Section 11

Discussion

Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease of the brain and spinal cord, characterised by optic neuritis (inflammation of the optic nerve) and myelitis (inflammation of the spinal cord)[1,2].

Myelin oligodendrocyte glycoprotein Antibody Disease (MOG) is an inflammatory condition that causes inflammation in the optic nerve but can also cause inflammation in the spinal cord and brain[3,4]. Previously, MOG patients may have been diagnosed with NMOSD, transverse myelitis acute disseminated encephalomyelitis, optic neuritis, or multiple sclerosis. MOG patients do not test positive for aquaporin-4 (AQP4) antibodies, and are less likely to have other autoimmune conditions[5].

In this PEEK study, there were 18 participants who diagnosed with NMOSD and 8 participants diagnosed with MOG that completed the online questionnaire and had an interview.

Incidence, prevalence and mortality statistics

NMOSD is a rare disorder previously thought to be a type of multiple sclerosis. NMOSD was difficult to distinguish from multiple sclerosis until the discovery of aquaporin 4 (AQP4 antibodies)[6]. A systematic review of reported incidence and prevalence worldwide of NMOSD reported highest estimates in Afro-Caribbean region and lowest incidence and prevalence of NMOSD were found in Australia and New Zealand[7].

Complications

Deterioration in NMOSD patients is irreversible and almost always takes place during clinical attacks[8]. Without treatment, within five years of the first attack, about half of NMOSD will be blind, and will be wheelchair users, and approximately a third will die[9]. Prognosis has improved with the identification of the AQP4 antibody[10,11]. Disabilities accumulate with relapses, it is therefore important to aggressively treat relapses and prevent relapses with maintenance therapies[12].

Risks and Symptoms

Although NMOSD can affect men and women of all ages and ethnicities, middle-aged and elderly women are most commonly affected[13]. The average age of onset is 40 years of age[14], and NMOSD is more common in African and Asian ethnicities[15,16]. Familial cases are recognised but rare[17].

Symptoms include optic neuritis (damage to optic nerve that may cause pain and temporary vision loss in one eye), acute myelitis (inflammation of spinal cord), area postrema syndrome (uncontrollable hiccups or nausea and vomiting), and narcolepsy (sleep disorder)[2].

Comorbidities

NMOSD is familial in about 3% of cases[17]. It is associated with other systemic autoimmune diseases such as thyroid autoimmunity, systemic lupus erythematosus, and Sjögren syndrome[18]. In this PEEK study, 61% that reported at least one other autoimmune disorder. Compared to healthy controls, people with NMOSD have more symptoms of anxiety and depression[19].

The most commonly reported health conditions in participants with NMOSD in this PEEK study were chronic pain (78%), sleep problems (61%), and depression either self-diagnosed or diagnosed by a doctor (50%).

Poor sleep quality in NMOSD is associated with longer illness duration, and higher fatigue[19], sleep problems were noted by 61% of NMOSD participants in this PEEK study.

There were few studies reporting co-morbidities of people with NMOSD. One study reported 45% of participants with NMOSD had mental health disorders, in this PEEK study, 61% described having either anxiety or depression (39% diagnosed by a doctor). The higher rate of anxiety and depression in this PEEK study could in part be explained by the current pandemic. Autoimmune disorders have been reported at rates of (19% to 25%)[20,21], compared to 61% in this current study. One study reported that 15% of NMOSD participants had previous malignancies[21], while no PEEK participants reported any cancer.

The National Health Survey was conducted in 2017 to 2018, it is an Australia wide survey conducted by the Australian Bureau of statistics. Almost half of the Australian population have one chronic condition%)[22]. Common chronic health conditions experienced in Australia in 2017-18 were: mental and behavioural conditions (20%), back problems (16%), arthritis (15%), asthma (11%), diabetes mellitus (5%), heart, stroke and vascular disease

(4.8%), osteoporosis (3.8%), chronic obstructive pulmonary disease (COPD) (3%), cancer (2%), and kidney disease (1%)[22]. The Australian Bureau of statistics reports that 10% of Australians have depression or feelings of depression and 13.1% have an anxiety-related condition%)[22].

Compared to the findings from the National Health Survey, the rates of chronic diseases in the PEEK NMOSD population were higher for anxiety, depression, and arthritis.

Baseline health

The Short Form Health Survey 36 (SF36) measures baseline health, or the general health of an individual[23]. The SF36 comprises nine scales: physical functioning, role functioning/physical, role functioning/emotional, energy and fatigue, emotional well-being, social function, pain, general health, and health change from one year ago. The scale ranges from 0 to 100, a higher score denotes better health or function.

Population norms for the SF36 dimensions in Australia were assessed in the 1995 National health survey, while this was conducted 25 years ago, it can give an indication of how the PMOSD community in this PEEK study compares with the Australian population[24]. Compared to the Australian population, participants in this PEEK study on average scored lower (worse health outcomes) in all SF36 domains.

Other studies focusing on health related quality of life, have reported that the NMOSD community have physical limitations, limiting work and participation in social activities [25,26]. Physical and emotional health related quality of life scores were lower in participants with fatigue [27,28]. People with NMOSD in general scored worse compared to healthy controls, [19], and worse than people with multiple sclerosis[29], and reported lower physical function scores compared to multiple sclerosis[20].

Symptoms and disability

Symptoms include optic neuritis (damage to optic nerve that may cause pain and temporary vision loss in one eye), acute myelitis (inflammation of spinal cord), area postrema syndrome (uncontrollable hiccups or nausea and vomiting), and narcolepsy (sleep disorder)**[2].**

Other reported symptoms of NMOSD include fatigue pain, painful tonic spasms sexual dysfunction restless leg syndrome depression pruritus, and cognitive dysfunctions[25,28,30-41].

Participants with NMOSD in this PEEK study had a median of 7.5 symptoms before diagnosis, ranging from two to 12 symptoms. The most common symptoms reported in a Unite Kingdomstudy were were visual symptoms, mobility impairment, and neuropathic pain[42]. Similar patterns were seen in the current study, where loss of clear vision, eye pain, muscle spasms, and sensory loss (n=12, 66.67%) were most commonly reported. The most common symptom leading to diagnosis was visual problems, similar to another study that reported presenting symptoms as visual disturbances, numbness and/or tingling, and difficulty walking[26].

The participants in this PEEK study described what they meant by mild or severe symptoms or side effects. Mild side effects were described using the example of numbness, and neuropathic pain, and severe using the examples of pain and vison loss. Fatigue was described both as a mild and severe side effect, and in another NMOSD study, fatigue was commonly rated as being moderate to severe as it may interfere with activities of daily living [25].

Pain was common for optic neuritis[32], neuropathic pain is more severe and disabling as compared with multiple sclerosis and early involvement of a local pain team is helpful[33]. Pain may interfere with activities of daily living [25], and may contribute to fatigue[30]. Painful tonic spasm was reported in NMOSD, and was associated with a higher age at onset, and a more frequent relapse rate[34].

Diagnostic criteria

The core clinical characteristics of NMOSD are optic neuritis, acute myelitis, anti-phospholipid syndrome, brainstem syndrome, symptomatic narcolepsy or acute diencephalic syndrome with NMOSD-typical diencephalic MRI lesions, and symptomatic cerebral syndrome with NMOSD-typical brain lesions[2]. Patients that are seropositive for AQP4 require at least one core clinical characteristic for diagnosis[2]. Patients that are seronegative or unknown status for AQP4 require two core clinical characteristics with at least one of optic neuritis, ongitudinally extensive transverse myelitis, or anti-phospholipid syndrome[2].

Diagnostic tests

There is little information about standard diagnostic tests for NMOSD in Australia. The Neuromyelitis Optica Unite Kingdom Specialist Services lists the following tests used to diagnose NMOSD; medical history, MRI of brain and spinal cord, lumbar puncture, blood tests, ophthalmological examination, visual evoke potential, visual field tests, low contrast test, Ishihara test, and optical coherence tomography[43].

Participants with NMOSD reported between seven and nine diagnostic tests, with a median of six tests. Nearly all participants had blood tests, MRI of brain, optic nerves, or spinal cord, and physical examination. Most participants also had a neurologic exam, lumbar puncture and ophthalmology studies. Very few had a family history taken, or CT scans.

Biomarkers

NMOSD is classified into AQP4 antibody positive and AQP4 antibody negative diseases[44]. NMOSD includes cases of MOG-antibody-positive disease with its unique clinical spectrum that is different from AQP4-antibody positive disease[44]. NMOSD with MOG antibodies have fewer attacks and better recovery from relapses than those with AQP4 antibodies, or those that are negative for both MOG and AQP4[42,45].

Few participants with NMOSD in this PEEK study could remember having conversations about biomarker, genomic, or gene testing that might be relevant to treatment. Over 60% said they did not have these tests, yet half of the participants in the study knew their AQP4 status. This may indicate that patients need more information and discussion about biomarkers, the purpose of testing, and what the relevance of their antibody status is in terms of treatment and prognosis.

Early diagnosis and treatment is important to reduce the risk of disability and death for people with NMOSD[12,46]. A range of 29 to 43% of people with NMOSD will have had a misdiagnosis of multiple sclerosis, causing delays in preventative treatments[47,48]. In addition, some treatments for multiple sclerosis increases relapse severity and frequency, increasing disability[49,50]. Diagnostic delay has been reduced with the specificity of the AQP4 antibody, which reliably distinguishes NMOSD from multiple sclerosis[6,48,51]. In addition, the application of the International consensus diagnostic criteria for neuromyelitis optica spectrum disorders in 2015[2], has led to an increase in the diagnosis of NMOSD[52].

About a third of the participants with NMOSD in this PEEK study were diagnosed more than a year after first noticing symptoms, very few were diagnosed within a month of noticing symptoms. In addition, delays between testing and diagnosis were common. Other studies in the NMOSD community reported average time between noticing symptoms and diagnosis between one and 3.3 years[25,26].

Most participants in a United Kingdom study described having difficulty with getting an NMOSD diagnosis. This was mostly due to misdiagnosis with multiple sclerosis[42]. Over a quarter of participants with NMOSD in the current study were misdiagnosed with multiple sclerosis, contributing to the delay with an NMOSD diagnosis.

Relapse

A relapse, or an attack of NMOSD, occurs when there is inflammation within the nervous system, attacks commonly include transverse myelitis optic neuritis, but can also include area postrema syndrome, and brainstem syndrome, or combinations of any of these[53]. People with NMOSD that have MOG antibodies have fewer attacks and better recovery from [42,45], relapse rates have been reported to be higher in African ethnicity, children and in those of shorter disease duration[54].

About a third of the participants with NMOSD in this PEEK study had one or two relapses, and about a third had three or four relapses. Physical disability was measured in this study in the SF36 physical function, and role functioning/physical domains, however, no differences were seen between those that had fewer than two relapses and those that had more.

Support at diagnosis

Almost all participants in this PEEK study felt that they either had no support or not enough support at diagnosis, similar to another study in an NMOSD population that reported participants wanted more support than they had received, especially during the early stage of diagnosis[42].

Decision making

The decision-making process in healthcare is an important component in care of chronic or serious illness[55]. Knowledge of prognosis, treatment options, symptom management, and how treatments are administered are important aspects of a person's ability to make decisions about their healthcare[56,57] highlighting the importance of healthcare professional communication.

Important aspects of health-related decision making for the participants in the current study were side effects, efficacy, and cost. Approximately a third of participants felt they did not have the opportunity to take part in decision making for the treatment and management of their condition, and only about 20% of participants felt they played an active role in decision making. The participants displayed a willingness to take part in decision making when it comes to deciding how their condition is managed, especially as they feel more informed and assertive, and are aware of their own health and limitations

In addition, the role of family members in decision making is important, with many making decisions following consultation with family[58]. In the current study, participants with NMOSD did not discuss the role of their family in decision making, however, 30% of family and carers discussed taking an active role.

Treatment

Acute treatment of an NMOSD attack consists of high dose steroids for five days, oral prednisolone then continues for weeks, reducing over the course of months. Plasma exchange is used when improvement is not seen within days of high dose steroids [12,23]. Plasma exchange has been shown to be more effective in improving recovery following relapse compared to high dose steroids, suggesting that escalation to plasma exchange may reduce long term disability in NMOSD**[23,59].**

All participants with NMOSD in this PEEK study had IV high dose steroids, nearly all had side effects, and on average quality of life on high dose steroids was low. However, on average, they rated this treatment as effective.

Less than half of the participants with NMOSD in this PEEK study had plasma exchange, about a quarter reported no side effects from this treatment. Quality of life from the treatment was low, but participants rated it as very effective.

Progression of neurological disability in NMOSD is thought to mainly occur during clinical attack/relapse[9], suggesting that preventing clinical attacks is the most important therapeutic target in NMOSD[8]. Management of NMOSD consists of preventative immunotherapy treatment, monitoring safety of treatment and adherence to treatment[18]. Immunosuppressive treatments reduce but do not stop relapses, however, they may reduce the disabling effects of optic neuritis and transverse myelitis[54]. Relapse prevention therapy is recommended for all patients that are AQP4 positive, and for AQP4 negative patients with established relapsing disease[60]. Following relapse, it is recommended to switch to a drug with a different mechanism of action, combination therapy is an option but data is limited[18]. Disease modifying drugs used in multiple sclerosis have been shown to with not work in NMOSD or may exacerbate NMOSD and should be avoided [61-63]

The most common prevention therapies used include azathioprine, mycophenolate mofetil and rituximab resulting in relapse free rates of between 25% and 66%[64-69]. Oral prednisolone is often given long-term, as the combination may be more protective than mycophenolate mofetil or rituximab alone[70]. Other immunosuppressants that are occasionally used include tocilizumab, methotrexate, cyclophosphamide, mitoxantrone, intravenous immunoglobulins, tacrolimus, and ciclosporin[70].

All participants with NMOSD in the current study had taken at least one long term treatment for the management of their condition. The most common types were rituximab, and prednisone. Most participants had side effects from prednisone, and reported low quality of life, however, on average found the treatment effective. Almost half of the participants taking rituximab reported no side effects, quality of life was rated as average. Peek participants rated rituximab as effective, which has been reported elsewhere[26].

Allied health

There is little published information about the use of allied health to manage NMOSD. In this PEEK study, 61% of participants with NMOSD used at least one allied health service in the management of NMOSD. As NMOSD is a progressively disabling condition, there is a gap in services for this cohort. The most common allied health services were occupational therapy (56%), physiotherapy (50%) and psychology

(44%), participants found these moderately effective to effective.

Lifestyle changes

There is little published information about lifestyle changes in the NMOSD community. In the current study, 83% of participants with NMOSD made at least one lifestyle change, most commonly exercise, and diet changes. Exercise was used by participants for both their mental health and physical health. Information about lifestyle changes was not given to many participants, one participant was given information about exercise, and no participants given information about diet. More than half of the NMOSD participants searched independently for information about diet and/or exercise. There is clearly interest in lifestyle changes for the management of NMOSD, and a need for more information.

Complementary therapies

There is little published data about complementary therapies in the NMOSD community. In this PEEK study, over 75% used at least one type of complementary therapy, the most common types were mindfulness or relaxation techniques, supplements, and massage therapy. Participants were given no information about complementary therapies, yet over 60% searched for information independently. More discussions are needed in this area so that people with NMOSD can safely use complementary therapies alongside their other treatments.

Clinical Trials

Clinical trials are essential for development of new treatments. The benefits to participants include access to new treatments, an active role in healthcare, and closer monitoring of health condition. The risks to participants include new treatment may not be as effective, and side effects.

A search of the Australian New Zealand Clinical Trials Registry was conducted on 9 February 2021. The search included any study that included NMOSD participants, was conducted in Australia, and began recruitment at any time. A total of four studies were identified that had a target recruitment of between 56 and 231 participants, all studies were international studies with Australian sites in NSW or Victoria. Currently, only one study is recruiting.

In this PEEK study, very few had discussions with their doctor about clinical trials, and no participants had taken part in a clinical trial for NMOSD. However, there is a wiliness to take part in a clinical trial (89%).

Patient treatment preferences

Clinical guidelines that are aligned to patient preferences are more likely to be used and lead to higher rates of patient compliance[71-73]. Patient preferences and priorities vary across different health issues[71], preferences are associated with health care service satisfaction, they refer to the perspectives, values or priorities related to health and health care, including opinions on risks and benefits, the impact on their health and lifestyle[71,74].

To help inform patient preferences in the NMOSD community, participants discussed side effects, treatment administration, adherence to treatment Participants were asked to describe what a mild side effect was. Some participants described side effects using specific examples such as numbness/paraesthesia, or neuropathic pain. Others described mild side effects as those that do not interfere with their daily life. In a similar way, participants describe severe side effects either as those that impact daily life, and using examples or severe side effects such as pain and vision loss. Discussing both a list of side effects and the potential impact on daily life may be important for treatment decision making.

When discussing adhering to treatments, there were those that would continue as long as side effects are tolerable, others described never giving up on treatments, while some described adhering to treatment on advice of their doctor. Participants described changes needed for them to feel like a treatment was working, most commonly reduction in a specific symptom, improvements in pain, prevention of relapse and improved mobility. Treatment adherence may be improved by discussing expected side effects and mechanisms and support to manage side effects. In addition to discussing the clinical aspects of treatment goals, discussing other aspects such as symptom reduction and weather improvements should be expected in current disabilities may improve adherence by setting expectations of signs that the treatment is working.

Affordability of healthcare

Almost half of the Australian population have private health insurance with hospital cover[75]. This can be used to partially or completely fund stays in public or private hospitals. Between 2006 and 2016, the proportion of private health care funded hospitalisations in public hospitals rose from about 8% to 14%[75]. In this PEEK study, 61% had private insurance, which is more than the Australian population. It should also be noted that participants in this study were grateful for the low cost medical care and access to treatment and hospital through Medicare.

Self-management

Self-management of chronic disease encompasses the tasks that an individual must do to live with their condition. Self-management is supported by education, support, and healthcare interventions. It includes regular review of problems and progress, setting goals, and providing support for problem solving[76]. Components of self-management include information, activation and collaboration[76].

Patient activation is measured in the PEEK study using the Partners in Health questionnaire[77]. The NMOSD participants in this study had good scores for knowledge, , recognition and management of symptoms, very good scores for adherence to treatment, and moderate scores for coping.

Information is a key component of health self-management[78,79]. The types of information that help with self-management includes information about the condition, prognosis, what to expect, information about how to conduct activities of daily living with the condition, and information about lifestyle factors that can help with disease management[78,79].

The most common types of information given to participants in this PEEK study were about treatment options, and disease management, however, about a third of the participants had little to no information given to them by their healthcare professionals.

The type of information that participants in this PEEK study searched for independently most often were disease management, disease cause, complementary therapies, and treatment options. Half of the participants looked for information about dietary information, and physical activity.

Regarding access to information, participants in the PEEK study had prefered online information, speaking to someone or a combination of both. In this study, participants with NMOSD looked for information on the internet in general, on Facebook, and through the Guthy-Jackson Foundation. Journal articles, treating clinician and other patient's experience were noted as important to some. In terms of timing of information, again, PEEK participants benefited from information at different times, from the time they were diagnosed, sometime after diagnosis

Activation (skills and knowledge)

Patient activation is the skills, knowledge, and confidence that a person has to manage their health and care; and is a key component to health self-management. Components of patient activation are support for treatment adherence and attendance at medical appointments, action plans to respond to signs and symptoms, monitoring and recording physiological measures to share with healthcare professionals, and psychological strategies such as problem solving and goal setting.

Communication and collaboration

Collaboration is an important part of health self-management, the components of collaboration include healthcare communication, details for available information, psychosocial and financial support[78,79]. Communication between healthcare professionals and patients can impact the treatment adherence, self-management, health outcomes, and patient satisfaction[80-83].

An expert panel identified the fundamental elements of healthcare communication that encourages a caring, trusting relationship for patient and healthcare professional that enables communication, information sharing, and decision-making[84]

Building a relationship with patient, families and support networks is fundamental to establishing good communication[84]. Healthcare professionals should encourage discussion with patients to understand their concerns, actively listen to patients to gather information using questions then summarising to ensure understanding[84]. It is important for healthcare professionals to understand the patient's perspective and to be sympathetic to their race, culture, beliefs, and concerns. It is important to share information using

language that the patient can understand, encourage questions and make sure that the patient understands[84]. The healthcare professional should encourage patient participation in decision-making, agree on problems, check for willingness to comply with treatment and inform patient about any available support and resources[84]. Finally, the healthcare professional should provide closure, this is to summarise and confirm agreement with treatment plan and discuss follow up.

In interviews with 15 participants with NMOSD from the United Kingdom, a common theme of negative encounters with healthcare professionals was reported. This was mostly due to a lack of knowledge, resulting in treatment delays[42]. Similarly, most participants with NMOSD in the current study had a negative experience of communication with healthcare professionals. This was because health care professionals had limited understanding of NMOSD, dismissive, or just very limited.

Positive communication in this PEEK study, was usually a result of a two-way supportive and comprehensive conversation between patient and clinician. This was also reported in another study, where participants appreciated honesty alongside health professionals listening to their needs[42].

Communication and collaboration with healthcare professionals was measured in this PEEK study by the Care Coordination questionnaire[61,85]. Participants had moderate scores for navigation of the healthcare system, and they rated their overall care as good, coordination of care as moderate. They had a poor score for communication with healthcare professionals.

Quality of life

NMOSD has a negative effect on quality of life[27,29], fatigue and pain have a negative impact on daily activities[26,28,33,86-88], and depression and anxiety have an impact on physical and emotional health[27,28,86,89].

Most participants with NMOSD in this PEEK study reported an overall negative impact on their quality of life due to their condition. The main reasons for this were changes in relationships, reduced physical activity, social interactions, anxiety about prognosis, fatigue and disability.

Almost all participants in this PEEK study reported that NMOSD had an impact on their mental health. The regular activities to maintain mental health were, physical exercise, mindfulness, consulting a mental health professional, remain engaged in social activities and hobbies.

Participants used physical activity to maintain both their mental and physical health. Other ways that participants in this PEEK study maintained their health was to understand their limitations, self-care, and treatment compliance. Similar to another study of NMOSD participants that described ways of dealing with fatigue, and needing to pace themselves[42].

Having NMOSD impacted relationships for participants in this study. Relationships were impacted because of difficulty in socialising and others withdrawing from relationships. Many NMOSD participants described being a burden on their family, mostly because family members had to take on extra responsibilities, and assist with getting to appointments. This is similar to another study that reported frustrations in having to depend on others due their physical limitations, and the difficulties in friendships due to ignorance of NMOSD, and difficulties socialising[42].

Anxiety associated with condition

In this PEEK study, anxiety associated with NMOSD was measured by the fear of progression questionnaire[90]participants in this study had high levels of anxiety concerning disease progression. The greatest concerns were about disease progression, reaching professional or personal goals, relatives being diagnosed with disease, being able to pursue hobbies, treatment will damage body, worried about family if anything happens to them, and not being able to work. In addition, themes from the structured interviews included reduced quality of life due to limitations on social interactions, and the inability to complete activities of daily living. This is similar to other studies, where NMOSD participants reported being fearful of relapse, symptom progression, changes to life plans, ability to complete daily activities and engage in social activities[26,42].

Characterisation

There were 18 participants with NMOSD, eight participants with MOG and 10 people who cared for people with NMOSD or MOG, in the study from

across Australia. This characterisation of the study will focus on participants with NMOSD. The majority of participants lived in major cities, they lived in all levels of economic advantage. Most of the of participants identified as Caucasian or white, and were aged mostly between 45 and 64. Under half of the participants had completed some university, and less than a third were employed either full time or part time. Less than a third of participants were carers to family members or spouses.

Participants in this PEEK study most commonly had between two and four relapses, and were diagnosed after they turned 40. This patient population was also characterised by comorbidities with an average of four other conditions in addition to NMOSD. More than half of the participants had chronic pain, sleep problems, or depression.

This is a patient population that sought medical attention relatively soon after noticing symptoms The most common symptoms before an NMOSD diagnosis were loss of clear vision, eye pain, muscle spasms, and sensory loss, causing a poor quality of life. Visual problems was the symptom that most often led to a diagnosis.

On average, this group had six diagnostic tests for their condition, they were diagnosed by a neurologist at hospital. They were most commonly diagnosed after being admitted to the emergency department or hospital. They didn't have enough emotional support or enough information at diagnosis. This is a cohort that did not have conversations about biomarker, genomic, or gene testing, but were able to recall having had this type of test.

This is a study cohort that knew nothing or very little about their condition at diagnosis. They commonly associated the condition with multiple sclerosis and poor prognosis, often describing their prognosis in relation to the long-term permanent effects they have suffered from it.

This is a patient population that mostly had discussions about multiple treatment options, some participated in the decision-making process while others did not. The most common specific treatment discussed was rituximab.

This is a study cohort that considered the side effects, efficacy and costs when making decisions about treatment. The participants felt that the way they made decisions had changed over time because they had become more informed or assertive.

When asked about their personal goals of treatment or care, participants wanted to maintain their condition, and prevent relapses.

This is a group who felt that throughout their experience, they were treated with respect , with the exception of one or two occasions. They were all cared for by a neurologist.

This is a cohort that had private health insurance that were often treated as public patients in public hospitals. They had no problems with paying for healthcare appointments, filling prescriptions, paying for basic essentials. The monthly out of pocket spending for NMOSD wasn't usually a significant burden.

Participants in this study had to quit their job, though carers and family did not have to change employment status. The loss of income due to NMOSD was a burden on many participants.

All participants had been treated with high dose steroids, while this was found to be effective, the quality of life was low. The most common immunosuppressant taken was rituximab, about half had no side effects from rituximab, participants found this treatment effective.

There were very few conversations about clinical trials, however, they would take part in a clinical trial if there was a suitable one for them.

This is a patient population that described mild side effects using examples like numbness or paresthesia, and neuropathic pain. They also described severe side effects using examples, such as pain, or vision loss.

Within this patient population, participants adhered to a treatment plan as long as side effects were tolerable. This is a study cohort that needed to see a reduction in a specific symptoms in order to feel that treatment is working as well as needed to see an improvements in pain levels.

Participants preferred to have treatment at home rather than in hospital because it was more comfortable and convenient, with less interruption to daily life. Participants in this study would need to be checked regularly by a GP or nurse at home if they

were having treatment at home to ease their anxiety.

This study cohort largely had some access to allied health services the most common being occupational therapists, physiotherapists, and psychologists. They found that services from allied health were generally effective.

Almost all participants made lifestyle changes to help manage their NMOSD, they usually exercised or made diet changes. They also tried complementary therapies to help manage their condition.

This participant population largely did not have access to telehealth services. Access was usually due to COVID-19, and those who used telehealth were pleased with their experience.

Within this patient population, it was most commonly felt that if treatment worked it would allow them to engage more with social activities and family life.

Participants in this study had good knowledge about their condition, were good at recognizing and managing symptoms, were excellent at adhering to treatment, and were average at coping with their condition,

Participants weren't given a lot of information about NMOSD. They were mostly given information treatment options, and disease management. Participants searched for information about many aspects of NMOSD including disease management, disease causes, treatment options, complementary therapies, and physical activity. This is a group who accessed information from non-profit, charity or patient organisations most often.

This is a patient population that accessed information through the internet, Facebook and the Guthy-Jackson Foundation. There was no information that wasn't helpful, but they found other people's experiences especially helpful.

This is a group that preferred to get their information online, talking to someone, or a mixture of both. They generally felt most receptive to information from the beginning, at diagnosis, or wanted to wait a bit after diagnosis to be given information.

Participants had a negative experience of communication when the healthcare profession had limited knowledge about NMOSD. They had positive experience of communication when conversations with healthcare professionals were two-way, supportive and comprehensive.

The participants in this study experienced good quality of care, and average coordination of care. They had an average ability to navigate the healthcare system, and experienced poor communication from healthcare professionals.

This is a patient population that most commonly did not receive care and support, though when they did, it was mainly through domestic services, for transport and from a hospital or clinical setting.

This is a patient population that experienced a negative impact on quality of life generally due to emotional strain on family/change in relationship dynamics and reduced capacity for physical activity. Emotional strain on family and changes in relationship dynamics had a negative impact on quality of life, as did the reduced capacity for physical activity

This is a study cohort that experienced at least some impact on their mental health and to maintain their mental health they exercised or used mindfulness techniques and meditation.

Within this patient population, participants described the importance of being understanding of their limitations, and practising self-care in order to maintain their general health.

This cohort most commonly felt there was a negative impact on their relationships due to having difficulties socialising.

This patient population felt their condition was a burden on their family, usually it was because of the extra household duties or responsibilities their family had to take on, and being taken to appointments.

Most participants felt there was some cost burden which was primarily in relation to time off work, and the cost of treatments.

The participants in this PEEK study had high levels of anxiety in relation to their condition, and overall, NMOSD had a negative impact on quality of life.

Participants would like future treatments to have fewer or less intense side effects, for there to be

more options to treat NMOSD, and more affordable treatments.

This is a study cohort that would like more information that is specific to NMOSD, and information about where to find services.

Participants in this study would like future communication to be more transparent and for healthcare professionals to be more forthcoming with information. They would like specialist clinics or services for NMOSD where they can talk to professionals, either in person, online or by telephone.

This patient population was grateful for healthcare staff, the entire health system, and low cost or free medical care through the government.

It was important for this cohort to control weakness or paralysis of arms and legs, loss of clear vision, and loss of bowel or bladder control. Participants in this study would consider taking a treatment for more than ten years if quality of life is improved with no cure.

Participants in this study valued knowing the safety of medication, and side effects when making treatment decisions, and thought that the government should consider the quality of life of patients when making decisions that impact treatment and care.

The message to decision-makers given by participants in this study was to invest in new treatments and make them more accessible. They would like more NMOSD research, and better access to support and care.

This is a patient population that wished they had known what to expect from their condition, the treatments available to prevent attacks, and they wish they had known to ask more questions and advocate for themselves.

Most participants in this cohort would not change their care and treatment primarily because they were satisfied with the care they received, though there were some that would have liked better communication and continuity of care.

References

1. Bukhari W, Barnett MH, Prain K, Broadley SA. Molecular pathogenesis of neuromyelitis optica. *Int J Mol Sci* 2012; **13**(10): 12970-93.
2. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015; **85**(2): 177-89.
3. Fan S, Xu Y, Ren H, et al. Comparison of myelin oligodendrocyte glycoprotein (MOG)-antibody disease and AQP4-IgG-positive neuromyelitis optica spectrum disorder (NMOSD) when they co-exist with anti-NMDA (N-methyl-D-aspartate) receptor encephalitis. *Mult Scler Relat Disord* 2018; **20**: 144-52.
4. Kezuka T, Ishikawa H. Diagnosis and treatment of anti-myelin oligodendrocyte glycoprotein antibody positive optic neuritis. *Jpn J Ophthalmol* 2018; **62**(2): 101-8.
5. Weber MS, Derfuss T, Metz I, Bruck W. Defining distinct features of anti-MOG antibody associated central nervous system demyelination. *Ther Adv Neurol Disord* 2018; **11**: 1756286418762083.
6. Lennon VA, Wingerchuk DM, Kryzer TJ, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004; **364**(9451): 2106-12.
7. Papp V, Magyari M, Aktas O, et al. Worldwide Incidence and Prevalence of Neuromyelitis Optica: A Systematic Review. *Neurology* 2021; **96**(2): 59-77.
8. Akaishi T, Takahashi T, Misu T, et al. Progressive patterns of neurological disability in multiple sclerosis and neuromyelitis optica spectrum disorders. *Sci Rep* 2020; **10**(1): 13890.
9. Wingerchuk DM, Hogancamp WF, O'Brien PC, Weinshenker BG. The clinical course of neuromyelitis optica (Devic's syndrome). *Neurology* 1999; **53**(5): 1107-14.
10. Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitis optica. *Neurology* 2006; **66**(10): 1485-9.
11. Mealy MA, Kessler RA, Rimler Z, et al. Mortality in neuromyelitis optica is strongly associated with African ancestry. *Neurol Neuroimmunol Neuroinflamm* 2018; **5**(4): e468.
12. Huda S, Whittam D, Bhojak M, Chamberlain J, Noonan C, Jacob A. Neuromyelitis optica spectrum disorders. *Clin Med (Lond)* 2019; **19**(2): 169-76.
13. Etemadifar M, Nasr Z, Khalili B, Taherioun M, Vosoughi R. Epidemiology of neuromyelitis optica in the world: a systematic review and meta-analysis. *Mult Scler Int* 2015; **2015**: 174720.
14. Quek AM, McKeon A, Lennon VA, et al. Effects of age and sex on aquaporin-4 autoimmunity. *Arch Neurol* 2012; **69**(8): 1039-43.
15. Flanagan EP, Cabre P, Weinshenker BG, et al. Epidemiology of aquaporin-4 autoimmunity and neuromyelitis optica spectrum. *Ann Neurol* 2016; **79**(5): 775-83.
16. Ochi H, Fujihara K. Demyelinating diseases in Asia. *Curr Opin Neurol* 2016; **29**(3): 222-8.
17. Matiello M, Kim HJ, Kim W, et al. Familial neuromyelitis optica. *Neurology* 2010; **75**(4): 310-5.
18. Weinshenker BG, Wingerchuk DM. Neuromyelitis Spectrum Disorders. *Mayo Clin Proc* 2017; **92**(4): 663-79.
19. Barzegar M, Sadeghi Bahmani D, Nehzat N, et al. Comparison of sleep complaints and quality of life between patients with neuromyelitis optica spectrum disorder (NMOSD) and healthy controls. *Mult Scler Relat Disord* 2019; **32**: 81-7.
20. Chen H, Liu SM, Zhang XX, et al. Clinical Features of Patients with Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorders. *Chin Med J (Engl)* 2016; **129**(17): 2079-84.
21. Akaishi T, Takahashi T, Fujihara K, et al. Risk factors of attacks in neuromyelitis optica spectrum disorders. *J Neuroimmunol* 2020; **343**: 577236.
22. Australian Bureau of Statistics 2018, National Health Survey: First Results, 2017-18, cat. no. 4364.0.55.001, ABS, Canberra.
23. Kleiter I, Gahlen A, Borisow N, et al. Neuromyelitis optica: Evaluation of 871 attacks and 1,153 treatment courses. *Ann Neurol* 2016; **79**(2): 206-16.
24. Australian Bureau of Statistics 1995, National Health Survey: SF36 Population Norms, Australia, 1995. cat. no. 4399.0, ABS, Canberra
.
25. Eaneff S, Wang V, Hanger M, et al. Patient perspectives on neuromyelitis optica spectrum

disorders: Data from the PatientsLikeMe online community. *Mult Scler Relat Disord* 2017; **17**: 116-22.
26. Beekman J, Keisler A, Pedraza O, et al. Neuromyelitis optica spectrum disorder: Patient experience and quality of life. *Neurol Neuroimmunol Neuroinflamm* 2019; **6**(4): e580.
27. Seok JM, Choi M, Cho EB, et al. Fatigue in patients with neuromyelitis optica spectrum disorder and its impact on quality of life. *PLoS One* 2017; **12**(5): e0177230.
28. Pan J, Zhao P, Cai H, et al. Hypoxemia, Sleep Disturbances, and Depression Correlated with Fatigue in Neuromyelitis Optica Spectrum Disorder. *CNS Neurosci Ther* 2015; **21**(7): 599-606.
29. Barzegar M, Badihian S, Mirmosayyeb O, et al. Comparative study of quality of life, anxiety, depression, and fatigue among patients with neuromyelitis optica spectrum disorder and multiple sclerosis: The first report from Iran. *Mult Scler Relat Disord* 2018; **22**: 161-5.
30. Bradl M, Kanamori Y, Nakashima I, et al. Pain in neuromyelitis optica--prevalence, pathogenesis and therapy. *Nat Rev Neurol* 2014; **10**(9): 529-36.
31. Chavarro VS, Mealy MA, Simpson A, et al. Insufficient treatment of severe depression in neuromyelitis optica spectrum disorder. *Neurol Neuroimmunol Neuroinflamm* 2016; **3**(6): e286.
32. Brody J, Hellmann MA, Marignier R, Lotan I, Stiebel-Kalish H. Neuromyelitis Optica Spectrum Disorder: Disease Course and Long-Term Visual Outcome. *J Neuroophthalmol* 2016; **36**(4): 356-62.
33. Kanamori Y, Nakashima I, Takai Y, et al. Pain in neuromyelitis optica and its effect on quality of life: a cross-sectional study. *Neurology* 2011; **77**(7): 652-8.
34. Liu J, Zhang Q, Lian Z, et al. Painful tonic spasm in neuromyelitis optica spectrum disorders: Prevalence, clinical implications and treatment options. *Mult Scler Relat Disord* 2017; **17**: 99-102.
35. Zhang Y, Zhang Q, Shi Z, et al. Sexual dysfunction in patients with neuromyelitis optica spectrum disorder. *J Neuroimmunol* 2020; **338**: 577093.
36. Chanson JB, Zephir H, Collongues N, et al. Evaluation of health-related quality of life, fatigue and depression in neuromyelitis optica. *Eur J Neurol* 2011; **18**(6): 836-41.
37. Hyun JW, Kim SH, Jeong IH, et al. Increased frequency and severity of restless legs syndrome in patients with neuromyelitis optica spectrum disorder. *Sleep Med* 2016; **17**: 121-3.
38. He Z, Ren M, Wang X, Guo Q, Qi X. Pruritus may be a common symptom related to neuromyelitis optica spectrum disorders. *Mult Scler Relat Disord* 2017; **13**: 1-3.
39. Eizaguirre MB, Alonso R, Vanotti S, Garcea O. Cognitive impairment in neuromyelitis optica spectrum disorders: What do we know? *Mult Scler Relat Disord* 2017; **18**: 225-9.
40. Moore P, Methley A, Pollard C, et al. Cognitive and psychiatric comorbidities in neuromyelitis optica. *J Neurol Sci* 2016; **360**: 4-9.
41. Blanc F, Zephir H, Lebrun C, et al. Cognitive functions in neuromyelitis optica. *Arch Neurol* 2008; **65**(1): 84-8.
42. Mutch K, Methley A, Moore P, Jacob A. Life on hold: the experience of living with neuromyelitis optica. *Disabil Rehabil* 2014; **36**(13): 1100-7.
43. Nmouk.nhs.uk. 2021. Diagnosis | NMO NHS | NMO Advice & Support UK. [online] Available at: <http://www.nmouk.nhs.uk/what-is-nmo/diagnosis> [Accessed 9 February 2021].
44. Fujihara K. Neuromyelitis optica spectrum disorders: still evolving and broadening. *Curr Opin Neurol* 2019; **32**(3): 385-94.
45. Sato DK, Callegaro D, Lana-Peixoto MA, et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. *Neurology* 2014; **82**(6): 474-81.
46. Mealy MA, Mossburg SE, Kim SH, et al. Long-term disability in neuromyelitis optica spectrum disorder with a history of myelitis is associated with age at onset, delay in diagnosis/preventive treatment, MRI lesion length and presence of symptomatic brain lesions. *Mult Scler Relat Disord* 2019; **28**: 64-8.
47. Mealy MA, Wingerchuk DM, Greenberg BM, Levy M. Epidemiology of neuromyelitis optica in the United States: a multicenter analysis. *Arch Neurol* 2012; **69**(9): 1176-80.
48. Jarius S, Ruprecht K, Wildemann B, et al. Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: A multicentre

study of 175 patients. *J Neuroinflammation* 2012; **9**: 14.
49. Kim SH, Kim W, Li XF, Jung IJ, Kim HJ. Does interferon beta treatment exacerbate neuromyelitis optica spectrum disorder? *Mult Scler* 2012; **18**(10): 1480-3.
50. Yamout BI, Beaini S, Zeineddine MM, Akkawi N. Catastrophic relapses following initiation of dimethyl fumarate in two patients with neuromyelitis optica spectrum disorder. *Mult Scler* 2017; **23**(9): 1297-300.
51. Hyun JW, Jeong IH, Joung A, Kim SH, Kim HJ. Evaluation of the 2015 diagnostic criteria for neuromyelitis optica spectrum disorder. *Neurology* 2016; **86**(19): 1772-9.
52. Hamid SH, Elsone L, Mutch K, Solomon T, Jacob A. The impact of 2015 neuromyelitis optica spectrum disorders criteria on diagnostic rates. *Mult Scler* 2017; **23**(2): 228-33.
53. Khalilidehkordi E, Clarke L, Arnett S, et al. Relapse Patterns in NMOSD: Evidence for Earlier Occurrence of Optic Neuritis and Possible Seasonal Variation. *Front Neurol* 2020; **11**: 537.
54. Tackley G, O'Brien F, Rocha J, et al. Neuromyelitis optica relapses: Race and rate, immunosuppression and impairment. *Mult Scler Relat Disord* 2016; **7**: 21-5.
55. Steinhauser KE, Christakis NA, Clipp EC, McNeilly M, McIntyre L, Tulsky JA. Factors considered important at the end of life by patients, family, physicians, and other care providers. *JAMA* 2000; **284**(19): 2476-82.
56. Barnes S, Gardiner C, Gott M, et al. Enhancing patient-professional communication about end-of-life issues in life-limiting conditions: a critical review of the literature. *J Pain Symptom Manage* 2012; **44**(6): 866-79.
57. Fellowes D, Wilkinson S, Moore P. Communication skills training for health care professionals working with cancer patients, their families and/or carers. *Cochrane Database Syst Rev* 2004; (2): CD003751.
58. Lamore K, Montalescot L, Untas A. Treatment decision-making in chronic diseases: What are the family members' roles, needs and attitudes? A systematic review. *Patient Educ Couns* 2017; **100**(12): 2172-81.
59. Abboud H, Petrak A, Mealy M, Sasidharan S, Siddique L, Levy M. Treatment of acute relapses in neuromyelitis optica: Steroids alone versus steroids plus plasma exchange. *Mult Scler* 2016; **22**(2): 185-92.
60. Wingerchuk DM, Weinshenker BG. Neuromyelitis optica. *Curr Treat Options Neurol* 2008; **10**(1): 55-66.
61. Min JH, Kim BJ, Lee KH. Development of extensive brain lesions following fingolimod (FTY720) treatment in a patient with neuromyelitis optica spectrum disorder. *Mult Scler* 2012; **18**(1): 113-5.
62. Jacob A, Hutchinson M, Elsone L, et al. Does natalizumab therapy worsen neuromyelitis optica? *Neurology* 2012; **79**(10): 1065-6.
63. Palace J, Leite MI, Nairne A, Vincent A. Interferon Beta treatment in neuromyelitis optica: increase in relapses and aquaporin 4 antibody titers. *Arch Neurol* 2010; **67**(8): 1016-7.
64. Costanzi C, Matiello M, Lucchinetti CF, et al. Azathioprine: tolerability, efficacy, and predictors of benefit in neuromyelitis optica. *Neurology* 2011; **77**(7): 659-66.
65. Elsone L, Kitley J, Luppe S, et al. Long-term efficacy, tolerability and retention rate of azathioprine in 103 aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder patients: a multicentre retrospective observational study from the UK. *Mult Scler* 2014; **20**(11): 1533-40.
66. Huh SY, Kim SH, Hyun JW, et al. Mycophenolate mofetil in the treatment of neuromyelitis optica spectrum disorder. *JAMA Neurol* 2014; **71**(11): 1372-8.
67. Kim SH, Huh SY, Lee SJ, Joung A, Kim HJ. A 5-year follow-up of rituximab treatment in patients with neuromyelitis optica spectrum disorder. *JAMA Neurol* 2013; **70**(9): 1110-7.
68. Cree BA, Lamb S, Morgan K, Chen A, Waubant E, Genain C. An open label study of the effects of rituximab in neuromyelitis optica. *Neurology* 2005; **64**(7): 1270-2.
69. Jacob A, Weinshenker BG, Violich I, et al. Treatment of neuromyelitis optica with rituximab: retrospective analysis of 25 patients. *Arch Neurol* 2008; **65**(11): 1443-8.
70. Palace J, Leite MI, Jacob A. A practical guide to the treatment of neuromyelitis optica. *Pract Neurol* 2012; **12**(4): 209-14.
71. Kim C, Armstrong MJ, Berta WB, Gagliardi AR. How to identify, incorporate and report patient preferences in clinical guidelines: A

scoping review. *Health Expect* 2020; **23**(5): 1028-36.
72. Cronin RM, Mayo-Gamble TL, Stimpson SJ, et al. Adapting medical guidelines to be patient-centered using a patient-driven process for individuals with sickle cell disease and their caregivers. *BMC Hematol* 2018; **18**: 12.
73. Sleath B, Carpenter DM, Slota C, et al. Communication during pediatric asthma visits and self-reported asthma medication adherence. *Pediatrics* 2012; **130**(4): 627-33.
74. Ross CK, Steward CA, Sinacore JM. The importance of patient preferences in the measurement of health care satisfaction. *Med Care* 1993; **31**(12): 1138-49.
75. Australian Institute of Health and Welfare 2017. Private health insurance use in Australian hospitals, 2006–07 to 2015–16: Australian hospital statistics. Health Services Series no. 81. Cat. no. HSE 196. Canberra: AIHW.
76. In: Adams K, Greiner AC, Corrigan JM, eds. The 1st Annual Crossing the Quality Chasm Summit: A Focus on Communities. Washington (DC); 2004.
77. Petkov J, Harvey P, Battersby M. The internal consistency and construct validity of the partners in health scale: validation of a patient rated chronic condition self-management measure. *Qual Life Res* 2010; **19**(7): 1079-85.
78. Grande SW, Faber MJ, Durand MA, Thompson R, Elwyn G. A classification model of patient engagement methods and assessment of their feasibility in real-world settings. *Patient Educ Couns* 2014; **95**(2): 281-7.
79. Taylor SJC, Pinnock H, Epiphaniou E, et al. A rapid synthesis of the evidence on interventions supporting self-management for people with long-term conditions: PRISMS - Practical systematic Review of Self-Management Support for long-term conditions. Southampton (UK); 2014.
80. Williams S, Weinman J, Dale J. Doctor-patient communication and patient satisfaction: a review. *Fam Pract* 1998; **15**(5): 480-92.
81. Stewart M, Brown JB, Boon H, Galajda J, Meredith L, Sangster M. Evidence on patient-doctor communication. *Cancer Prev Control* 1999; **3**(1): 25-30.
82. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract* 2000; **49**(9): 796-804.
83. Glasgow RE, Davis CL, Funnell MM, Beck A. Implementing practical interventions to support chronic illness self-management. *Jt Comm J Qual Saf* 2003; **29**(11): 563-74.
84. Makoul G. Essential elements of communication in medical encounters: the Kalamazoo consensus statement. *Acad Med* 2001; **76**(4): 390-3.
85. Young JM, Walsh J, Butow PN, Solomon MJ, Shaw J. Measuring cancer care coordination: development and validation of a questionnaire for patients. *BMC Cancer* 2011; **11**: 298.
86. Akaishi T, Nakashima I, Misu T, Fujihara K, Aoki M. Depressive state and chronic fatigue in multiple sclerosis and neuromyelitis optica. *J Neuroimmunol* 2015; **283**: 70-3.
87. Muto M, Mori M, Sato Y, et al. Current symptomatology in multiple sclerosis and neuromyelitis optica. *Eur J Neurol* 2015; **22**(2): 299-304.
88. Tackley G, Vecchio D, Hamid S, et al. Chronic neuropathic pain severity is determined by lesion level in aquaporin 4-antibody-positive myelitis. *J Neurol Neurosurg Psychiatry* 2017; **88**(2): 165-9.
89. Shi Z, Chen H, Lian Z, Liu J, Feng H, Zhou H. Factors that impact health-related quality of life in neuromyelitis optica spectrum disorder: anxiety, disability, fatigue and depression. *J Neuroimmunol* 2016; **293**: 54-8.
90. Hinz A, Mehnert A, Ernst J, Herschbach P, Schulte T. Fear of progression in patients 6 months after cancer rehabilitation-a- validation study of the fear of progression questionnaire FoP-Q-12. *Support Care Cancer* 2015; **23**(6): 1579-87.