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ORIGINAL RESEARCH

Patient Pathway to Diagnosis of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD): Findings from a Multinational Survey of 204 Patients

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ABSTRACT

Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare demyelinating disorder of the central nervous system. Despite increased recognition of MOGAD as a distinct disease and the availability of sensitive methods of MOG antibody testing, diagnostic challenges remain. We conducted a survey to explore the patient experience from the start of symptoms to final MOGAD diagnosis.

Methods: A 23-question online survey (including multiple-choice and free-text responses) covering symptom history, healthcare interactions and impact of diagnosis was emailed to people living with MOGAD by The MOG Project patient advocacy group. People living with MOGAD could share the survey with their caregivers. Anonymised responses were analysed.

Results: In total, 204 people living with MOGAD or their caregivers from 21 countries completed the survey; most respondents were from North America. Age of symptom onset ranged from 1 to 66 (median 28) years. Symptoms that prompted patients to seek medical care included blurred vision/loss of vision (58.2%), eye pain (35.8%) and difficulty walking (25.4%). Patients most frequently presented to emergency care physicians (38.7%) and primary care doctors (26.0%), with the MOGAD diagnosis most often made by general neurologists (40.4%) or neuro-immunologists (30.0%).Patients saw a median of four doctors before diagnosis, with 26.5% of patients seeing at least six doctors. Although 60.6% of patients received a MOGAD diagnosis within 6 months of experiencing initial health problems, 17.7% experienced a ≥ 5-year delay. More than half of patients (55.4%) received an alternative primary diagnosis before final MOGAD diagnosis. Most respondents (60.6%) reported receiving insufficient information/resources at the time of MOGAD diagnosis. Diagnostic delay was

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associated with long-term negative consequences for physical health.
Conclusion: This survey provides unique insights from people living with MOGAD and their caregivers that could help address the challenges faced in the pathway to final MOGAD diagnosis.

Keywords: Demyelination; Diagnosis; Myelin oligodendrocyte glycoprotein (MOG); Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD); Neurology; Patient perspective; Survey; Symptoms

Key Summary Points

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is increasingly recognised as a disease distinct from other inflammatory central nervous system demyelinating diseases, including multiple sclerosis and aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder.

Despite antibody testing, MOGAD diagnosis can remain challenging due to its heterogeneous disease course and low awareness of MOGAD among healthcare professionals.

We conducted an online survey of people living with MOGAD and their caregivers to explore the challenges faced in the pathway to final MOGAD diagnosis.

This survey revealed that many patients faced a protracted and multi-step pathway towards MOGAD diagnosis, although it is likely that some of these patients sought diagnoses before MOG antibody testing was available.

This survey provides important insights into the patient and caregiver perspectives of the challenges associated with the diagnosis of MOGAD to help facilitate improvement of the diagnostic pathway.

INTRODUCTION

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare, inflammatory, demyelinating condition of the central nervous system (CNS), caused by pathogenic serum antibodies that target MOG expressed on the surface of the myelin sheath [1–3]. The prevalence of MOGAD is estimated to be 1–4 cases per 100,000 people [3], and the disease is equally likely to affect males and females [4]. The disease course can be relapsing (reported for 44– 83% of patients) or monophasic, the latter subtype being more common in MOGAD than in other neurological demyelinating disorders, such as neuromyelitis optica spectrum disorder (NMOSD) or multiple sclerosis (MS) [3, 5]. The clinical phenotypes of MOGAD are variable and include transverse myelitis (TM), optic neuritis (ON), acute disseminated encephalomyelitis (ADEM), NMOSD and cerebral cortical encephalitis, making diagnosis challenging [5–13].

Despite the introduction of MOG antibody (MOG-Ig) diagnostic testing in some regions and countries, MOGAD diagnosis can remain challenging due to its heterogeneous disease course, its overlapping clinical presentations with other CNS demyelinating diseases and low awareness of MOGAD among healthcare professionals. In patients with clinical features consistent with MOGAD, evidence supports the use of a cell-based assay (preferably live cells) using a target antigen of full-length human MOG to detect MOG immunoglobulin G (IgG) in serum [5, 14–16]. In addition to MOG-Ig and aquaporin 4 (AQP4)-IgG testing, neurological examination, magnetic resonance imaging and spinal fluid analysis can also facilitate the differentiation of MOGAD, AQP4 + NMOSD and MS [5, 17–21]. The International Classification of Diseases (ICD) 11th Revision (updated February 2022) implies that MOGAD is a subtype of neuromyelitis optica [22]. Distinct ICD coding for MOGAD that recognises MOGAD as a distinct rare disease in global classification systems could help the patient diagnostic pathway. An international survey of neurologists conducted in 2019 reported highly varied

treatment strategies for MOGAD [23]. Disease management strategies for MS and NMOSD have been applied to MOGAD, with some treatments showing high effectiveness [15, 24]; however, treatments for MOGAD adopted from MS and NMOSD may be ineffective or even harmful in some cases [15, 25–27]. Earlier and correct diagnosis of MOGAD may mitigate the risks associated with potentially inappropriate treatments. New expert consensus recommendations for MOGAD disease definition and diagnostic criteria [28], and refined diagnostic criteria for MS to help exclude patients with MOGAD, will help to reduce diagnostic delay and raise awareness of MOGAD.

Published data on MOGAD and the challenges of timely diagnosis are in general presented through the lens of the physician and the medical system. The patient perspective in rare disease can be informative, providing additional insights into disease-specific needs. To assess gaps in clinical care, we conducted a survey of people living with MOGAD and their caregivers covering the time from initial symptom onset and the pathway to diagnosis.

METHODS

Patient Population

The MOG Project (Olney, MD, USA) is a patient advocacy group that provides resources for doctors, people living with MOGAD and caregivers, while also providing support for the community, raising awareness of MOGAD and advocating for research into a cure [29]. The MOG Project is an important global resource for people living with MOGAD. The only inclusion criterion for this survey was to be a person living with MOGAD or the caregiver of a person living with MOGAD; there were no exclusion criteria. Confirmation of diagnosis of MOGAD was not required for feasibility reasons.

Survey Development

The survey was designed by UCB Pharma (ZP) in collaboration with The MOG Project (authors JG and JL) and a paediatric neuro-immunologist (author JDS). The survey comprised 23 multiple-choice and free-text questions (Table 1) covering patient and caregiver perspectives on patient disease history and healthcare interactions up to MOGAD diagnosis. Free-text questions were included to elicit patient and caregiver perspectives that could potentially highlight any unmet educational needs of healthcare professionals, adding value to the multiple-choice questions. Some questions only required a response if the response to the preceding question was affirmative. Although the survey was presented only in English, non-English responses were permitted and were translated into English prior to analysis.

The survey received ethics approval from the University of Southern California Institutional Review Board (ID:21-0082). As the study did not involve clinical data or involve data collection from other institutions, only one centre was used to approve study material and perform ethics review. Ethics approval was waived after expedited review as there was no clinical or identifying information collected. Survey participants were informed of the intention to publish the anonymised results before they began the survey. All survey respondents provided informed consent to participate in the study on the survey landing page prior to being able to start the survey. An option to opt out of the survey was available on all displayed pages. As the study was an anonymous patient and caregiver survey to report perspectives on the pathway to MOGAD diagnosis, no verification of individual patient data was required. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Survey Administration

The survey was distributed by The MOG Project to people living with MOGAD who had already signed up to The MOG Project email distribution list ($n = 225$). The survey was also shared on three social media platforms: Facebook ($n = 1800$ members in The MOG Project group), Instagram (approximately 150 views of the

Table 1 Survey questions

Question number	Question	Response option(s)
Pre-survey question	Which country are you from?	No response type specified
1	How old were you (or your child) when you first started experiencing symptoms associated to myelin oligodendrocyte glycoprotein antibody disease (MOGAD)? This can be before you were diagnosed by a doctor.	_____ *<numerical value 1–99>*
2	At what age were you (or your child) diagnosed with MOGAD? ***Select one response.***	a. 0–9 years b. 10–18 years c. 19–29 years d. 30–39 years e. 40–49 years f. 50–59 years g. 60–69 years h. 70+ years i. NA; not formally diagnosed (if selected, respondent was screened out of survey)

Question number	Question	Response option(s)
3	Thinking back to before you (or your child) were diagnosed with MOGAD, which of the following was the very first health problem you remember experiencing?† ***Select all appropriate responses.***	a. Back pain b. Blurred vision/loss of vision c. Tiredness/fatigue d. Eye pain e. Cold/flu-type symptoms f. Confusion g. Difficulty walking h. Headache i. Leg/arm tingling/loss of sensation j. Leg/arm weakness k. Memory problems l. Seizures m. Urinary problems/incontinence n. Other pain o. Other; please specify: _____

post), and Twitter (approximately 850 views of the post). Instagram and Twitter post views may not represent unique users of these social media platforms. Caregivers could complete the survey on behalf of individuals, if required (e.g. person living with MOGAD had visual impairment). Here, 'respondents' refers to people living with MOGAD, whether responses were self- or proxy-reported. Anonymised survey responses, collected from 18 January to 1 March 2022, were collated using QuestionPro [30]. Any identifying free-text information was removed by The MOG Project organisation before being shared with UCB Pharma for analysis. Respondents consented to publication of the resulting data through active acknowledgement on the survey landing page. Results were reviewed and analysed by UCB Pharma; only completed surveys were used in the analysis.

Table 1 continued

Question number	Question	Response option(s)
4	Thinking back to before you (or your child) were diagnosed with MOGAD, what other MOGAD-related health problems developed after your first health problem of *<insert response from Q3>*? As best as you can recall, in what order did these other health problems occur?† *<Drop and drag exercise where respondents select and order from the list>.*	a. Back pain b. Blurred vision/loss of vision c. Tiredness/fatigue d. Eye pain e. Cold/flu-type symptoms f. Confusion g. Difficulty walking h. Headache i. Leg/arm tingling/loss of sensation j. Leg/arm weakness k. Memory problems l. Seizures m. Urinary problems/incontinence n. Other pain o. Other; please specify: _____ p. I did not have any other health problems
5	What were the main MOGAD-related health problems that eventually made you (or your child) seek medical advice from a healthcare professional? In other words, what were your most severe symptoms that required you to seek medical care? *Select all appropriate responses.*	a. Back pain b. Blurred vision/loss of vision c. Tiredness/fatigue d. Eye pain e. Cold/flu-type symptoms f. Confusion g. Difficulty walking h. Headache i. Leg/arm tingling/loss of sensation j. Leg/arm weakness k. Memory problems l. Seizures m. Urinary problems/incontinence n. Other pain o. Other; please specify: _____
6	How long did it take between your first MOGAD symptom and seeking medical advice?	a. Less than 2 months b. 2 to 5 months c. 6 to 12 months d. >1 year; specify number of years: _____

Statistical Analysis

All statistical analyses were performed using SAS v.9.4 for data cleaning, data manipulation and analysis; R v.4.0.2 was used for data visualisations. Given the nature of the raw data, some data cleaning was required before analysis could proceed. This included translation of some survey responses from Dutch and Spanish into English, removal of invalid responses (for example, where each question had the same response or responses had no relation to the

Table 1 continued

Question number	Question	Response option(s)
7	<ASK IF Q6 = D> Please explain the reason for waiting more than 1 year to seek medical advice.	_____ *<open end w/ significant number of characters, e.g. 2000>*
8	What type of doctor did you (or your child) see when you first sought medical advice for your initial MOGAD health problems?	a. Primary care doctor (general practitioner/family medicine/internist) b. Paediatrician (doctor who treats children) c. Ophthalmologist (doctor who treats disorders of the eye) d. Neuro-ophthalmologist (doctor who treats disorders of the eye caused by brain disease) e. General neurologist (doctor who treats brain disorders) f. Neuro-immunologist (doctor who treats brain disorders caused by the immune system) g. Movement disorder specialist (doctor who treats brain disorders with muscular issues) h. Emergency care doctor i. Geneticist (doctor who treats people with genetic disorders) j. Other specialty, please specify: _____ k. NA; you (or your child) were not referred to another physician

Question number	Question	Response option(s)
9	What type of doctor were you (or your child) referred to next?	a. Primary care doctor (general practitioner/family medicine/internist) b. Paediatrician (doctor who treats children) c. Ophthalmologist (doctor who treats disorders of the eye) d. Neuro-ophthalmologist (doctor who treats disorders of the eye caused by brain disease) e. General neurologist (doctor who treats brain disorders) f. Neuro-immunologist (doctor who treats brain disorders caused by the immune system) g. Movement disorder specialist (doctor who treats brain disorders with muscular issues) h. Emergency care doctor i. Geneticist (doctor who treats people with genetic disorders) j. Other specialty, please specify: _____ k. NA; you (or your child) were not referred to another physician

survey), and removal of responses outside the scope of the question.

Quantitative data [survey question (Q)1–6, Q8–13, Q15, Q18–20] were summarised with number of responses, mean, standard deviation, median, minimum and maximum values; categorical variables were summarised using number and percentage of responses. Qualitative data (Q7, Q14, Q16, Q17, Q21–23) were categorised by two independent reviewers and adjudicated by a third independent reviewer in the case of differences. These data were then summarised in a manner similar to that used for the categorical variables, presenting summary statistics for the number of respondents that fell within each category. Categories for the analysis of free-text responses are listed in Supplemental Table 1.

Table 1 continued

Question number	Question	Response option(s)
10	How long did you (or your child) have to wait to see the doctor to which you were referred?	a. 1 week b. 2 to 3 weeks c. 4 to 6 weeks d. 2 months e. 3 months f. 4 months g. 5 months h. 6 months i. Longer than 6 months j. Other; please specify: _____
11	What type of doctor eventually made your (or your child's) diagnosis of MOGAD?	a. Primary care doctor (general practitioner/family medicine/internist) b. Paediatrician (doctor who treats children) c. Ophthalmologist (doctor who treats disorders of the eye) d. Neuro-ophthalmologist (doctor who treats disorders of the eye caused by brain disease) e. General neurologist (doctor who treats brain disorders) f. Neuro-immunologist (doctor who treats brain disorders caused by the immune system)
		g. Movement disorder specialist (doctor who treats brain disorders with muscular issues) h. Emergency care doctor i. Geneticist (doctor who treats people with genetic disorders) j. Other specialty, please specify: _____
12	How many different doctors did you (or your child) see in total before you finally received your diagnosis of MOGAD?	_____ *<numerical value 1–99>*
13	From the time that you (or your child) **first experienced health issues** related to MOGAD, how long did it take to get diagnosed?	a. Less than 6 months b. 6 to 11 months c. 1 year d. 2 years e. 3 years f. 4 years g. 5 years h. 6 years i. 7 years or more

RESULTS

Respondents

A total of 204 respondents from 21 countries completed the survey. Most respondents (73.5%, 150/204) were from North America (Canada and USA), followed by 15.2% (31/204) from Europe (Belgium, Croatia, France, Germany, Norway, Switzerland, Spain and the UK), 6.4% (13/204) from Australia and New Zealand, 2.0% (4/204) from Asia (India, Japan and

Table 1 continued

Question number	Question	Response option(s)
14	<ASK IF Q13 = I> Please explain why it took 7 years or more to get a MOGAD diagnosis **from the point of your initial symptoms**.	No response type specified
15	From the time that you (or your child) saw the **very first doctor for your initial health problems**, how long did it take to get diagnosed with MOGAD?	a. Less than 6 months b. 6 to 11 months c. 1 year d. 2 years e. 3 years f. 4 years g. 5 years h. 6 years i. 7 years or more
16	<ASK IF Q15 = I> Please explain why it took 7 years or more to get a MOGAD diagnosis **from the point of when you saw your first doctor**.	
17	Thinking back to before you (or your child) had the diagnosis of MOGAD, were you (or your child) misdiagnosed with another illness?	a. Yes, please specify other medical diagnoses: _____ b. No c. I don't remember
18	Do you feel you (or your child) were provided with enough information and/or resources at the time of your (or your child's) MOGAD diagnosis?	a. Yes b. No
19	<IF Q18 = B> What information and/or resources would you have liked to receive at the time of your MOGAD diagnosis?	a. Pamphlets b. Brochure c. Online video resources d. Advocacy website information e. Support group information f. Other: _____*<open end w/ significant number of characters, e.g. 2000>*

Turkey), 1.5% (3/204) from Africa (South Africa) and the Middle East (Egypt and Lebanon) and 1.5% (3/204) from South America (Brazil, Chile and Mexico). Free-text responses were reviewed by a physician author and a MOG Project representative author prior to arbitration by a clinician author. Responses were consistent with a diagnosis of MOGAD, and there was no evidence that fraudulent responses (i.e. from people who did not receive a diagnosis of MOGAD) were received.

Experience from Time of Initial Symptoms

The age of onset of initial symptoms associated with MOGAD (Survey Q1, 105 respondents) ranged from 1 to 66 years, with a mean (median) of 27.4 (28.0) years. Age at MOGAD diagnosis (Survey Q2) was most often reported in children at < 10 years of age (19.1%, 39/204) or between 30 and 49 years of age (40.2%, 82/204) (Fig. 1). Approximately 30% of respondents (62/204) were aged ≤ 18 years when they received a diagnosis of MOGAD.

Table 1 continued

Question number	Question	Response option(s)
20	Which type of doctor **do you currently see** for the management of your MOGAD?	a. Primary care doctor (general practitioner/family medicine/internist) b. Paediatrician (doctor who treats children) c. Ophthalmologist (doctor who treats disorders of the eye) d. Neuro-ophthalmologist (doctor who treats disorders of the eye caused by brain disease) e. General neurologist (doctor who treats brain disorders) f. Neuro-immunologist (doctor who treats brain disorders caused by the immune system) g. Movement disorder specialist (doctor who treats brain disorders with muscular issues) h. Emergency care doctor i. Geneticist (doctor who treats people with genetic disorders) j. Other specialty, please specify: _____
21	Please share any thoughts you have about your 'journey' from first experiencing health issues related to MOGAD, to when you were finally diagnosed with MOGAD. Please include your thoughts about the importance or the value that you give to having a proper and timely diagnosis and how the diagnostic process could be improved.	_____ *<open end w/ significant number of characters, e.g. 2000>*

Question number	Question	Response option(s)
22‡	Prior to your (or your child's) MOGAD diagnosis, if any, what sort of activities were you unable to perform because of your (or your child's) health problems related to MOGAD? How did having a final MOGAD diagnosis change anything?	_____ *<open end w/ significant number of characters, e.g. 2000>*
23	Have you (or your child) had any long-term health consequences as a result of not being diagnosed earlier with MOGAD? Please provide details.	_____ *<open end w/ significant number of characters, e.g. 2000>*

MOGAD myelin oligodendrocyte glycoprotein antibody-associated disease, *NA* not applicable
*Response options were presented in a random order for all multiple-choice questions
†Questions 3 and 4 were presented as one question; respondents were asked to place health problems in the order in which they occurred, starting with the first health problem experienced
‡Question 22 was divided into Questions 22a and 22b prior to analysis

The most common initial health problems experienced (Survey Q3) included headache (21.0%, 41/195), followed by eye pain (13.3%, 26/195) and cold/flu-like symptoms (12.3%, 24/195) (Fig. 2). After the initial health problems (Survey Q4), headache and eye pain continued to be experienced by 56.2% (113/201) and 60.7% (122/201) of respondents, respectively (Table 2). Patients experienced other health problems including blurred vision/loss of vision (68.7%, 138/201), tiredness/fatigue (57.7%, 116/201) and leg/arm tingling/loss of sensation (47.3%, 95/201) among a wide range of other symptoms (Table 2). The MOGAD-related health problems that led respondents to seek medical care (Survey Q5) included blurred vision/loss of vision (58.2%, 117/201), eye pain

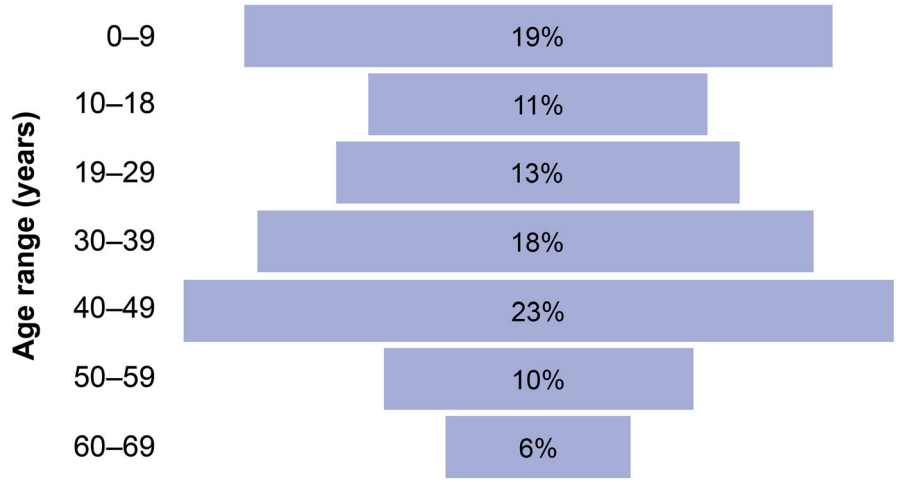

Fig. 1 Age at time of MOGAD diagnosis*. *Survey Question 2; data from 204 respondents. *MOGAD* myelin oligodendrocyte glycoprotein antibody-associated disease

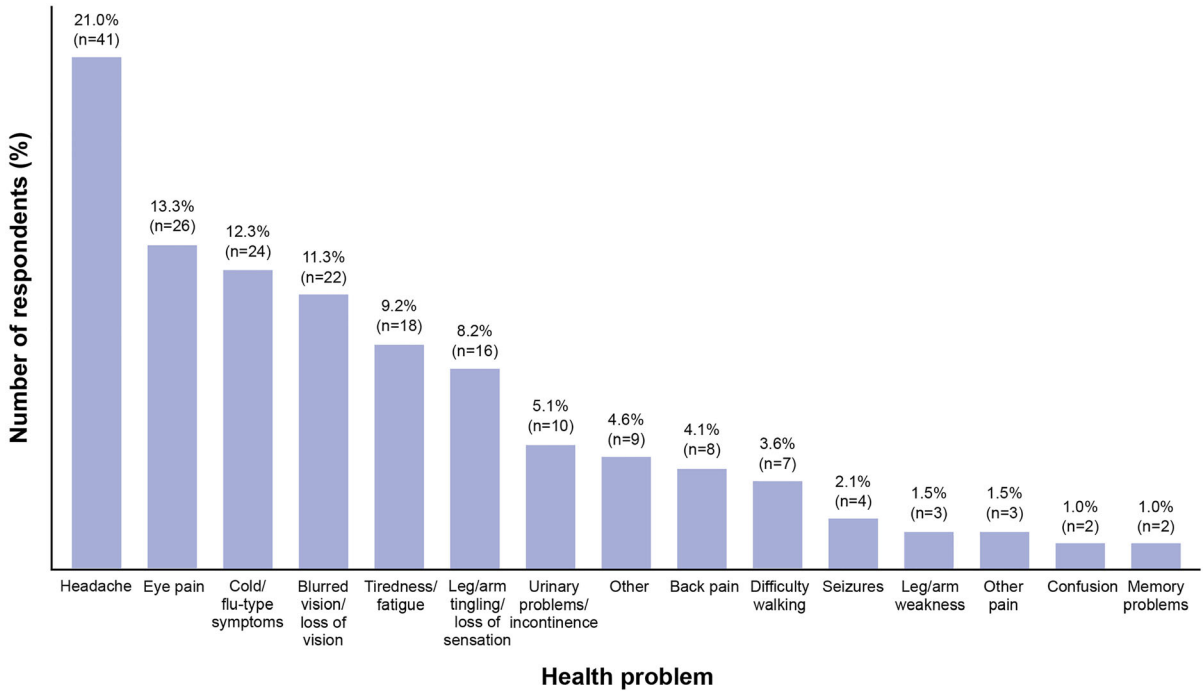

Fig. 2 Initial health problems experienced by patients*. *Survey Question 3; data from 195 respondents

(35.8%, 72/201) and difficulty walking (25.4%, 51/201) (Fig. 3).

From Initial Symptoms to MOGAD Diagnosis

Most respondents (81.3%, 165/203) sought medical care within 2 months of first experiencing MOGAD-associated symptoms (Survey Q6); almost 4% (8/203) and 8% (16/203) of patients sought medical care between 6–12 months and > 1 year, respectively. Free-text responses that elaborated on the > 1-year delay to seeking medical care (Survey Q7) revealed that 46.7% of respondents (7/15) had sought medical care but faced problems

Table 2 Health problems that patients experienced after initial health problems

Health problem experienced by patients, *n* (%)	Patient population (*n* = 201)
Blurred vision/loss of vision	138 (68.7)
Eye pain	122 (60.7)
Tiredness/fatigue	116 (57.7)
Headache	113 (56.2)
Leg/arm tingling/loss of sensation	95 (47.3)
Difficulty walking	90 (44.8)
Urinary problems/incontinence	88 (43.8)
Leg/arm weakness	79 (39.3)
Back pain	62 (30.8)
Cold/flu-type symptoms	57 (28.4)
Memory problems	52 (25.9)
Other	47 (23.4)
Other pain	45 (22.4)
Confusion	39 (19.4)
Seizures	29 (14.4)

Survey Question 4
MOGAD myelin oligodendrocyte glycoprotein antibody-associated disease

receiving a diagnosis or received an alternative primary diagnosis. One-third of respondents (33.3%, 5/15) felt that their symptoms were not severe or long-term enough to seek medical support, while 13.3% of patients (2/15) did not or could not prioritise seeking medical advice.

> "I immediately sought out advice when the urinary issues began. My provider just told me it's normal; I'll get over it. Urinary tract infection is a normal problem for any sexually active female. I was not sexually active, and I would get one urinary tract infection a month."—Survey Respondent (Survey Q7).
>
> "I could explain away symptoms, I didn't eat right, etc…."—Survey Respondent (Survey Q7).
>
> "Scared and felt my symptoms would go away."—Survey Respondent (Survey Q7).

In the global patient population, most individuals first sought medical care (Survey Q8) from emergency care doctors (38.7%, 79/204) or primary care doctors (general practitioner, family medicine doctor/internist; 26.0%, 53/204). Ophthalmologists and paediatricians were the first healthcare point of contact for 15.2% (31/204) and 6.9% (14/204) of patients, respectively. In contrast, specialist doctors, such as general neurologists, neuro-ophthalmologists, and neuro-immunologists, were consulted by comparatively few patients (Supplemental Table 2). After the initial consultation with the first doctor, the next type of doctor that patients were referred to (Survey Q9) demonstrated a shift towards more specialist involvement (Supplemental Table 2): 28.0% of patients (56/200) saw general neurologists, while ophthalmologists and neuro-ophthalmologists were each consulted by 14.5% (29/200) of patients. The type of doctor who eventually made the MOGAD diagnosis (Survey Q11) was in most cases a specialist: general neurologists and neuro-immunologists for 40.4% (82/203) and 30.0% (61/203) of patients, respectively, in addition to other specialists. Only 3.0% of MOGAD diagnoses were made by emergency care doctors (Supplemental Table 2).

Subgroup analyses of the diagnostic pathway were performed for: (1) the USA and (2) Europe, Australia and New Zealand (Australia, Belgium, Croatia, France, Germany, New Zealand, Norway, Spain, Switzerland and the UK). For respondents in the USA ($n = 136$), emergency care doctors were typically the first point of contact, with general neurologists being the doctors to whom patients were most frequently referred next and the ones to make the diagnosis (Fig. 4). In the Europe, Australia, and New Zealand subgroup ($n = 42$), the first point of contact was most often a primary care doctor, with the next most common referral being to an ophthalmologist; however, most diagnoses were made by a general neurologist (Fig. 5). In both the USA and the Europe, Australia and New Zealand subgroups, a prominent shift of patient referrals toward specialist involvement

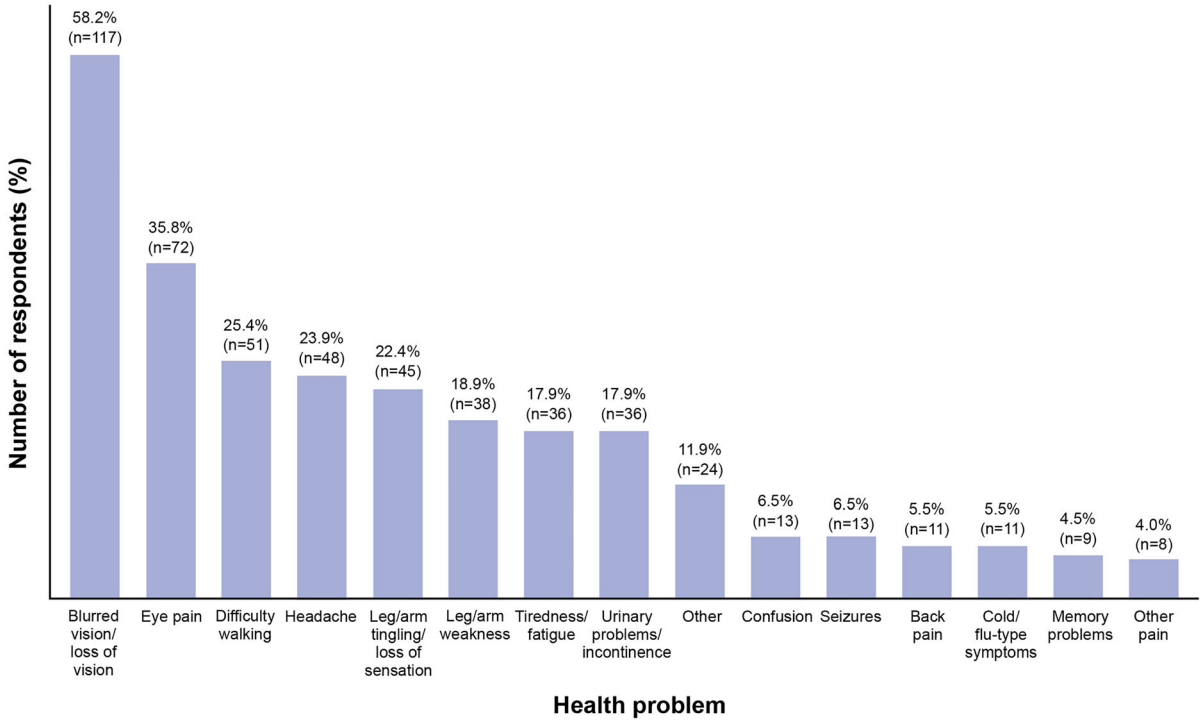

Fig. 3 Health problems that led respondents to seek medical care*. *Survey Question 5; data from 201 respondents

was observed from the 'next doctor' to the 'diagnosing doctor' stages of the diagnostic pathway.

The time from referral to consultation with a doctor (Survey Q10) was 1 week and 4–6 weeks for 68.5% (126/184) and 10.9% (20/184) of patients, respectively. The wait from referral to consultation was only 1 week for 68.4% (13/19) and 65.6% (80/122) of patients in the UK and USA, respectively. Only 2.7% (5/184) of respondents waited ≥ 6 months for a referral (Supplemental Table 3). The mean number of doctors seen prior to MOGAD diagnosis (Survey Q12) was 5.3 (median: 4.0; 181 respondents). Most patients (73.5%, 133/181) saw ≤ 5 doctors, but almost a quarter (26.5%, 48/181) saw ≥ 6 doctors before receiving a diagnosis of MOGAD. The time from the initial MOGAD-related health problems experienced to time of MOGAD diagnosis (Survey Q13) was < 6 months for 60% of patients (60.6%, 123/203), but ≥ 5 years for almost one-fifth of patients (17.7%, 36/203) (Table 3). Free-text responses that elaborated on the delay of ≥ 7 years from first symptoms to diagnosis (Survey Q14) highlighted unmet medical needs or lack of awareness of MOGAD in the medical community (24.1%, 7/29), unavailability of the MOG-Ig test (6.9%, 2/29), or that doctors did not believe patients about their symptoms (6.9%, 2/29) (Supplemental Table 4). The time to diagnosis from the first consultation with a doctor (Survey Q15) was < 6 months for most patients (61.3%, 125/204), but ≥ 7 years for 15.2% (31/204) of patients (Table 3).

> "They simply had no clue what was going on and were unable to put the symptoms together."—Survey Respondent (Survey Q16).
> "Doctors didn't know what I had, lack of knowledge. Some tests were not available at that time."—Survey Respondent (Survey Q16).
> "For 25 years was told symptoms were all in my head."—Survey Respondent (Survey Q16).

Before MOGAD diagnosis, > 55% of patients (113/204) reported that they received an alternative primary diagnosis (Survey Q17; Fig. 6).

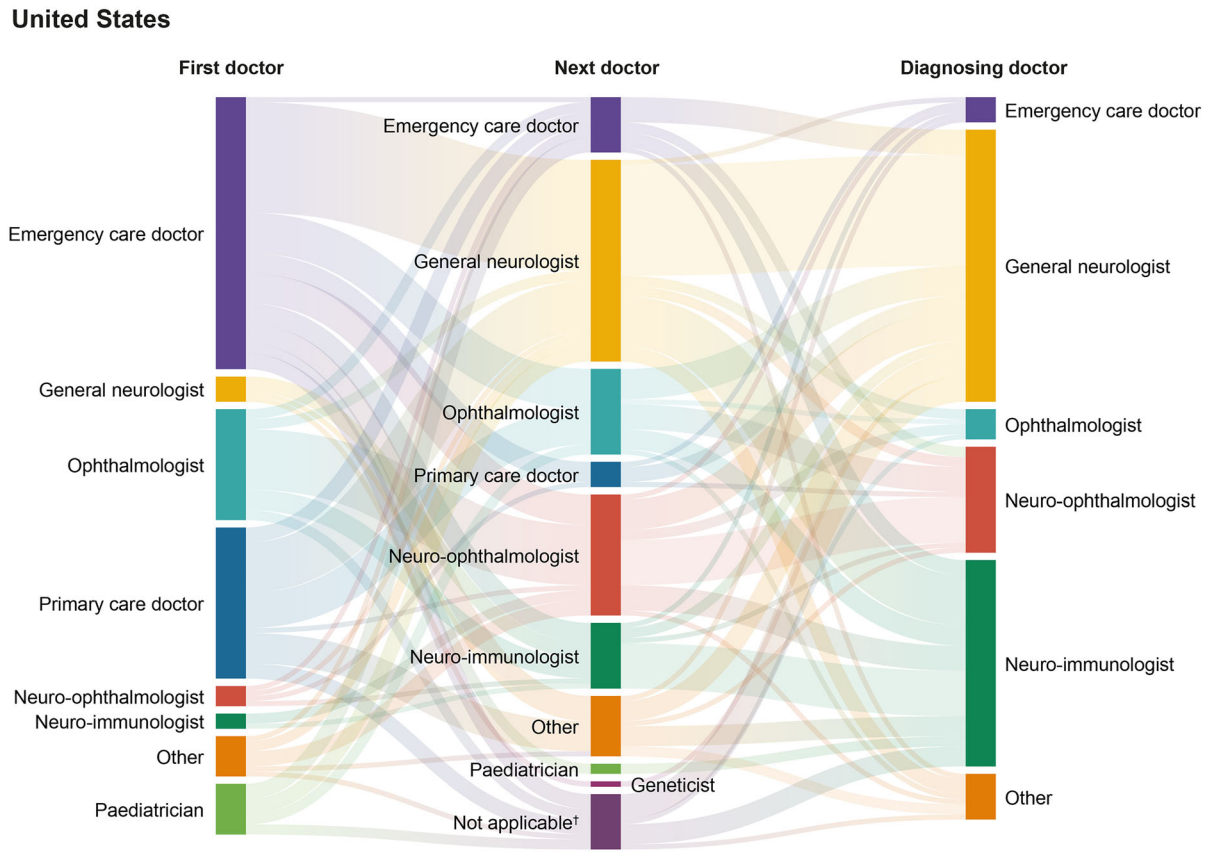

Fig. 4 Diagnostic pathway from initial consultation to MOGAD diagnosis in the USA*. *Survey Questions 8, 9 and 11; data from 136 respondents†Patients were not referred to another doctor. *MOGAD* myelin oligodendrocyte glycoprotein antibody-associated disease

The most common diagnosis received was MS (32.7%, 37/113), followed by neuromyelitis optica (11.5%, 13/113) and ADEM (8.8%, 10/113). Other primary alternative diagnoses received included meningitis (5.3%, 6/113), migraines (4.4%, 5/113), encephalitis (3.5%, 4/113), TM, chronic fatigue, chronic relapsing inflammatory optic neuropathy (each 2.7%, 3/113), psychiatric depression (1.8%, 2/113), common virus (0.9%, 1/113) and others.

MOGAD Diagnosis and Disease Management

Most respondents (60.6%, 123/203) felt they were not given sufficient information and/or resources at the time of MOGAD diagnosis (Survey Q18). At that time, respondents would have liked to receive (Survey Q19) information about support groups (79.5%, 159/200), advocacy website information (68.0%, 136/200), online video resources (62.0%, 124/200), pamphlets (55.0%, 110/200) and other resources.

After receiving a MOGAD diagnosis, patients often had more than one doctor managing the disease (Survey Q20), including general neurologists (53.9%, 110/204), neuro-ophthalmologists (46.6%, 95/204), neuro-immunologists (46.1%, 94/204), primary care doctors (24.5%, 50/204), ophthalmologists (20.1%, 41/204), paediatricians (6.9%, 14/204) and other specialist doctors (13.7%, 28/204).

Disease Burden Prior to, and After, MOGAD Diagnosis

Prior to MOGAD diagnosis, patients experienced a substantial MOGAD-related health

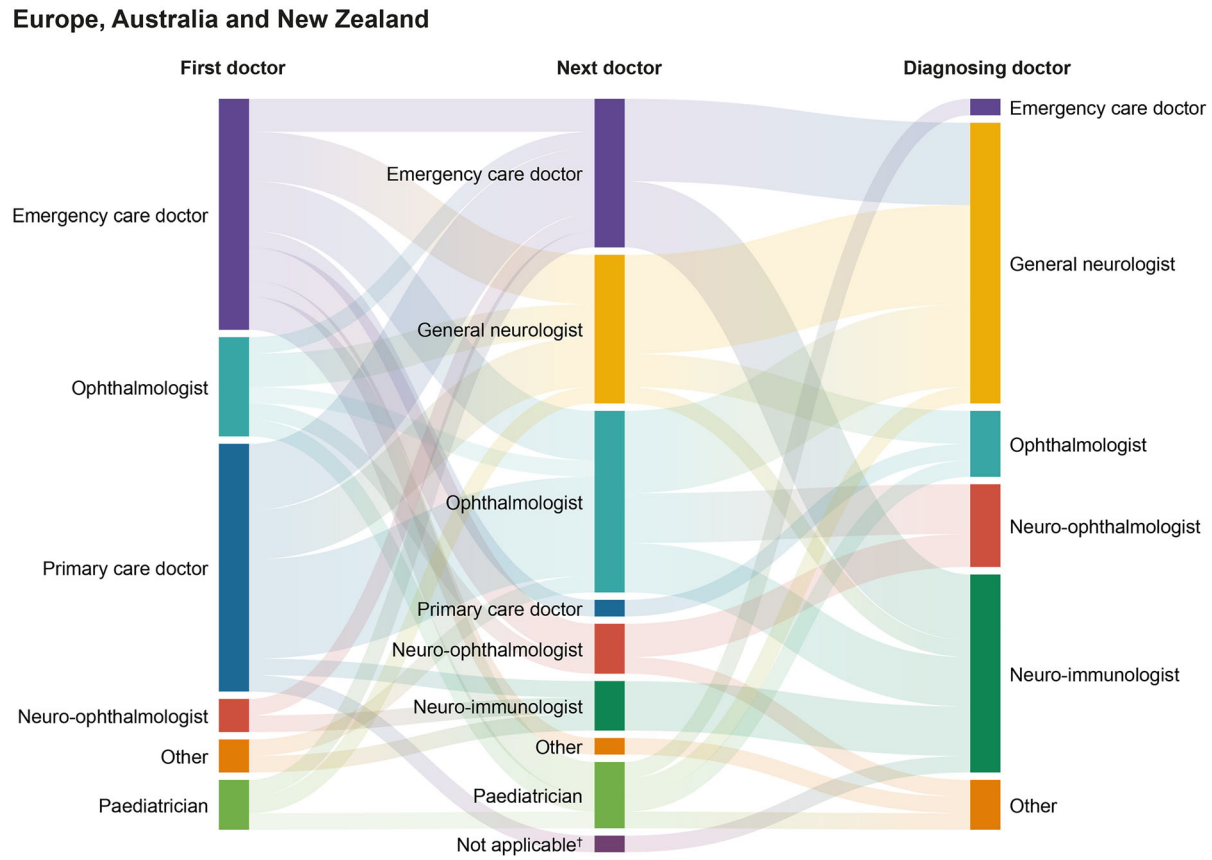

Fig. 5 Diagnostic pathway from initial consultation to MOGAD diagnosis in Europe, Australia and New Zealand*‡. *Survey Questions 8, 9 and 11; data from 42 respondents †Patients were not referred to another doctor ‡Europe, Australia and New Zealand subgroup included Australia, Belgium, Croatia, France, Germany, New Zealand, Norway, Spain, Switzerland and the UK. *MOGAD* myelin oligodendrocyte glycoprotein antibody-associated disease

burden (Survey Q22a). Over half of respondents (57.3%, 79/138) reported that overall health and well-being were negatively affected by the disease. In addition, impairment of patients' vision and mobility (including balance) were reported by 21.0% (29/138) and 13.0% (18/138) of respondents, respectively. Receiving a final MOGAD diagnosis (Survey Q22b) led to improvement in emotional responses, including reduced feelings of distress, depression, anxiety or fear, for more than half of respondents (61.1%, 11/18), whereas more than one-fifth of respondents reported that the final MOGAD diagnosis worsened emotional responses (22.2%, 4/18). Respondents perceived that the delay to MOGAD diagnosis led to long-term adverse health consequences (Survey Q23) including vision impairment (55.6%, 50/90), neurological disorders not including mental health (27.8%, 25/90) and bladder issues (20.0%, 18/90). Additionally, they reported other health problems, adverse impacts on the ability to perform daily living and social activities and on attendance and performance at work or school. Free-text responses describing the pathway to MOGAD diagnosis (Survey Q21) included frequently used words such as 'diagnosis', 'doctor(s)', 'hospital', 'time' and 'vision'.

> "Honestly, I wish doctors knew back then what was wrong with me and took my symptoms seriously. I'm so thankful now for my doctors, who are amazing and are knowledgeable about MOGAD […]. It was a

Table 3 Time to MOGAD diagnosis

Time to MOGAD diagnosis, *n* (%)	From first MOGAD-related health problems experienced (*n* = 203)[a]	From consultation with first doctor (*n* = 204)[b]
< 6 months	123 (60.6)	125 (61.3)
6–11 months	19 (9.4)	17 (8.3)
1 year	11 (5.4)	6 (2.9)
2 years	8 (3.9)	10 (4.9)
3 years	5 (2.5)	8 (3.9)
4 years	1 (0.5)	1 (0.5)
5 years	3 (1.5)	2 (1.0)
6 years	4 (2.0)	4 (2.0)
≥ 7 years	29 (14.3)	31 (15.2)

MOGAD myelin oligodendrocyte glycoprotein antibody-associated disease
[a]Survey Question 13
[b]Survey question 15

long and stressful journey and was not taken seriously by doctors."—Survey Respondent (Survey Q21).

"My […] daughter was misdiagnosed […]. It wasn't until she was completely blind that we returned to the hospital and demanded that they screen for other possibilities. Had we received a correct diagnosis from the beginning, […] she could have received treatment more quickly. She has permanent damage to her optic nerves and we often wonder if she could have avoided the permanent damage had she been diagnosed and treated more quickly."—Survey Respondent (Survey Q21).

"I felt like I was able to get a diagnosis very quick because all of the information was more prevalent at the time in 2018."—Survey Respondent (Survey Q21).

"I feel that lack of knowledge about MOGAD caused initial ophthalmologists to not explore this disease as a possibility of my symptoms and delayed effective treatment."—Survey Respondent (Survey Q21).

"When I was diagnosed, doctors didn't know much about MOGAD. It was very scary and frustrating."—Survey Respondent (Survey Q21).

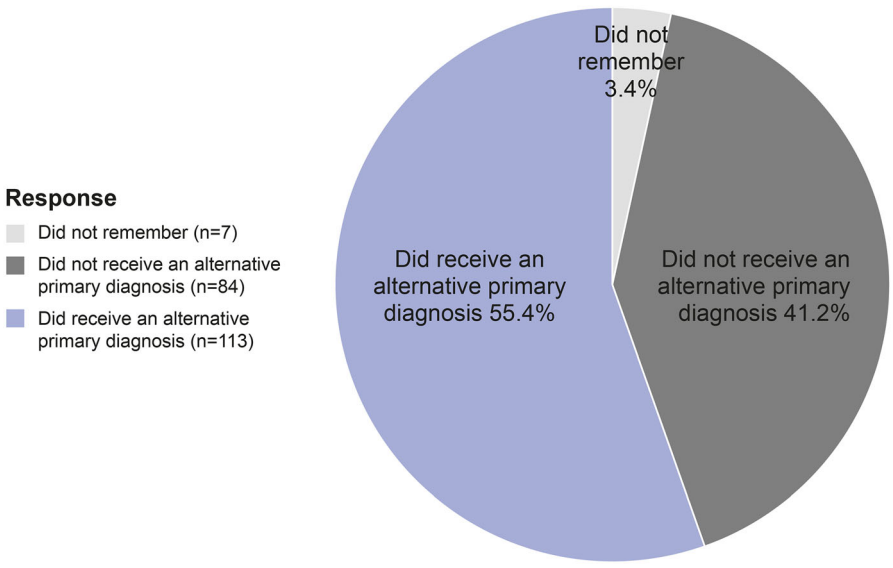

Fig. 6 Proportion of patients who received an alternative primary diagnosis before receiving a MOGAD diagnosis*. *Survey Question 17; data from 204 respondents. *MOGAD* myelin oligodendrocyte glycoprotein antibody-associated disease

DISCUSSION

Our understanding of rare neurological diseases such as MOGAD is expanding, but challenges remain. Indeed, one of the goals of the International Rare Disease Research Consortium is that, by 2027, patients with a suspected rare disease will receive an accurate diagnosis within 1 year of seeking medical care if the disease is established within the medical literature [31]. Patients with rare diseases commonly face a difficult and protracted diagnostic pathway [32], compounded in cases where the required diagnostic expertise may be limited to specialised medical centres [33]. Despite the fact that MOGAD is now recognised as a distinct demyelinating CNS disease, and that more sensitive/specific diagnostic testing is available, there remains a need to increase awareness of MOGAD in the medical community to help better address the needs of people living with MOGAD and their caregivers. Our findings from a multinational survey of 204 people living with MOGAD and their caregivers reveal that many individuals experienced a protracted and multistep pathway from initial symptoms to final MOGAD diagnosis, which can potentially result in adverse long-term physical and/or psychological health outcomes. Understanding the multi-factorial variables that influenced the diagnostic pathway is important to achieve earlier diagnosis.

It is likely that the variety of different phenotypes encountered in people living with MOGAD complicates diagnosis. Blurred vision/loss of vision was the MOGAD-related health problem that catalysed > 58% of respondents to seek medical care, although ON may not have been present in all of these cases. Most respondents (81.3%) sought medical care within 2 months of symptom onset. The first point of contact with a healthcare professional was most commonly with emergency care and primary care doctors, respectively, for patients in the USA subgroup and the Europe, Australia and New Zealand subgroup. Globally, MOGAD diagnosis was most frequently made by specialist doctors such as general neurologists (40.4%) or neuro-immunologists (30.0%).

Over one-quarter of patients (48/181) consulted with ≥ 6 doctors before receiving a MOGAD diagnosis. Although our survey did not capture the year a MOGAD diagnosis was received, the authors feel it is reasonable to assume that some patients with protracted delays to MOGAD diagnosis represent cases that predate the recognition of MOGAD as a distinct disease. Varied access to MOG-Ig testing may also have negatively affected the time to diagnosis. However, the correlation between serum presence of MOG antibodies and MOGAD is not absolute; MOG antibody levels may disappear over time, according to disease status and treatment [4, 7, 9]. Standardisation of MOG-Ig tests is recommended to improve clinical care for patients with MOGAD and future research of the disease [15, 34].

Some patients delayed seeking medical help within the first year of symptom onset. For several patients, the symptoms were not considered severe enough and/or were experienced intermittently. Survey responses also revealed a subset of patients who sought medical care, but their symptoms were dismissed by doctors as 'an isolated event' or 'all in your head'. This finding may be related to the fact that, even when untreated, acute demyelinating events can often improve after the symptom onset causing less noticeable symptoms if evaluation is delayed. A study of misdiagnosis of MS found that women were more likely to be misdiagnosed with a mental health condition than men; the latter were also offered more investigative tests [35]. Increased education and training related to MOGAD diagnosis, targeted at both specialist and non-specialist healthcare professionals, are needed to increase awareness of this disease so that symptoms are investigated thoroughly, rather than dismissed or misinterpreted. While it may not be practical to provide bespoke education to healthcare professionals for all rare neurological conditions, general education about treatment approaches for neurological conditions may be more feasible. Healthcare professionals should be educated about the importance of early referral to neurologists and ophthalmologists for patients with suspected rare neurological conditions such as MOGAD.

Of 113 patients who received an alternative primary diagnosis, 32.7% received a diagnosis of MS. Relapsing MOG-encephalomyelitis has been misdiagnosed as MS due to a significant overlap in clinical and radiological presentation [16]. Although the survey did not record the year that these patients received a diagnosis of MS, one may assume that these diagnoses did not incorporate MOG-Ig testing and/or other recommendations to differentiate MOGAD from other inflammatory CNS demyelinating diseases [16, 28].

MOGAD can have a significant detrimental impact on patients' health and may result in potentially irreversible consequences such as blindness, paralysis, cognitive decline or behavioural issues [5, 15, 27, 36]. MOGAD relapses are associated with disability [27]. In a cohort study (n = 252, adult and paediatric), 41% of patients did not have any disability at last follow-up, but approximately one-quarter had moderate-to-severe disability [11]. However, other studies in children with overlapping phenotypes, such as ADEM, have reported significant neurocognitive and structural changes longitudinally, highlighting the possibility of hidden disability in individuals with MOGAD [37–40]. Early diagnosis and appropriate treatment may prevent future relapses and lead to more urgent relapse treatment with reduced permanent disability.

Once patients received a MOGAD diagnosis, disease management included doctors of differing specialities, but many patients remained dissatisfied with their care. Over half of respondents (60.3%) reported that insufficient information and/or resources were provided at the time of diagnosis; the initial management of MOGAD at diagnosis may be compromised by a lack of longitudinal data and general experience. Although high levels of dissatisfaction were recorded in this study, it is hoped that, as MOGAD is more routinely reported in the literature and identified in clinical practice, medical professional knowledge and comfort treating this condition will improve.

This study is not without limitations. In our study, two-thirds of respondents were from the USA, which has an extraordinarily complex healthcare system different from the majority of the rest of the world. Compounding this is that insurance status was not collected in this study, which could have skewed coverage and been related to some delays in diagnosis and access to care. Availability of the survey in several languages and inclusion of higher numbers of patients in different countries may have allowed assessment of the relative success of different healthcare systems in identifying and treating MOGAD. Although no association between ethnicity and MOGAD is known [4], ethnicity and race are important factors that should be explored in the diagnosis and treatment of MOGAD; exclusion of these data in the survey design is a limitation of our study. As with any survey, recall bias is likely to have been present in this study, especially for patients who have been symptomatic for long periods of time. An additional limitation is that survey responses were not stratified as self- or proxy-reported, or paediatric versus adult, and the sex of patients was not recorded. Selection bias was likely to be present as people with relapsing MOGAD were more likely to be involved with The MOG Project than patients with monophasic MOGAD. However, the strength is that this is the only study to report the impact of MOGAD and the diagnostic pathway from the patients' perspective; even if there are biases towards overemphasis, we highlight areas that require improvement. There is precedent for patient direct surveys in neurology [41, 42], which we considered the most feasible approach for patients with a rare disease such as MOGAD. As MOGAD is poorly understood and under-recognized as a distinct disease, we believe the potential for false-positive or false-negative data to be low, and there was no evidence of fraudulent responses. Given the rarity of MOGAD and the dependence on the presence of MOG antibodies for diagnosis, it would be anticipated that false identification would be rare, although not impossible. Of particular concern would be the interpretation of low-titre MOG antibodies as causative of neurological or quasi-neurological disease. A final limitation is that the diagnostic pathway, particularly in MOGAD, which only had commercial testing available in the past half-decade, is likely to be different depending on the age of symptom

onset. The year that patients experienced initial symptoms or the year that a MOGAD diagnosis was received was not asked; these questions should be included in future surveys. Re-evaluation of the diagnostic pathway and clinical experience of patients would be beneficial as MOGAD testing and diagnosis improve in the future.

CONCLUSIONS

This study highlights several challenges in the often protracted and multi-step patient pathway towards MOGAD diagnosis. Receiving an alternative primary diagnosis and delay to final MOGAD diagnosis were associated with increased frustration, physical impairment and reduced health-related quality of life. The data from this survey highlight the need for improved awareness of MOGAD in the medical community and the importance of early MOGAD diagnosis. New expert consensus recommendations for MOGAD disease definition and diagnostic criteria [28] will help in this respect. Further research is needed to assess the impact of earlier MOGAD diagnosis on long-term disease burden and health-related quality of life from patient and caregiver perspectives.

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Author Contributions. Jennifer Gould, Zoya Panahloo, and Julia Lefelar conceptualised the study and study design. Jonathan D. Santoro, Jennifer Gould, Zoya Panahloo and Julia Lefelar developed the survey. Jennifer Gould and Julia Lefelar distributed the survey. Ella Thompson performed the statistical analysis. All authors contributed to interpretation of the results and critical revision of the manuscript.

Prior Presentation. Study results, with the exception of free-text response data, were presented as a poster at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) 2022 meeting.

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Compliance with Ethics Guidelines. The survey received ethics approval from the University of Southern California Institutional Review Board (ID:21–0082). As the study did not involve clinical data nor involve data collection from other institutions, only one centre was used to approve study material and perform ethics review. Ethics approval was waived after expedited review as there was no clinical or

identifying information collected. Survey participants were informed of the intention to publish the anonymized results before they began the survey. All survey respondents provided informed consent to participate in the study on the survey landing page prior to being able to start the survey. An option to opt out of the survey was available on all displayed pages. As the study was an anonymous patient and caregiver survey to report perspectives on the pathway to MOGAD diagnosis, no verification of individual patient data was required. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Data Availability. Data from non-clinical studies are outside of UCB Pharma's data sharing policy and are unavailable for sharing.

REFERENCES

1. Zamvil SS, Slavin AJ. Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder? Neurol Neuroimmunol Neuroinflamm. 2015;2(1): e62.
2. Johns TG, Bernard CC. The structure and function of myelin oligodendrocyte glycoprotein. J Neurochem. 1999;72(1):1–9.
3. Reindl M, Waters P. Myelin oligodendrocyte glycoprotein antibodies in neurological disease. Nat Rev Neurol. 2019;15(2):89–102.
4. Sechi E, Cacciaguerra L, Chen JJ, Mariotto S, Fadda G, Dinoto A, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): a review of clinical and mri features, diagnosis, and management. Front Neurol. 2022;13: 885218.
5. Wynford-Thomas R, Jacob A, Tomassini V. Neurological update: MOG antibody disease. J Neurol. 2019;266(5):1280–6.
6. Hegen H, Reindl M. Recent developments in MOG-IgG associated neurological disorders. Ther Adv Neurol Disord. 2020;13:1756286420945135.
7. Shahriari M, Sotirchos ES, Newsome SD, Yousem DM. MOGAD: how it differs from and resembles other neuroinflammatory disorders. AJR Am J Roentgenol. 2021;216(4):1031–9.
8. Juryńczyk M, Jacob A, Fujihara K, Palace J. Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease: practical considerations. Pract Neurol. 2019;19(3):187–95.
9. Jarius S, Ruprecht K, Kleiter I, Borisow N, Asgari N, Pitarokoili K, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 1: frequency, syndrome specificity, influence of disease activity, long-term course, association with AQP4-IgG, and origin. J Neuroinflammation. 2016;13(1):279.
10. Lana-Peixoto MA, Talim N. Neuromyelitis optica spectrum disorder and anti-MOG syndromes. Biomedicines. 2019;7(2):42.
11. Jurynczyk M, Messina S, Woodhall MR, Raza N, Everett R, Roca-Fernandez A, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. Brain. 2017;140(12):3128–38.
12. Narayan R, Simpson A, Fritsche K, Salama S, Pardo S, Mealy M, et al. MOG antibody disease: a review of MOG antibody seropositive neuromyelitis optica spectrum disorder. Mult Scler Relat Disord. 2018;25: 66–72.
13. Valencia-Sanchez C, Guo Y, Krecke KN, Chen JJ, Redenbaugh V, Montalvo M, et al. Cerebral cortical encephalitis in myelin oligodendrocyte glycoprotein antibody-associated disease. Ann Neurol. 2023;93(2):297–302.

14. Waters PJ, Komorowski L, Woodhall M, Lederer S, Majed M, Fryer J, et al. A multicenter comparison of MOG-IgG cell-based assays. Neurology. 2019;92(11):e1250–5.

15. Ambrosius W, Michalak S, Kozubski W, Kalinowska A. Myelin oligodendrocyte glycoprotein antibody-associated disease: current insights into the disease pathophysiology, diagnosis and management. Int J Mol Sci. 2020;22(1):100.

16. Jarius S, Paul F, Aktas O, Asgari N, Dale RC, de Seze J, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. J Neuroinflammation. 2018;15(1):134.

17. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85(2):177–89.

18. Fujihara K. Neuromyelitis optica spectrum disorders: still evolving and broadening. Curr Opin Neurol. 2019;32(3):385–94.

19. Filippatou AG, Mukharesh L, Saidha S, Calabresi PA, Sotirchos ES. AQP4-IgG and MOG-IgG related optic neuritis-prevalence, optical coherence tomography findings, and visual outcomes: a systematic review and meta-analysis. Front Neurol. 2020;11: 540156.

20. Prasad S, Chen J. What you need to know about AQP4, MOG, and NMOSD. Semin Neurol. 2019;39(6):718–31.

21. Carnero Contentti E, Rojas JI, Criniti J, Lopez PA, Daccach Marques V, Soto de Castillo I, et al. Towards imaging criteria that best differentiate MS from NMOSD and MOGAD: Large multi-ethnic population and different clinical scenarios. Mult Scler Relat Disord. 2022;61:103778.

22. World Health Organization. (2022). ICD-11: International classification of diseases (11th revision). https://icd.who.int/.

23. Whittam DH, Karthikeayan V, Gibbons E, Kneen R, Chandratre S, Ciccarelli O, et al. Treatment of MOG antibody associated disorders: results of an international survey. J Neurol. 2020;267(12):3565–77.

24. Palace J, Leite MI, Jacob A. A practical guide to the treatment of neuromyelitis optica. Pract Neurol. 2012;12(4):209–14.

25. Chen JJ, Flanagan EP, Bhatti MT, Jitprapaikulsan J, Dubey D, Lopez Chiriboga ASS, et al. Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder. Neurology. 2020;95(2): e111–20.

26. Seneviratne SO, Marriott M, Ramanathan S, Yeh W, Brilot-Turville F, Butzkueven H, et al. Failure of alemtuzumab therapy in three patients with MOG antibody associated disease. BMC Neurol. 2022;22(1):84.

27. Healy S, ElHadd KT, Gibbons E, Whittam D, Griffiths MJ, Jacob A, et al. Treatment of myelin oligodendrocyte glycoprotein immunoglobulin G–associated disease. Clin Exp Neuroimmunol. 2021;12:22–41.

28. Banwell B, Bennett JL, Marignier R, Kim HJ, Brilot F, Flanagan EP, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023;22(3):268–82.

29. The MOG Project. How we support the MOGAD Community 2022 https://mogproject.org/about/. Accessed 10 Mar 2023.

30. QuestionPro. Homepage. https://www.questionpro.com/. Accessed 2 Mar 2022.

31. Austin CP, Cutillo CM, Lau LPL, Jonker AH, Rath A, Julkowska D, et al. Future of rare diseases research 2017–2027: an IRDiRC perspective. Clin Transl Sci. 2018;11(1):21–7.

32. Benito-Lozano J, Arias-Merino G, Gómez-Martínez M, Ancochea-Díaz A, Aparicio-García A, Posada de la Paz M, et al. Diagnostic process in rare diseases: determinants associated with diagnostic delay. Int J Environ Res Public Health. 2022;19(11):6456.

33. Stoller JK. The Challenge of Rare Diseases. Chest. 2018;153(6):1309–14.

34. Reindl M, Schanda K, Woodhall M, Tea F, Ramanathan S, Sagen J, et al. International multicenter examination of MOG antibody assays. Neurol Neuroimmunol Neuroinflamm. 2020;7(2):e674.

35. Levin N, Mor M, Ben-Hur T. Patterns of misdiagnosis of multiple sclerosis. Isr Med Assoc J. 2003;5(7):489–90.

36. Parrotta E, Kister I. The expanding clinical spectrum of myelin oligodendrocyte glycoprotein (MOG) antibody associated disease in children and adults. Front Neurol. 2020;11:960.

37. Aubert-Broche B, Weier K, Longoni G, Fonov VS, Bar-Or A, Marrie RA, et al. Monophasic demyelination reduces brain growth in children. Neurology. 2017;88(18):1744–50.

38. Longoni G, Brown RA, MomayyezSiahkal P, Elliott C, Narayanan S, Bar-Or A, et al. White matter changes in paediatric multiple sclerosis and

monophasic demyelinating disorders. Brain. 2017;140(5):1300–15.

39. Shilo S, Michaeli O, Shahar E, Ravid S. Long-term motor, cognitive and behavioral outcome of acute disseminated encephalomyelitis. Eur J Paediatr Neurol. 2016;20(3):361–7.

40. Burton KLO, Williams TA, Catchpoole SE, Brunsdon RK. Long-term neuropsychological outcomes of childhood onset acute disseminated encephalomyelitis (ADEM): a meta-analysis. Neuropsychol Rev. 2017;27(2):124–33.

41. Law N, Davio K, Blunck M, Lobban D, Seddik K. The Lived experience of myasthenia gravis: a patient-led analysis. Neurol Ther. 2021;10(2):1103–25.

42. National Multiple Sclerosis Society. Surveys and Other Research Studies 2023. https://www.nationalmssociety.org/Research/Participate-in-Research-Studies/Surveys#section-6. Accessed 10 Mar 2023.