Section 1

Introduction and methods

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About this condition

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].

Although NMOSD can affect men and women of all ages and ethnicities, middle-aged and elderly women are most commonly affected[5]. The average age of onset is 40 years of age[6], and NMOSD is more common in non-white ethnicities[7,8].

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 prostrema syndrome (uncontrollable hiccups or nausea and vomiting), and narcolepsy (sleep disorder)**[2].**

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]. Disabilities accumulate with relapses, it is therefore important to aggressively treat relapses and prevent relapses with maintenance therapies**[10].** Prognosis has improved with the identification of the AQP4 antibody[11,12].

Participants

To be eligible for the study, participants needed to have been diagnosed with NMOSD, or MOG, or have cared for someone who had one of these conditions, have experienced the healthcare system in Australia, be 18 years of age or older, be able to speak English, and be able to give consent to participate in the study.

Personal Experience, Expectations and Knowledge (PEEK): Study position

In this PEEK study, 18 people diagnosed with NMOSD throughout Australia participated in the study that included a qualitative structured interview and quantitative questionnaire. This study in NMOSD is the only mixed methods study reported in an Australian population, and it includes the most patient interviews worldwide. In addition, PEEK is a comprehensive study covering all aspects of disease experience from symptoms, diagnosis, treatment, healthcare communication, information provision, care and support, quality of life, and future treatment and care expectations.

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].

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 MS until the discovery of aquaporin 4 (AQP4 antibodies)[3]. The estimated incidence of NMOSD in Australia and NZ is 0.37 per million per year, and estimated prevalence is 0.7 per 100,000[4].

Risks and Symptoms

Although NMOSD can affect men and women of all ages and ethnicities, middle-aged and elderly women are most commonly affected[5]. The average age of onset is 40 years of age[6], and NMOSD is more common in non-white ethnicities[7,8].

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 prostrema syndrome (uncontrollable hiccups or nausea and vomiting), and narcolepsy (sleep disorder)**[2].**

Complications

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]. Disabilities accumulate with relapses, it is therefore important to aggressively treat relapses and prevent relapses with maintenance therapies[10]. Prognosis has improved with the identification of the AQP4 antibody[11,12].

Personal Experience, Expectations and Knowledge (PEEK)

Patient Experience, Expectations and Knowledge (PEEK) is a research program developed by the Centre for Community-Driven Research (CCDR). The aim of PEEK is to conduct patient experience studies across several disease areas using a protocol that will allow for comparisons over time (both quantitative and qualitative components). PEEK studies give us a clear picture and historical record of what it is like to be a patient at a given point in time, and by asking patients about their expectations, PEEK studies give us a way forward to support patients and their families with treatments, information and care.

The research protocol used in PEEK studies is independently driven by CCDR. PEEK studies include a quantitative and qualitative component. The quantitative component is based on a series of validated tools. The qualitative component is the result of two years of protocol testing by CCDR to develop a structured interview that solicits patient experience data and provides patients with the opportunity to provide advice on what they would like to see in relation to future treatment, information and care. The structured interview has also been designed so that the outcomes of PEEK studies can inform policy, research, care, information, supportive care services and advocacy efforts.

Methodology

Participants

To be eligible for the study, participants needed to have been diagnosed with NMOSD, or MOG, or have cared for someone who had one of these conditions, have experienced the healthcare system in Australia, be 18 years of age or older, be able to speak English, and be able to give consent to participate in the study. Recruitment commenced in September 2020 to December 2020.

Ethics

Ethics approval for this study was granted (as a low or negligible risk research study) by the Centre for Community-Driven Research Ethics Committee (Reference CS_Q4_03).

Data collection

Data for the online questionnaire was collected using Zoho Survey (Zoho Corporation Pvt. Ltd. Pleasanton, California, USA, www.zoho.com/survey). Participants completed the survey from September 2020 to December 2020.

There were three researchers who conducted telephone interviews and used standardised prompts throughout the interview. The interviews were recorded and transcribed verbatim. Identifying names and locations were not included

in the transcript. All transcripts were checked against the original recording for quality assurance. Interview data was collected from September 2020 to December 2020.

Online questionnaire (quantitative)

The online questionnaire consisted of the 36-Item Short Form Health Survey (SF36) (RAND Health)[13], a modified Cancer Care Coordination Questionnaire for Patients (CCCQ)[14], the Short Fear of Progression Questionnaire (FOP12)[15], and the Partners in Health version 2 (PIH)[16]. In addition, investigator derived questions about demographics, diagnosis, treatment received and future treatment decisions making were included.

Structured Interview (qualitative)

Interviews were conducted via telephone by registered nurses who were trained in qualitative research. The first set of interview questions guided the patient through their whole experience from when symptoms were noticed up to the present day.

Questionnaire analysis

Statistical analysis was conducted using R included in the packages "car", "dplyr" and "ggplot2" (R 3.3.3 GUI 1.69 Mavericks build (7328). The aim of the statistical analysis of the SF36, CCCQ, FOP12, and PIH responses was to identify variations by participant type, relapses, fear of progression, physical function, gender, age, location of residence, education status and socio-economic status. Scales and subscales were calculated according to reported instructions[13-16].

The Location of participants was evaluated by postcode using the Australian Statistical Geography Maps (ASGS) Remoteness areas accessed from the Australian Bureau of Statistics[17].

The level of socio-economic status of participants was evaluated by postcode using the Socio-economic Indexes for Areas (SEIFA) accessed from the Australian Bureau of Statistics[18].

For comparisons by disability, participant type, and age, a one-way analysis of variance (ANOVA) analysis was conducted. A Tukey HSD test was used post-hoc to identify the source of any differences identified in the one-way ANOVA test. Where the assumptions for the one-way ANOVA were not met, a Kruskal-Wallis rank sum test on care was conducted with post-hoc pairwise comparisons using Wilcoxon rank sum test. When the assumption of equal variances were not met, a Welch one-way test was used with post-hoc pairwise t-tests with no assumption of equal variances.

For all other comparisons, a two-sample t-test was used when assumptions for normality and variance were met, or when assumptions were not met, a Wilcoxon rank sum test with continuity correction was used. Questions where participants were asked to rank preferences were analysed using weighted averages. Weights were applied in reverse, the most preferred option was given the largest weight equal to the number of options, the least preferred option was given the lowest weight of 1.

Structured interviews analysis

A content analysis was conducted using conventional analysis to identify major themes from structured interviews. Text from the interviews were read line-by-line by the lead researcher and then imported into NVivo 8 (QSR International)/MaxQDA. Each question within the interview was individually analysed. Initial categories and definitions were identified and registered in NVivo 8 (QSR International)/MaxQDA. The minimum coded unit was a sentence with paragraphs and phrases coded as a unit.

A second researcher verified the codes and definitions, and the text was coded until full agreement was reached using the process of consensual validation. Where a theme occurred less than 5 times it was not included in the study results, unless this result demonstrated a significant gap or unexpected result.

Data analysis and final reporting was completed in January 2021.

Position of this study

A search was conducted in Pubmed (August 18, 2020) to identify NMOSD quality of life or patient experience studies of adults that had been conducted in the past ten years worldwide (Table 1.1). Meta-analysis studies, studies conducted in developing countries, and studies of less than five participants were excluded.

There were 14 studies identified that collected patient self-reported data. There was a single

qualitative study of 15 NMOSD participants [19], where 15 interviews were focused on quality of life. There were 13 quantitative studies of between five and 522 participants with NMOSD. There were seven studies focused on symptoms[20-26], two studies on COVID-19[27,28], two Quality of life studies[29], one focused on co-morbidities [30], and one on Reproductive history[31]. There were no studies that were conducted in an Australian population.

In this PEEK study, 18 people diagnosed with NMOSD throughout Australia participated in the study that included a qualitative structured interview and quantitative questionnaire. This study in NMOSD is therefore the only mixed methods study reported in an Australian population, and it includes the most patient interviews worldwide. In addition, PEEK is a comprehensive study covering all aspects of disease experience from symptoms, diagnosis, treatment, healthcare communication, information provision, care and support, quality of life, and future treatment and care expectations.

Table 1.1: PEEK position

Author, Year	Disease and Number of participants (Number of NMOSD in mixed studies)	Location	Design	Focus	PEEK section							
					2: Health status, co-morbidities, health-related quality of life	3: Diagnosis experience, information, support and costs	4: Decision making and healthcare professional discussions	5: Treatment, healthcare system use and access, economic implications	6: Information, communication and self-management	7: Care, support and navigating healthcare system	8: Quality of life, mental health, relationships	9 Expectations, preferences and messages
Beekman, 2019[32]	NMOSD,193	North America	Quantitative	Quality of life	X	X		X			X	X
Mealy, 2019[29]	NMOSD, 21	USA	Quantitative	Quality of life	X							
Seok, 2017[20]	NMOSD, 35	Korea	Quantitative	Symptoms	X	X					X	
Bove, 2017[31]	NMOSD, 217	UK	Quantitative	Reproductive history				X				
Salama, 2020[27]	NMOSD, 186	USA	Quantitative	COVID 19			X	X	X		X	
Eaneff, 2017[21]	NMOSD, 522	International	Quantitative	Symptoms	X	X		X				
Mealy, 2020[22]	NMOSD, 22	USA	Quantitative	Symptoms		X		X			X	
Milewska, 2020[23]	Demyelinating diseases, 64(8)	Poland	Quantitative	Symptoms		X						
Kawahara, 2014[24]	MS/NMO, 45(10)	Japan	Quantitative	Symptoms		X						
Vanotti, 2013[25]	NMOSD, 14	Spain	Quantitative	Symptoms							X	
Shin, 2019[30]	MS/NMO, 59(35)	Korea	Quantitative	Co-morbidities	X	X					X	
Ciampi, 2020[28]	MS/NMO, 409(5)	Chile	Quantitative	COVID 19	X			X				
Methley, 2017[19]	NMOSD, 15	UK	Qualitative (interviews)	Quality of life	X	X				X	X	X
Asseyer, 2018[26]	NMOSD, 49	Germany	Quantitative	Symptoms	X	X					X	

Abbreviations and terminology

AQP4	Aquaporin-4
ASGS	The Australian Statistical Geography Standard from the Australian Bureau of Statistics, defines remoteness and urban/rural definitions in Australia
CCDR	Centre for Community-Driven Research
dF	Degrees of Freedom. The number of values in the final calculation of a statistic that are free to vary.
f	The F ratio is the ratio of two mean square values, used in an ANOVA comparison. A large F ratio means that the variation among group means is more than you'd expect to see by chance.
FOP	Fear of Progression. Tool to measure anxiety related to progression
IQR	Interquartile range. A measure of statistical dispersion, being equal to the difference between 75th and 25th percentiles, or between upper and lower quartiles.
MOG	Myelin oligodendrocyte glycoprotein
NMOSD	Neuromyelitis optica spectrum disorders
p	Probability value. A small *p*-value (typically ≤ 0.05) indicates strong. A large *p*-value (> 0.05) indicates weak evidence.
PEEK	Patient Experience, Expectations and Knowledge
PIH	Partners in Health
SD	Standard deviation. A quantity expressing by how much the members of a group digger from the mean value for the group/
SEIFA	Socio-Economic Indexes for Areas (SEIFA) ranks areas in Australia according to relative socio-economic advantage and disadvantage. This is developed by the Australian Bureau of Statistics.
SF36	Short Form Health Survey 36
t	t-Statistic. Size of the difference relative to the variation in your sample data.
Tukey HSD	Tukey's honestly significant difference test. It is used in this study to find 5significantly different means following an ANOVA test.
W	The W statistic is the test value from the Wilcoxon Rank sum test. The theoretical range of W is between 0 and (number in group one) x (number in group 2). When W=0, the two groups are exactly the same.
X^2	Chi-squared. Kruskal-Wallis test statistic approximates a chi-square distribution. The Chi-square test is intended to test how likely it is that an observed distribution is due to chance.

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