 1.22 on a five-point scale.

Most patients expressed concerns about their inability to afford DMTs (see Figure 2). Out of the 321 patients on DMTs, 135 (42.06%) believed that the drug cost was the greatest barrier to treatment access. Primary challenges for 89 patients included a lack of effective treatment, whereas 60 patients faced difficulties in diagnosis. Among the 37 patients who were most anxious about treatment availability, the greatest inconvenience was the need to travel out of town to obtain drugs, and some drugs required hospitalization for administration or insurance reimbursement.

The patients' demands regarding the focus of rare disease legislation are summarized in Figure 3. The results were consistent with the primary challenges faced by patients during treatment. Increasing the inclusion of DMTs into NRDL and improving the coverage rates for reimbursed drugs was the most frequent suggestion, followed by suggestions for patient advocacy through legislation and a budget increase in orphan drug development. Other patient demands were related to information and treatment access.

TSQM

Table 4 describes the mean TSQM scores of patients by current or most recent DMT. Patients on rituximab perceived the highest satisfaction except in the convenience domain, though convenience was the only domain that a significant difference was observed among groups ($p < 0.001$).

All patient factors, including patient characteristics, treatment access (sources and travel time required to obtain DMTs), and treatment costs, were analyzed to assess their correlations with TSQM global satisfaction scores. Statistical analysis revealed that only age ($p = 0.002$) and travel time required ($p = 0.036$) exhibited significant differences between groups (Table 5). *Post hoc* analysis suggested that patients aged 18–30 years were significantly more satisfied with their current DMT compared to all other age groups; however, patients aged 31–40 years reported significantly greater satisfaction than patients 41–50 years old only. Patients who had to travel over 2 h to obtain medications were significantly less satisfied.

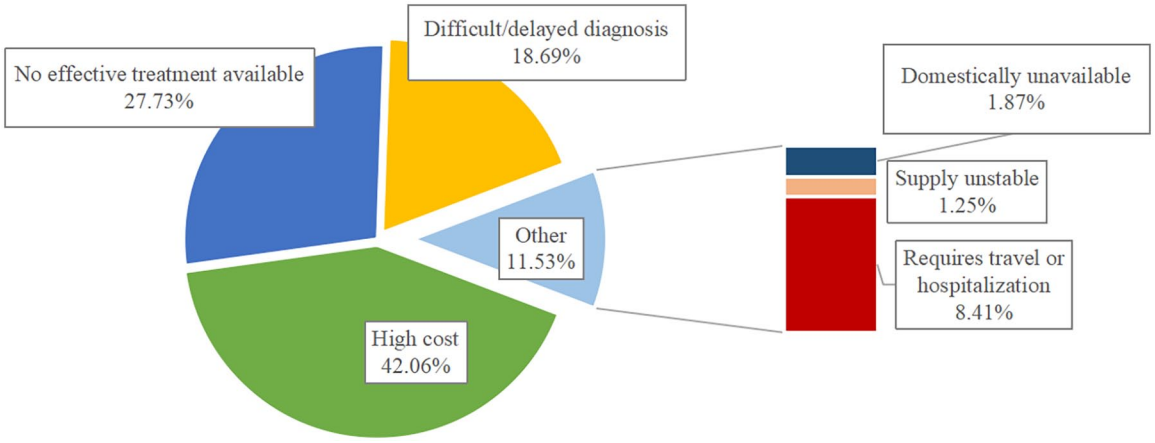

Figure 2. Primary challenge perceived by NMOSD patients in DMT treatment.
DMT, disease-modifying therapy; NMOSD, neuromyelitis optica spectrum diseases.

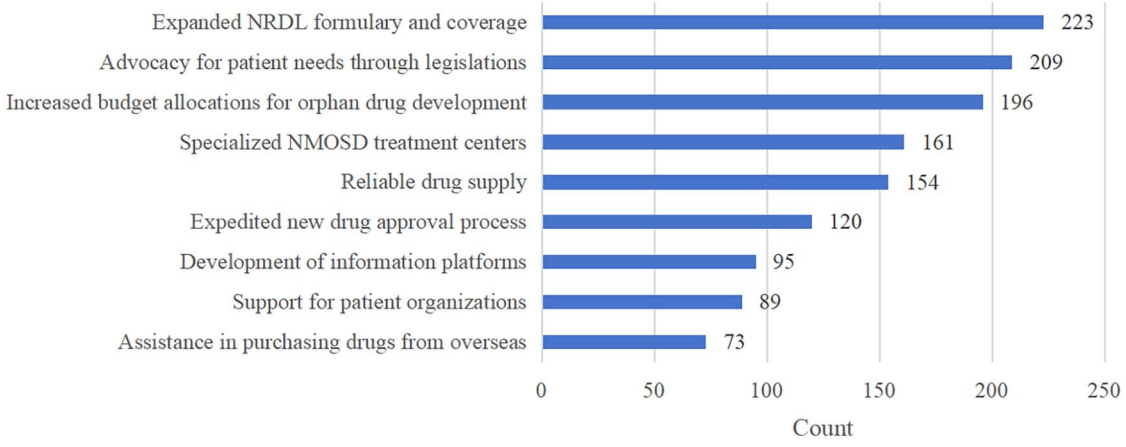

Figure 3. Demands of NMOSD patients by count of selections.
NMOSD, neuromyelitis optica spectrum disorder; NRDL, national reimbursement drug list.

Age and travel time required were identified as FDR-corrected candidate factors for regression analysis. Age values were transformed to log scale to ensure a normal distribution prior to inclusion in the linear regression model. The model was significant ($F = 4.927$, $p < 0.001$), $R^2 = 0.073$, adjusted $R^2 = 0.058$, D–W = 1.878. Age ($p = 0.001$) and a commuting time of over 2 h to obtain DMT ($p = 0.016$) were found to be negatively associated with global satisfaction (Table 6).

Discussion

This cross-sectional study investigated the treatment status, DMTs accessibility, and treatment satisfaction among patients with NMOSD in China. Through a patient survey, the study explored factors influencing barriers to accessing DMTs and treatment satisfaction from patients' perspective. The study results not only expanded the population evaluated with TSQM to include NMOSD patients but also emphasized the impact of DMT availability, cost, and affordability on treatment satisfaction in Chinese NMOSD patients.

Despite recent advances in disease awareness, challenges persist in achieving timely diagnosis. The time from symptom onset to a definitive diagnosis could range from a couple months to decades.[17–21] Our patients typically waited for more than 3 months for their first medical visit

Table 4. TSQM scores of NMOSD patients by DMT.

DMT	*n*	Effectiveness	SD	Side effects	SD	Convenience	SD	Global satisfaction	SD
Azathioprine	40	60.48	19.50	66.50	30.33	63.30	16.66	56.23	21.00
MMF	167	58.11	16.49	67.56	29.33	53.52	15.46	54.49	16.77
Rituximab	70	60.96	17.36	77.43	25.53	50.46	18.24	57.84	17.80
Tacrolimus	19	59.53	21.42	59.68	26.67	53.79	15.74	50.84	18.42
Others	25	54.72	13.29	66.68	27.46	45.56	19.20	50.04	20.22

'Others' includes multi-drug regimens and DMTs used by less than five patients.
DMT, disease-modifying therapy; NMOSD, neuromyelitis optica spectrum diseases; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

and another year to receive a definitive diagnosis, which required three to four visits on the journey. They generally had to travel to a major city for both diagnosis and to obtain their medications. In fact, almost 20% of the patients in our study claimed that 'difficult diagnosis' was the main obstacle to treatment access. A Spanish study also found that geographical distance, the number of medical visits required for diagnosis, and waiting over 6 months to see a specialist were the main factors contributing to diagnostic delay in rare diseases.[22] Notably, studies have identified the gender of female, an onset age of 30–44 years, and suffering from a rare disease of the nervous system as individual determinants associated with diagnostic delay,[22,23] all of which align with the characteristics of NMOSD. The complexity of diagnostic testing and issues with the availability of diagnostic tools for neurological diseases could contribute to this diagnostic odyssey.[5,24,25] In China, more than half of the rare disease patients were diagnosed at an average distance of 562 km from home.[26] This probably resulted from the inadequate and uneven distribution of medical resources in China, from diagnostic tools to qualified neurologists.[27]

Economic disparities may result in an uneven distribution of resources. The Middle and Western areas of China often face economic disadvantages compared to the Eastern area, leading to a shortage of medical resources and lower socioeconomic status among patients. These factors have been identified as key influencers in obtaining a definitive diagnosis.[26,28] Policy as a foundational factor upstream in promoting health equity is in great demand to alleviate the health disparities among regions.[29] Encouragement of academic communication and legislative support in resource sharing are examples that may allow easier access to diagnostic resources for all patients and professionals in the country.

Insufficient disease knowledge could be another reason that delays accurate diagnosis and treatment. Mistaking NMOSD for multiple sclerosis or myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease can easily occur especially under a deficit of disease knowledge.[30] A misdiagnosis of NMOSD can delay proper treatment or even incorrect treatment, potentially causing harm.[2,31] However, 33% of the medical staff in tertiary hospitals in China barely had any knowledge of or exposure to rare diseases.[32] This lack of awareness may contribute to the suboptimal patient satisfaction with healthcare professionals as a source of disease information. Therefore, disease education for healthcare professionals is crucial to reduce misdiagnosis and to expedite the diagnostic process.

Inconvenience in obtaining medication significantly affected patient satisfaction. Most patients relied on hospitals for medication, so a routine commute was required. This includes patients living outside a 2-h radius from the hospital. The complexity of the techniques used in NMOSD diagnosis[30] limited both diagnosis and treatment capabilities to only a handful of hospitals in regions with advanced medical facilities, primarily in major metropolitan areas. Patients residing in other regions, particularly those in remote areas, have to travel to access medical resources.

Certain DMTs such as MMF, rituximab, and AZA used to treat common immune-related

Table 5. Candidate factors that affect global satisfaction scores of NMOSD patients.

Factors	Global satisfaction (mean ± SD)	*F*	*p*	FDR
Age (years)		4.407	0.002	0.028
18–30	61.26 ± 19.70			
31–40	55.90 ± 17.98			
41–50	49.63 ± 17.61			
51–60	52.12 ± 15.07			
>60	51.30 ± 13.47			
Gender		0.2	0.655	0.781
Male	55.14 ± 21.32			
Female	54.85 ± 17.65			
Residence type		2.11	0.147	0.442
Urban	55.53 ± 17.86			
Rural	53.96 ± 18.13			
Area in China		0.611	0.544	0.781
Eastern	55.54 ± 17.42			
Western	54.64 ± 20.67			
Middle	52.54 ± 18.36			
Level of education		0.402	0.669	0.781
Up to high school level	52.50 ± 18.07			
Undergraduate level	56.68 ± 17.72			
Graduate level	55.47 ± 18.52			
Disease duration (years)		0.422	0.656	0.781
⩽3	54.25 ± 17.79			
4–6	54.43 ± 19.44			
⩾7	55.85 ± 16.90			
Number of visits prior to diagnosis		2.155	0.074	0.345
1	50.48 ± 19.29			
2	54.38 ± 17.99			
3	58.44 ± 15.07			
4–6	53.50 ± 18.85			
⩾7	60.91 ± 16.51			

(Continued)

Table 5. (Continued)

Factors	Global satisfaction (mean ± SD)	*F*	*p*	FDR
Annual household income (CNY)		1.051	0.351	0.702
<50,000	51.77 ± 19.18			
50,000–100,000	56.10 ± 16.81			
>100,000	57.34 ± 17.25			
Main source to obtain DMTs		0.375	0.541	0.781
Hospital	54.09 ± 18.20			
Non-hospital	56.55 ± 17.43			
Travel time required (hour)		2.605	0.036	0.252
Home delivery or mail order	57.38 ± 15.18			
<0.5	57.96 ± 19.49			
0.5–1	56.71 ± 16.59			
1–2	56.20 ± 16.17			
>2	49.55 ± 20.08			
Frequency of follow-up visits		1.747	0.158	0.442
Monthly	50.00 ± 17.77			
Quarterly	55.68 ± 18.79			
Biannually	57.14 ± 17.02			
Annually	55.78 ± 17.55			
Out-of-pocket drug expenditure per month (CNY)		1.349	0.261	0.609
<1000	56.75 ± 16.71			
1000–5000	53.56 ± 19.04			
>5000	56.50 ± 15.23			
NRDL drug coverages		0.088	0.767	0.826
Full or partial	55.10 ± 17.67			
None	54.37 ± 18.69			
Current DMT choice		0.119	0.976	0.976
AZA	56.23 ± 21.00			
MMF	54.49 ± 16.77			
Rituximab	57.84 ± 17.80			
Tacrolimus	50.84 ± 18.42			
Others	50.04 ± 20.22			

AZA, azathioprine; DMT, disease-modifying therapy; FDR, false discovery rate; MMF, mycophenolate mofetil; NMOSD, neuromyelitis optica spectrum diseases; NRDL, national reimbursement drug list; SD, standard deviation.

Table 6. Linear regression of the candidate factors that affect global satisfaction scores of NMOSD patients.

Factors	Coefficient	SE	*T*	*p*	95% CI
Constant	97.286	11.949	8.142	0.000	73.866, 120.706
Travel time required (h)					
Ref: 0.5–1					
>2	−7.117	2.944	−2.418	0.016	−12.887, −1.348
1–2	−0.178	3.412	−0.052	0.958	−6.867, 6.510
<0.5	1.485	3.492	0.425	0.671	−5.358, 8.329
Home delivery or mail order	0.502	3.063	0.164	0.870	−5.501, 6.505
Age (in log scale)	−25.554	7.382	−3.462	0.001	−40.022, −11.086

CI, confidence interval; NMOSD, neuromyelitis optica spectrum diseases; SE, standard error.

conditions are readily available in many hospitals. However, not all hospitals that use these DMTs have specialists in NMOSD, leading to a clustering of patients in top-tier tertiary hospitals. The Chinese government has been promoting the relocation of medical resources since 2015. As increased attention has been paid to the rare disease population, there is a growing effort of medical training in rare diseases for practitioners at secondary and primary institutions. Local care for NMOSD should be attainable in the near future.

High cost of treatment has discouraged many NMOSD patients from accessing better treatment options. China implements universal healthcare coverage that requires substantial political and financial commitment.[33,34] With a relatively limited health expenditure per capita in China,[35,36] the primary objective of NBMI is to ensure fair access to basic medical services for all citizens, resulting in a restricted coverage of high-cost orphan drugs. Consequently, little improvement was observed in economic burden on NMOSD patients compared to the literature results.[15] Cost was the main reason for the patients to opt for acute treatment only instead of using DMTs. It was also found to be the primary reason for the patients to discontinue rituximab, especially the branded product. Among AZA, MMF, and rituximab, only AZA is fully covered by NBMI; the coverage rates for the other two vary by province and are currently only partially reimbursed. Patients from regions with lower medical budgets may reach their payout cap sooner, leading to higher out-of-pocket expenses. Furthermore, none of the three DMTs are officially indicated for NMOSD treatment. Off-label use is generally not supported and reimbursed by NBMI.

There has been a rapid expansion of DMTs in recent years.[37] Satralizumab and inebilizumab were recently launched in China with an indication for NMOSD, and eculizumab has also received a recent approval for NMOSD treatment. Patience is necessary for policies to take effect on drug affordability of these innovative drugs. With the inclusion of inebilizumab in the NRDL starting in 2023, future inclusions of DMTs is anticipated. The use of innovative drugs will therefore increase among patients, leading to improved treatment outcomes and reduced long-term total disease burden for patients and society.

Treatment satisfaction results were less than ideal. All TSQM scores were in the range of 50s–60s except for rituximab, which scored over 77 in satisfaction of side effects. However, as the only injectable drug in comparison, rituximab was considered the least convenient, which could be explained by its route of administration. Patients on rituximab may require premedication before infusion, making it less favorable. Additionally, the necessity for regular hospital visits poses a burden, particularly for NMOSD patients who have to travel long distances for treatment. Other than the inconvenience, rituximab was preferred for its effectiveness and low side effects, further contributing to the existing evidence of the

superiority of rituximab in NMOSD treatment compared to other DMTs like MTX and AZA.[38–40]

In our study, rituximab was the second most widely used DMT both in current therapies and as the switch-to drug, following MMF. MMF consistently ranked first as the initial DMT and the current/last DMT. AZA was switched-off most often with effectiveness being the main reason for change of therapy. Judging from their respective TSQM scores and literature findings on efficacy and safety,[41,42] no definitive conclusion could be drawn yet to explain the dominance of MMF in the study patients. In fact, evidence regarding treatment sequences and switching remains inconclusive.[37] MMF was favored over rituximab probably due to its convenience as an oral drug and the significant cost reduction; as compared to AZA, it is supposed that MMF was preferred for its slight advantage in observed safety in the Chinese patient population.[43–45] Drug supply may be another real-world factor influencing the choice of therapy by prescribers, which is beyond the scope of this study.

Patients were not satisfied with their current therapy on traditional immunosuppressive agents. New treatment alternatives such as satralizumab and inebilizumab were rarely used since they have only recently become available in the Chinese market within the last 2 years. In our study, younger patients were associated with higher satisfaction scores, possibly due to their shorter disease duration and earlier access to novel, more effective therapies compared to older patients over the disease course. An improvement in effectiveness and overall treatment satisfaction is anticipated with the growing use of the latest treatment options for NMOSD patients in China.

Patient suggestions aligned with the study findings. High treatment cost was the primary concern, given the universal challenge of affordability for rare disease patients.[5,11,46] Additionally, nearly two-thirds of the NMOSD patients expressed the pressing need for attention to drug research and development, indicating dissatisfaction with current treatment options. Efforts to improve drug accessibility in NMOSD should prioritize enhancements in diagnosis and treatment effectiveness rather than solely focusing on costs. The survey also underlined the importance of developing credible and publicly accessible information platforms for rare diseases. Such platforms could mitigate the lack of disease education in patients, encouraging early visits to specialist.

Limitations

The geographical concentration of the recruited respondents could introduce potential selection bias, as their experiences might not fully represent patients in other regions across the country. However, the regional distribution of the patients in this study is comparable to a previous survey of the NMOSD patients in China.[15] The similar patient distribution implies that our study results could remain representative of patients from different regions. Recall bias may also exist due to the nature of patient-reported outcomes and online surveys. Furthermore, since this study focused on drug accessibility, the patients' clinical status including physical disability, comorbidities, and mental status were not considered. Therefore, potential impacts of the clinical factors on treatment effectiveness and patient satisfaction were not investigated in this study. A more structured survey using point scales that takes clinical aspects into consideration would be necessary in future studies for a more comprehensive and objective measurement.

Conclusion

NMOSD patients in China experienced significant challenges in treatment access, owing to the delayed diagnosis, extended travel times to obtain medications, and treatment costs that exceed the threshold for catastrophic health expenditure. Treatment satisfaction was generally suboptimal. Policy interventions should prioritize reducing the economic burden of appropriate treatment and enhancing disease education and information access for both healthcare professionals and patients to facilitate early and accurate diagnosis.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Huashan Hospital, Fudan University (KY2022-727). All participants provided an infomed, signed consent.

Consent for publication

Not applicable.

Author contributions

Yue Yu: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Visualization; Writing – original draft; Writing – review & editing.

Mingkang Zhong: Conceptualization; Investigation; Resources; Software; Writing – review & editing.

Chao Quan: Funding acquisition; Methodology; Resources; Supervision; Writing – review & editing.

Chunlai Ma: Conceptualization; Investigation; Methodology; Supervision; Validation; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

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

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Supplemental material

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