The Lived Experience of Narcolepsy in Australia: An Exploration of the Needs, Concerns, and Barriers to Care

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Statement of Originality

The work presented in this thesis is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material in full or in part for a degree at this or any other institution.

Aaron Schokman
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Date: 26/05/2023

Publications, communication, and awards

The body of work is presented for examination as a thesis with publications. Four publications have resulted from the body of work undertaken during the PhD. Two manuscripts have been submitted for publication, and two are currently undergoing peer review by the relevant journals.

The publications are listed below in the order they appear in the thesis:

Publications

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Abstracts

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Authorship attribution statement

The PhD candidate is the principal author of all four publications and co-designed, collected and analysed the data and wrote the draft manuscripts for all four studies.

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As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Professor Nick Glozier
Primary Supervisor

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Dedication

I want to dedicate this thesis to my friend and mentor, Melissa Jose, who is no longer with us. Your passion and relentless drive to improve the lives of people with narcolepsy have always been an inspiration. You will always have my heartfelt gratitude for the support and guidance you gave me personally and in navigating the advocacy space.

Abstract

This thesis explored the needs, concerns, and barriers to care experienced by persons and their families/carers living with narcolepsy in Australia. It also aimed to explore how person-centric the healthcare system is in practice, using narcolepsy as the example, and determine what persons with narcolepsy and their families/carers perceive 'well-managed' narcolepsy to be. The rationale behind this thesis stems from the substantial burden of disease associated with narcolepsy. We know from the literature that narcolepsy affects health-related quality of life, psychosocial health, capacity to work, functional impairment and absenteeism, and health-related stigma. However, little is known about the actual impact and healthcare needs of persons with narcolepsy in Australia, nor whether the healthcare system and support services are adequately addressing these concerns. This thesis comprises four studies: A qualitative study involving a document analysis using the framework approach, a systematic review involving the quantitative analysis of psychometric properties of outcome measures, and two qualitative studies involving 1:1 semi-structured interviews.

In my first study, I conducted a document analysis of the submissions written by persons with narcolepsy and their family and carers to the federal Parliamentary Inquiry on Sleep Health Awareness in Australia 2018. The aim of this study was to explore the needs, concerns and barriers to care for persons with narcolepsy and their family and carers. We found that although persons with narcolepsy and their family/carers prioritised issues that affected their daily lives (i.e. mental health sequela, workplace accommodations), the policy recommendations in the report focused mainly on issues of healthcare infrastructure, funding and engagement. The results of this study informed the hypothesis that perhaps there was a misalignment between persons affected by narcolepsy and other stakeholders around the perceived illness experience, impact, and healthcare priorities of narcolepsy.

The second study was a systematic review of outcome measures to assess treatment efficacy in narcolepsy randomised controlled trials and an assessment of the psychometric properties of any patient-reported outcome measure used. As narcolepsy management is almost entirely pharmacological, one of the aims of this study was to explore how 'well-managed' narcolepsy is determined and whether these outcome measures aligned with the priorities found in study one. The results indicate that frequently used patient-reported outcome measures lack validation for use in a narcolepsy population. Further, domains considered important to persons with narcolepsy and their family and carers (e.g. psychosocial) identified in study one were rarely assessed.

The third study involved 1:1 semi-structured interviews with parents who have a child with narcolepsy. This study aimed to explore the needs, concerns, and barriers to care identified in study one in further detail, using a more extensive and diverse sample. This study also sought to expand on families and carers perceive 'well-managed' narcolepsy. The results of this study contextualise the whole-person impact of narcolepsy from the perspective of parents and carers, highlighting the need for proactive inclusion of parents/carers in developing healthcare policy and practice.

The fourth study involved 1:1 semi-structured interviews with persons with narcolepsy. The aim of this study was similar to the third, where we explored the needs, concerns, and barriers to care and how persons with narcolepsy perceive 'well-managed' narcolepsy. Our results showed that descriptions of common symptoms often differed between participants and the existing literature, and that the severity of narcolepsy was sometimes determined by the level of functional impairment rather than the frequency of symptoms. The results also showed that almost all persons with narcolepsy often experienced anticipated stigma and subsequently internalised stigma, likely stemming from the societal devaluation of sleep and conflation of sleepiness with laziness.

Several key findings resulted from this thesis:

i) There is substantial dissatisfaction with the healthcare system likely due to misalignment in care priorities between persons with narcolepsy, healthcare professionals, and the healthcare system

ii) Effective treatment is inaccessible for most persons living with narcolepsy

iii) Consumers have limited avenues to voice healthcare concerns or meaningfully contribute to healthcare policy development.

iv) There is a lack of easily accessible information about narcolepsy, including its impact and the accommodations and services, in a format accessible to the public, workplaces, and schools

v) There is a lack of quality, validated outcome measures used in narcolepsy

vi) Persons with narcolepsy experience substantial anticipated and self-stigma that likely contributes to the high prevalence of depression and anxiety.

The findings of this thesis imply that the healthcare system does not appear to be person-centric when navigated by persons with narcolepsy. Little progress has been made towards addressing the needs and concerns of persons with narcolepsy, with some of the concerns identified in this thesis previously reported as early as 2001. Overall, it suggests a need for the proactive inclusion of persons with narcolepsy and their families and carers in healthcare policy and practice at all levels.

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List of Abbreviations

ACSQHC	Australian Commission on Safety and Quality in Health Care
ASAM	American Academy of Sleep Medicine
AUD	Australian Dollar
CHF	Consumer Health Foundation
CSF	Cerebrospinal Fluid
CwN	Child with Narcolepsy
DSM	Diagnostic and Statistical Manual of Mental Disorders
EDS	Excessive Daytime Sleepiness
EEG	Electroencephalogram
ESS	Epworth Sleepiness Scale
HLA	Human Leukocyte Antigen
ICSD	International Classification of Sleep Disorders
IH	Idiopathic Hypersomnia
KSS	Karolinska Sleepiness Scale
MSLT	Multiple Sleep Latency Test
MWT	Maintenance of Wakefulness Test
NT1	Narcolepsy Type 1
NT2	Narcolepsy Type 2
NREM	Non-Rapid Eye Movement
NSQHS	National Safety and Quality Health Service
NSS	Narcolepsy Severity Scale
OSA	Obstructive Sleep Apnoea
PBS	Pharmaceutical Benefits Scheme
PROM	Patient-Reported Outcome Measure
PREM	Patient-Reported Experience Measure
PSG	Polysomnography
PwN	Persons with Narcolepsy
REM	Rapid-Eye Movement
SOREMP	Sleep Onset Rapid Eye Movement Period
TGA	Therapeutic Goods Administration
USD	United States Dollars

Chapter 1: Introduction

1.1 Sleep

Sleep is a biological necessity shared by all humans. It is a reversible state of unconsciousness characterised by a dampening of sensory perception and muscle activity. There are four stages of sleep, each distinguishable by different frequencies and amplitudes of brain waves measurable via an electroencephalogram (EEG). Sleep stages 1-3 are grouped as non-rapid eye movement (NREM) sleep, with each stage considered progressively deeper sleep [1]. Stage 4 is known as rapid eye movement (REM) sleep and is where most dreaming occurs, marked by increased heart rate, brain activity, blood pressure, and muscle atonia that prevents dreams from being acted out. Sleep is also a tightly controlled process. Alexander Borbely (1980) proposed that sleep is maintained by a two-process model - the circadian and homeostatic processes [2]. The former refers to the body's internal clock, where hormone levels and body temperature are modified to maintain the divide between sleep and wakefulness.

On the other hand, a homeostatic process refers to the biological drive for sleep, which increases with time spent awake and decreases with time spent asleep. These two processes are not mutually exclusive. Instead, the homeostatic process drives the need for sleep, whereas the circadian process determines sleep timing.

Sleep disorders tend to be sleep quality, quantity, or timing disruptions. The International Classification of Sleep Disorders currently lists around 70 known sleep disorders, with the most frequent and most severe being obstructive sleep apnoea (OSA), narcolepsy, restless legs syndrome, periodic limb movement disorder, insomnia, parasomnias, circadian rhythm disorders including jet lag and shift work, and sudden infant death syndrome [3,4]. Considering sleep is a biological necessity for both personal health and is vital for productivity, it is no surprise that the likely impact of sleep disorders is high, estimated to cost Australia over $36 billion (AUD) every year[4].

1.2 Narcolepsy

1.2.1 – Background

Narcolepsy appears in literature and medical texts dating back to ancient Greece. Beginning in the late 19th century, French physician Jean-Baptiste-Édouard Gélineau published the first known case report of narcolepsy [5]. The report described a male, 38 years old, who experienced up to 200 'sleep attacks' per day and strange episodes of sleep or muscle atonia triggered by strong emotion, typically laughter or telling a joke. In his report, Gélineau describes his patient collapsing at the zoo while observing monkeys making faces [5]. It was not until research conducted by French-American physician Emmanuel Mignot and his colleagues discovered the genetic and immunological basis associated with narcolepsy [6].

In persons with narcolepsy, low levels of the neuropeptide orexin (also known as hypocretin) are observed in cerebrospinal fluid (CSF), as well as a selective loss of hypocretin-producing neurons in the lateral hypothalamus[7-9]. The loss of this neuropeptide was found to disrupt frontal, limbic, diencephalic and brainstem networks [10,11], resulting in instability between sleep and wakefulness and the loss of boundary control between the two states, where sleep intrudes into wakefulness and vice versa[12,13]. The loss of orexin in narcolepsy is considered to be primarily the result of an autoimmune-mediated loss of hypothalamic neurons, environmentally triggered, and strongly associated with the immune gene Human Leukocyte Antigen (HLA)-DQB1*06:02 [6]. Cases of secondary narcolepsy have also been reported in persons who have sustained a traumatic brain injury or other hypothalamic injury/lesion [14 15].

As our knowledge of sleep expanded and ways to measure sleep increased (i.e. polysomnography (PSG)), other inappropriate REM manifestations were also thought to be associated with narcolepsy, including sleep paralysis and hypnagogic and hypnopompic hallucinations [13].

The classic clinical presentation of narcolepsy is known as narcolepsy type 1 (NT1) [3]. At the start of the 21st century, narcolepsy also began to include cases of excessive daytime sleepiness that did not experience cataplexy and who mostly do not have hypocretin deficiency. This presentation is known as narcolepsy type 2 (NT2) per the International Classification of Sleep Disorders (3rd edition) [3].

1.2.2 – Symptoms

Five symptoms have become increasingly associated with narcolepsy over the last 20 to 30 years and are often labelled the narcolepsy pentad of symptoms. These include excessive daytime sleepiness (EDS), cataplexy, sleep paralysis, hypnagogic hallucinations and disrupted nighttime sleep [13]. People with narcolepsy also experience difficulty with cognition, concentrating and fatigue [16-18].

1.2.2.1 – Excessive daytime sleepiness (EDS)

EDS is often the most noticeable and impactful symptom associated with narcolepsy [13]. EDS is not specific to narcolepsy and presents in other sleep disorders, including obstructive sleep apnea, insomnia and idiopathic hypersomnia, general sleep deprivation and psychological disorders (e.g. depression) [3,19]. As such, EDS often describes a broad range of clinical presentations associated with sleepiness. Specific to narcolepsy, EDS describes several phenomena, including an inability to stay awake, an overwhelming feeling of needing to sleep, sleep attacks, involuntary napping, and sudden transitions into sleep that can occur in monotonous situations or the middle of a task [13]. It remains unclear whether persons with narcolepsy (PwN) perceive these terms as associated with their experience of symptoms or whether these terms are specific to certain constructs of sleepiness. Our ability to measure EDS also appears to lack specificity. Subjective measures of sleep propensity (i.e. Epworth Sleepiness Scale (ESS)) seem to lack concordance with objective measures of sleepiness (i.e. maintenance of wakefulness test (MWT) and the multiple sleep latency test (MSLT) ([20,21]).

1.2.2.2 – Cataplexy

Cataplexy is the only symptom considered specific to narcolepsy. It refers to intruding REM-associated muscle atonia into wakefulness, typically in response to a positive emotional stimulus [13]. While this emotion is usually positive, there have been reports that other emotions, such as anger/surprise, can trigger cataplexy attacks. This symptom may relate to the loss of orexin and the neurotransmitter's role in the brain's reward pathways, perhaps explaining why it usually occurs in response to laughter or making a witty comment [22]. Episodes of cataplexy (referred to as a 'cataplexy attack') can present as a full attack (i.e. sudden whole-body paralysis, consciousness is

maintained lasting < 2 minutes) or as a partial attack (i.e. sudden, brief loss of muscle tone in the legs or neck often described as a 'droop'). Identification of cataplexy is often made by self-report, with measurement of symptom frequency and severity collected using a daily diary. Several cataplexy mimicries are often mistaken for cataplexy, including syncope, epilepsy, hyperekplexia, drop attacks and pseudo-cataplexy [23]. These can be differentiated from cataplexy using thorough history-taking and at-home video recordings. Cataplexy may also present differently in children (i.e. protrusion of the tongue) that later normalizes into muscle weakness seen in adults [6,19,24]. This difference in presentation can often complicate the recognition of the symptom and prevent early diagnosis.

1.2.2.3 – Sleep Paralysis and hypnagogic/hypnopompic hallucinations

Sleep paralysis is a dissociated state where wakeful consciousness co-occurs with REM muscle atonia. It occurs during sleep onset or offset and can last for seconds or several minutes.

Hypnagogic and hypnopompic hallucinations are vivid hallucinations that occur during periods of transition between REM sleep and wakefulness. Hypnagogic hallucinations occur when falling asleep, while hypnopompic hallucinations occur while waking up. These hallucinations are usually vivid visual, auditory, tactile, or kinetic perceptions and estimated to occur in 40 – 80% of persons with narcolepsy type 1 [25].

It is important to note that neither sleep paralysis, hypnagogic or hypnopompic hallucinations are specific for narcolepsy type 1 or 2, occurring in the general population with relative frequency[26,27].

1.2.2.4 – Disrupted Night-time sleep

Disrupted nighttime sleep refers to the fragmented sleep and multiple awakenings observed in narcolepsy. Studies using 24-72hr EEG have shown that persons with narcolepsy type 1 have similar amounts (duration) of sleep over a 24-hour period. However, over these 24 hours, sleep and wake

times are fragmented with rapid transitions and intrusions of REM sleep during the day and night [6,28].

1.2.2.5 – Other symptoms, including those resulting from the lack of orexin

As a loss of orexin characterizes narcolepsy type 1, it stands to reason that those with type 1 experience disruption to systems orexin plays a role. Orexin loss has been implicated in includes reward-related pathways, cognition, temperature regulation, vigilance, feeding/eating regulation and psychological disorders (e.g. major depressive disorder, anxiety and stress) [29]. However, it is rare for clinical management of narcolepsy to consider nor manage symptoms outside the narcolepsy pentad [30].

1.2.3 – Types of narcolepsy and diagnosis

Narcolepsy onset typically occurs in adolescence, with earlier and later cases observed [31]. There is a substantial delay in getting a diagnosis, with a mean delay of up to 15 years from symptom onset, with some individual cases upwards of 60 years [32]. Healthcare professionals' lack of symptom recognition is often the main contributing factor to this delay [32,33].

1.2.3.1 – Background

Diagnostic criteria for narcolepsy have changed several times over the last 20 years to reflect increases in our knowledge of the disorder. The International Classification of Sleep Disorders (ICSD-1) is among the earliest criteria, published in 2005. ICSD-1 listed the diagnostic criteria for narcolepsy as present, associated with an irrepressible need to sleep, sudden muscle weakness, and recurrent daytime lapses into sleep occurring almost daily for three months. As our knowledge of sleep expanded, narcolepsy was found to be closely associated with the human leukocyte antigen (HLA) gene HLA DBQ1∗0602, with cataplexy seen to be a specific subtype of the disease. The second iteration (ICSD-2) described four subtypes of narcolepsy, narcolepsy cataplexy; narcolepsy without cataplexy; narcolepsy due to a medical condition; unspecified narcolepsy (REF). The third iteration (ICSD-3), published in 2014, is still used today (Table 1). Evidenced-based changes reflected our

increasing knowledge that narcolepsy with cataplexy resulted from low levels of the hypocretin/orexin protein in cerebrospinal fluid (CSF) that contributed to sleep-wake regulation[3,7,34]. Thus, low levels of hypocretin in CSF (<110 pg/ml) as an optional objective measure for the diagnosis of narcolepsy type 1 was included in the updated version. The ICSD-3 is the most recent version and classifies narcolepsy into two subtypes: Narcolepsy type 1 (NT1), otherwise known as narcolepsy with cataplexy, and narcolepsy type 2 (NT2), or narcolepsy without cataplexy.

The most recent version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR), published in 2022, contains similar diagnostic criteria for narcolepsy, bringing it into alignment with the ICSD-3. The DSM-5-TR classifies narcolepsy as either: Narcolepsy with cataplexy or hypocretin deficiency (type 1), Narcolepsy without cataplexy and normal hypocretin levels or hypocretin unmeasured (type 2), Narcolepsy with cataplexy or hypocretin deficiency due to a medical condition; and Narcolepsy without cataplexy and without hypocretin deficiency due to a medical condition [35].

Table 1: Current classification of hypersomnia using the international criteria of sleep disorders, 3rd edition [3]

Narcolepsy type 1 (NT1); narcolepsy with cataplexy	Narcolepsy type 2 (NT2); narcolepsy without cataplexy	Idiopathic hypersomnia (IH)
• Hypocretin-1 deficiency in cerebrospinal fluid (<110 pg/mL or less than 1/3 of normative values with the same standardised assay) **OR** • Mean latency of <8 mins on MSLT, two SOREMPs on MLST, or a SOREMP on the PSG coupled with at least one SOREMP on the MSLT **AND** • Clear cataplexy (defined as "more than one episode of generally brief [< 2 min], usually bilaterally symmetrical, sudden loss of muscle tone with retained consciousness")	• Cerebrospinal fluid hypocretin-1 levels, if measured, must not meet the narcolepsy type 1 criterion. **AND** • Mean latency < 8 min on MSLT and two SOREMPs (or one SOREMP on PSG and one or more on MSLT). **AND** • Cataplexy must be absent	• < 8 min on MSLT with fewer than two SOREMPs (including any SOREMP on the PSG from the preceding night), absence of cataplexy and hypocretin deficiency (if measured), and no other identifiable cause. • ≥ 660 min average daily sleep time

MSLT – Multiple Sleep Latency Test, PSG – Polysomnography, SOREMP – Sleep Onset Rapid Eye Movement Period

1.2.3.2 – Challenges with current diagnostic criteria

Narcolepsy type 1 is an autoimmune-mediated loss of hypocretin, a clear aetiology defined by a measurable reduction of hypocretin in CSF [7]. However, CSF hypocretin testing lacks a standardized, readily available assay and is invasive. Narcolepsy type 1 is considered a rare disease, with a prevalence estimated to be between 1-5/10000 [36] and distinguishing symptoms (i.e. cataplexy) that can aid in diagnosis. Recognising cataplexy can be difficult due to various cataplexy mimicries and a lack of objective measures.

In contrast, narcolepsy type 2 is far more heterogenous in its presentation and is often considered a diagnosis of exclusion [13]. Narcolepsy type 2 can be challenging to diagnose due to the non-specificity of symptoms (i.e. excessive daytime sleepiness present in other sleep disorders), absence of biomarkers and limited understanding of the pathophysiology underpinning this subtype. These challenges also likely explain why the prevalence of narcolepsy type 2 is largely unknown.

There are also limits to the current gold-standard diagnostic tools used for diagnosing narcolepsy. Diagnostic criteria such as short sleep latency and sleep-onset REM periods are not unique to narcolepsy, as observed in other disorders and healthy controls. There are also limitations with the gold standard objective diagnostic tool, the multiple sleep latency test (MSLT). While the MSLT has a high test-retest reliability for narcolepsy type 1, it is non-reproducible in persons with narcolepsy type 2[37]. Some experts have suggested this may have led to some being misdiagnosed as having narcolepsy type 2, contributing to an estimated prevalence above 0.16-0.32% [6].

Other studies have explored the link between the diagnostic protocol and the prevalence of narcolepsy type 2. European protocol for sleep studies utilises actigraphy to rule out sleep deprivation before ordering more tests for diagnosing disorders of central hypersomnolence [38]. In contrast, the US and other countries, including Australia[39], rely far more on patient history or sleep diaries. The prevalence of narcolepsy type 2 is minimal in Europe. However, in the US, diagnosis of

narcolepsy type 2 is far more frequent, with more than 2 – 3 times greater than narcolepsy type 1[40-42]. It suggests that some persons with narcolepsy type 2 may be misdiagnosed and instead have chronic sleep depression due to some other cause (e.g. mental health disorder, shiftwork) [43,44].

1.2.3.3 – Future changes to diagnostic criteria

There has been a recent push to amend the new version of the ICSD to reflect current knowledge of central disorders of hypersomnolence. A recent unsupervised cluster analysis of symptoms was conducted using data from a large European narcolepsy prospective database [45]. The study identified narcolepsy type 1 as a specific subgroup, while persons with narcolepsy type 2 and IH subgroups were divided over two subgroups that differed on clinical variables including quality of awakening, presence of sleep drunkenness and refreshed daytime sleep [45]. As such, leading European narcolepsy experts including Claudio L.A Bassetti, Guiseppe Plazzi and Yves Dauvilliers amongst others have proposed a reappraisal of the diagnostic criteria for central disorders of hypersomnolence[46]. The proposal separates the current criteria of Narcolepsy Type 1, Narcolepsy Type 2 and Idiopathic Hypersomnia into three diagnostic classifications: Narcolepsy, Idiopathic hypersomnia and Idiopathic Excessive Sleepiness (Table 2). The approach aligns with commentary made by Emmanual Mignot, who highlights the distinction between Narcolepsy Type 1 and Type 2 [6].

Table 2: Diagnostic criteria for narcolepsy, idiopathic hypersomnia, and idiopathic excessive sleepiness (Replicated from Lammers et al., 2020[46] under Creative Commons Licence CC BY 4.0.)

<table>
<tr><th rowspan="2">Level</th><th colspan="3">Diagnosis</th></tr>
<tr><th>Narcolepsy</th><th>Idiopathic Hypersomnia</th><th>Idiopathic excessive sleepiness</th></tr>
<tr><td rowspan="2">Level 1 – definite</td><td>A. EDS and/or typical cataplexy and orexin deficiency (CSF)</td><td rowspan="2">A. ENS (acquired)
B. Objective evidence for increased sleep using PSG and actigraphy**</td><td rowspan="2">A. EDS
B. MSLT: msl < 8 min##</td></tr>
<tr><td>B. EDS and typical cataplexy and MSLT with msl < 8 min and > 1 SOREMP*</td></tr>
<tr><td rowspan="4">Level 2 – probable</td><td>A. EDS and typical cataplexy and MSLT with either msl < 8 min or > 1 SOREMP</td><td rowspan="4">A. ENS (acquired)
B. Objective support*** for increased sleep using PSG and actigraphy</td><td>A. EDS
B. MSLT: msl > 8 min and < 12 min##</td></tr>
<tr><td rowspan="3">B. EDS (without typical cataplexy) but with HH and/ or SP and/or disturbed nocturnal sleep and MSLT with either msl < 5 min and > 1 SOREMP or msl < 8 min and > 2 SOREMP and HLA-DQB1*0602 positive</td><td>Subtype R (REM type):
MSLT/PSG: ≥ 1 SOREMP
SART: normal or abnormal</td></tr>
<tr><td>Subtype N (NREM type):
MSLT/PSG: no SOREMP
SART: normal</td></tr>
<tr><td>Subtype A (Attention):
MSLT/PSG: no SOREMP
SART: abnormal</td></tr>
</table>

EDS, excessive daytime sleepiness; ENS, excessive need for sleep; CSF, cerebrospinal fluid; MSLT, multiple sleep latency test; msl, mean sleep latency; SOREMP, sleep onset REM period; PSG, polysomnography; SART, sustained attention to response task. *Including nocturnal sleep. #Other causes for EDS need to be excluded. **Two weeks of actigraphy and 32 h polysomnography supporting at least 9 h nocturnal sleep or 10h sleep over the 24 h of the day. ***Similar to ** but with 24 h polysomnography or with results almost meeting the 9/10 h criterium. ##Diagnostic criteria for Narcolepsy or IH not fulfilled, and other causes for EDS need to be excluded

1.2.4 – Impact of Narcolepsy

Narcolepsy appears to have a substantial adverse impact on health-related quality of life (HRQoL), increased rates of healthcare resource utilization (e.g., increased hospitalization and emergency care), long-term disability and poor socioeconomic and psychosocial outcomes [47-51]. Most studies exploring the impact of narcolepsy have taken a 'burden of disease' approach rather than the impact of individual symptoms. While some studies have explored the impact of excessive daytime sleepiness in persons with narcolepsy, it is often unclear what specific symptoms or aspects of excessive daytime sleepiness are referred to (e.g. sleepiness, fatigue, automatic behaviors, sleep attacks etc.). Further, the mechanism in these studies is unknown as they rely upon label – outcome associations rather than exploring mediators. Little is known about the impact of narcolepsy on Australians, as our current understanding is based solely on studies conducted in the USA and Europe.

1.2.4.1 – Health-related stigma

Weiss and colleagues define health-related stigma as "a social process (experienced or anticipated) characterized by exclusion, rejection, blame or devaluation that results from experience, perception or reasonable anticipation of an adverse social judgment about a person or group" [52]. Adolescents with narcolepsy experience health-related stigma with similar frequency as HIV-positive persons [53]. However, the specific type of stigma (e.g. public, self, perceived, structural) experienced by persons with narcolepsy remains unknown, as is the impact on quality of life.

1.2.4.2 – Health-related quality of life (HRQoL)

A recent systematic analysis of the literature regarding health-related quality of life in narcolepsy found persons with narcolepsy experience substantially lower health-related quality of life when compared with general population norms across the US, UK, France and Norway [54]. Further, health-related quality of life was lower than others with chronic diseases such as multiple sclerosis, diabetes, hypertension, and epilepsy [54]. In particular, the domains of physical role limitation and

cognitive domains (social functioning and emotional role limitations) appeared to be most impacted by narcolepsy.

Persons with narcolepsy have a higher incidence of comorbid conditions, including obesity and other sleep disorders[55]. They also have higher rates of accidental injuries, burns and bone fractures than matched controls[55-57]. Narcolepsy is also associated with a 1.5-fold excess mortality relative to those without narcolepsy [58].

1.2.4.3 – Healthcare resource utilization

Several studies have characterised healthcare resource utilisation and associated costs in large populations of persons diagnosed with narcolepsy. These studies often do not distinguish between narcolepsy subtypes and instead, approach narcolepsy as a homogeneous disorder. Compared to healthy age-matched controls, persons with narcolepsy had an approximately two-fold higher annual rate of hospital inpatient admission, emergency department visits without admission, hospital outpatient visits, and other outpatient services and more than double the total number of specialist visits annually [48]. Other studies found similar Increases in healthcare utilisation and associated indirect and direct costs to both the individual and the healthcare system [41,49], with one study describing a health-related cost of €10,000 per year, for each person with narcolepsy [59].

1.2.4.4 – Disability

Limited studies have explored functional impairment in narcolepsy. In one study of persons with narcolepsy type 1, functional impairment and severe fatigue were found to be statistically related [16]. Severe fatigue was also highly prevalent in persons with narcolepsy with cataplexy, comparable to prevalence indicators in neuromuscular disorders such as facioscapulohumeral dystrophy, myotonic dystrophy and hereditary motor and sensory neuropathy type 1 [60] [16].

There is limited evidence exploring the cost of disability in persons with narcolepsy. Annual short-term disability costs were estimated to be 200% amongst employees with narcolepsy vs matched controls ($876 vs $292 USD, respectively; P <.0001)[48], with many estimated to be on long-term disability benefits[49,61].

1.2.4.5 – Socioeconomic impact

Narcolepsy is associated with higher unemployment, higher private insurance premiums (US-based healthcare), lower income from employment and found more likely to be single than matched controls [62]. There is also an increased risk for work-related or vehicular accidents [63,64]. Work productivity is also affected. Relative to matched controls of the general population, persons with narcolepsy report significantly higher costs related to work absenteeism ($7631 vs $12,839 USD, respectively; P <.001) and presenteeism ($4987 vs $7013 USD; P <.001)[49].

1.2.4.6 – Psychosocial impact

There is substantive evidence exploring the psychosocial impact of narcolepsy. There is a higher prevalence of depression, anxiety, suicidal ideation, and other psychological comorbidities in persons with narcolepsy [65-68]. Similarly, there is a higher prevalence of psychological comorbidities in adolescents with narcolepsy, who appear at higher risk for depression, anxiety, behavioural issues, social and emotional distress, and poor concentration and attention resulting in poor performance at school [69-71]. Narcolepsy can also impact personal relationships both directly (e.g. experiencing cataplexy during sex) and indirectly (e.g. EDS symptoms impacting equal distribution of chores in a relationship)[72].

A comparison of persons with epilepsy and narcolepsy type 1 found, in general, persons with narcolepsy type 1 were substantially more psychosocially impaired across domains, including reduced performance at work, poorer driving records, higher accident rates from smoking, greater problems in planning recreation, than those with epilepsy [73]. The increased psychosocial impairment appeared to stem from excessive daytime sleepiness between the diagnostic attacks, whereas persons with epilepsy are relatively alert between seizures [73].

1.2.5 – Management of narcolepsy

Current clinical guidelines for the management of narcolepsy focus almost entirely on the pharmacological management of symptoms [30,74]. Comparing the efficacy of various treatments is often difficult due to repeated changes to the diagnostic criteria of narcolepsy over the years. Many clinical trials exploring treatment efficacy in narcolepsy use a combination of persons with type 1 and type 2 narcolepsy. These studies often treat narcolepsy as a homogenous cohort, despite evidence suggesting differences between subtypes regarding symptom experience, physiology and treatment experience [3,74]. Treating narcolepsy subtypes as a single cohort can impact development and make recommending tailored treatment plans difficult. The most recent American Academy of Sleep Medicine guidelines for narcolepsy management is an example where evidenced-based treatment guidelines could not be made specifically for individual subtypes of narcolepsy[74].

1.2.5.1 – Current treatments for narcolepsy

Several types of pharmacotherapy are used to manage the various symptoms of narcolepsy, including wakefulness-promoting agents, antidepressants, and orexin replacement therapies. There is little difference in recommended pharmacological treatments for adult and pediatric narcolepsy [55,74]. These are summarised below, along with an assessment of the quality of the evidence supporting their use (i.e. efficacy studies) as rated by the American Academy of Sleep Medicine using the GRADE approach – (quality of evidence rated from Very Low/Low/Moderate/High) [74]:

- *Stimulant-based wakefulness promoters (Amphetamines and Methylphenidate)*

  Stimulant-based wakefulness promoters increase the availability of dopamine and norepinephrine in the central nervous system, thus improving wakefulness. This medication has been used as early as 1990 for persons with narcolepsy and is associated with several adverse side effects, including palpitations, weight loss and psychiatric disturbances. The American Academy of Sleep Medicine found that the quality of evidence supporting its use for treating excessive daytime sleepiness was very low [74].

- *Modafinil / Armodafinil*

  Both modafinil and armodafinil are wake-promoting medications that act via a different mechanism of action than stimulants. Armodafinil is the R- enantiomer of modafinil and is similarly used to treat excessive daytime sleepiness following large efficacy studies [75]. Modafinil has a lower potential for abuse and fewer side effects than stimulant-based wakefulness promoters [74]. However, armodafinil appears less efficacious than modafinil and is often recommended secondary to modafinil [74]. Both have also been found to have a higher risk of major congenital abnormalities for pregnancy and may reduce the effectiveness of contraception [76]. The American Academy of Sleep Medicine found that the evidence supporting Modafinil and Armodafinil for treating excessive daytime sleepiness was of moderate quality [74].

- *Pitolisant*

Pitolisant is a selective receptor antagonist, indirectly increasing histamine levels and is used to treat excessive daytime sleepiness and is purported to be efficacious for cataplexy. The American Academy of Sleep Medicine found that the quality of evidence supporting its use for treating excessive daytime sleepiness and cataplexy was moderate [74].

- *Solriamfetol*

Solriamfetol is a norepinephrine-dopamine reuptake inhibitor used to treat excessive daytime sleepiness. It has a rapid onset of action and a favorable safety profile [74]. The American Academy of Sleep Medicine found that the quality of evidence supporting its use for treating excessive daytime sleepiness was high [74].

- *Antidepressants*

Clinical consensus recommends the off-label use of antidepressants to treat cataplexy, including selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). However, there are numerous side effects associated with these treatment options, including SSRIs potentially being associated with an increased risk of suicidality in children, adolescents, and young adults with major depressive or other psychiatric disorders (REF) [77-79]. Antidepressants have been recommended as a second-line treatment for cataplexy. However, evidence supporting their effectiveness is limited. The American Academy of Sleep Medicine found insufficient and inconclusive evidence supporting its use for cataplexy [74]. Similarly, a Cochrane review of antidepressant use for narcolepsy found scarce evidence supporting the use of antidepressants to treat cataplexy [80].

- *Xyrem (sodium oxybate) and Xywav (low sodium oxybate version) and Lumryz*

Xyrem, Xywav and Lumryz are central nervous system depressants acting on the gamma-aminobutyric acid (GABA) system. Xyrem and Lumryz are sodium oxybate salts, whereas Xywav is a mixture of calcium, potassium, magnesium and sodium oxybate salts. Studies have shown that these medications decrease nocturnal awakenings, increase the amount of slow-wave sleep, and are used to treat cataplexy and excessive daytime sleepiness[74,81,82]. The American Academy of Sleep Medicine found that the quality of evidence supporting its use for treating excessive daytime sleepiness was moderate [74].

- *Cognitive behavioral therapy (CBT)*

Cognitive behavioural therapy is a psychological intervention modified for use in narcolepsy [83,84]. It is used to manage behaviours and develop cognitive strategies to minimise the impact of symptoms (e.g. having a daily nap schedule), and identify and modify dysfunctional patterns of thought that have a negative influence on emotion and well-being [85]. While cognitive behavioural therapy for narcolepsy does not result in a cessation of symptoms, studies have shown that it does have a positively impact perceived quality of life and is a useful adjunct to pharmacotherapy [84,86].

- *Lifestyle changes / other treatments*

L-carnitine, scheduled naps, and a low carbohydrate/ketogenic diet are non-pharmaceutical treatment options often used to manage narcolepsy. The American Academy of Sleep Medicine clinical guidelines reports insufficient evidence supporting the use of these interventions in the management of narcolepsy [74]. That said, scheduled napping and maintaining a sleep routine are effective and practical non-pharmacological approaches to managing narcolepsy[13,87]. Recent evidence also points to L-carnitine treatment being efficacious and tolerable for persons with narcolepsy type 1, perhaps offering a safer treatment alternative for pregnant women [88].

1.2.5.2 – Treatments in development

Several hypocretin/orexin agonist compounds at various development and testing stages mimic the action of hypocretin/orexin neuropeptides. Although not yet available, they have shown promising results in preclinical studies and early-phase clinical trials, potentially offering a more targeted treatment for narcolepsy type 1.

1.3 – The Australian Experience of Living with Narcolepsy

1.3.1 – Pathways to diagnosis

Pathway to diagnosis typically begins with complaints of daytime sleepiness and fatigue that impacts daily function (chapter 8). A visit to a general practitioner is the first port of call for persons with narcolepsy. However, general practitioners are trained to deal with more common health concerns (e.g. general fatigue, depression) and perhaps unsurprisingly, narcolepsy or other sleep disorders are rarely considered (chapter 8).

Navigating pathways to seek help and a diagnosis appear difficult (chapter 7 and 8) and often are unclear. Further, there are no sufficiently validated subjective outcome measures available to general practitioners to aid in diagnosis [75,89] (chapter 5). Narcolepsy is often attributed to be a disorder of excessive daytime sleepiness, which may explain the delay to diagnosis of up to 15 years[32,89].

Having a person-centric general practitioner that is willing to work with their patient is often key to obtaining a referral. Patients often have to challenge their practitioners opinion that their symptoms are related to more common health concerns (chapter 3, 7 and 8). Pathway to diagnosis involves a referral to a sleep and respiratory specialist, who may diagnose narcolepsy on history alone or by organising an overnight polysomnography study and a multiple sleep latency test, using the ICSD-3 criteria [39].

Diagnosis based on history is complicated considering the lack of validated subjective measurements and often unspecific symptoms associated with narcolepsy (i.e. excessive daytime sleepiness). It can also be difficult to distinguish cataplexy from pseudocataplexy [90,91] – a spectrum of somatic symptoms disorders (i.e. functional neurologic disorder)[35].

1.3.1 – Exploring the Impact and Management of Narcolepsy in Australia

There is limited research, published evidence or raw data exploring the impact or management of narcolepsy in Australia. In the early 2000s, Dorothy Bruck conducted studies exploring the impact of narcolepsy in Australia. These results highlight the impact of narcolepsy on psychological health, adjustment in salient role behaviours and vocational adjustment [92]. Bruck et al. (2001) found that a multidisciplinary team is necessary to manage narcolepsy. Notably, the study gives insight into some of the healthcare concerns persons with narcolepsy had in Australia as early as 2001:

"The overall health care needs of this group were not being well catered for, with the participants expressing dissatisfaction with the quality of care provided, access to information and treatments not meeting expectations. Hopefully, this finding will become dated as the practice of sleep medicine grows in Australia." [92]

Bruck (2001) gives further commentary on a possible cause, writing:

"It is also important that the typical location of sleep clinics within Departments of Respiratory Medicine in Australia does not mean that the expertise of specialists with knowledge of neurological sleep disorders is unavailable to those with narcolepsy."

Bruck and colleagues provided a unique insight into the healthcare needs of those with narcolepsy in Australia in 2001. However, the management of narcolepsy has progressed substantially. This includes a deepening of our knowledge around narcolepsy, development of the ICSD and DSM-5-TR diagnostic criteria, implementation of quality care standards around person-centred care, development of several efficacious treatments, the rise of digital information consumption, and creation of support services for a disability (i.e. NDIS). As such, it is unclear whether these findings will be applicable to narcolepsy management in 2023. However, they provide unique insight and a baseline to compare how management has changed in the last 20 years.

1.3.2 – Disparities in available treatments between other countries and Australia

There are several disparities in treatments available in Australia compared to similar countries [93] (table 2). International guidelines recommend modafinil, pitolisant, sodium oxalate, or Solriamfetol as first-line treatments for excessive daytime sleepiness in narcolepsy. Of those listed, only modafinil is registered for use and accessible in Australia. The Therapeutics Goods Administration (TGA) recommends Modafinil as a first-line treatment for excessive daytime sleepiness in narcolepsy. However, the Pharmaceutical Benefits Scheme (PBS) lists modafinil as a second-line treatment. In contrast, stimulant-based treatments (i.e. dexamphetamine) are listed as second-line by the TGA and first-line on the PBS, despite poor evidence and a less favorable side-effect profile than modafinil [74].

International guidelines recommend sodium oxybate and pitolisant as first-line treatments for cataplexy. In Australia, both treatments are inaccessible and not registered for use. The only medication available to manage cataplexy is the off-label use of antidepressants. As described, this approach does not appear to be best practice or evidenced-based (see 1.2.5.1). A similar approach to treating cataplexy with antidepressants also occurs in more vulnerable populations such as children, adolescents and young adults despite evidence suggesting an increased risk of suicidality [77-79]. Under the TGA Special Access Scheme B, individuals can still access sodium oxybate and pitolisant, even though these medications are not registered in Australia. However, this comes with a tremendous financial cost and is thus inaccessible for most Australians unless funding can be procured (i.e. for compassionate access through a local hospital formulary).

Table 3: Summary of treatments available for narcolepsy in Australia and their indicated uses.

Medication	TGA registration	PBS listing	AASM quality of evidence rating	Symptoms treated		
				Excessive Daytime Sleepiness	Cataplexy	Disrupted nocturnal sleepiness
Amphetamines	2nd line	1st line	Very low			
Modafinil / Armodafinil	1st line	2nd line	Moderate			
Pitolisant			Moderate			
Solriamfetol			High			
Antidepressants			N/A			
Sodium Oxybate			Moderate			

Green cells = Yes; Red cells = No, N/A means there was insufficient or inconclusive evidence available for AASM to make a judgement. AASM – American Academy of Sleep Medicine, TGA – Therapeutic Goods Administration, PBS – Pharmaceutical Benefits Scheme

1.3.3 – Disability/welfare support

There does not appear to be any formal recognition of narcolepsy as a disability in Australia. This approach is similar to the American Social Security system, which does not formally recognise narcolepsy as a disability yet considers narcolepsy as comparable in medical severity to epilepsy [94]. This contradiction likely stems from the heterogeneity of narcolepsy symptoms and perhaps reflects the lack of distinction between subtypes in healthcare policy.

Narcolepsy is not listed on The Department of Social Services List of Recognised Disabilities [95], nor on the National Disability Insurance Scheme (NDIS) list of conditions likely to result in permanent impairment [96]. These lists serve as a tool for fast-tracking eligibility when accessing support, and the absence of narcolepsy does not prevent individuals from accessing these supports. However, it does place an additional burden on the individual and their healthcare team to be aware of the existing services, eligibility, and how to access them.

Similarly, there appears to be very little information on workplace and school accommodations for persons with narcolepsy. Not only does this apply to persons with narcolepsy and their family and carers, but also employers who may be trying to navigate the space.

1.4 Person-Centred Healthcare

1.4.1 – Background – Models of care used in healthcare systems

1.4.1.1 – Paternalistic Healthcare

Paternalism has, for many years, been a defining characteristic of medicine. The belief underpinning this style of care is that physicians should make decisions about their patient's care, even if the patient can decide for themselves [97]. The underlying assumption is that the physician always knows what is best for the patient, more so than the patient [97,98]. There has been considerable pushback on this style of care over the last 50 years in democratic countries, as this model of care often receives harsh criticism due to the quality of the patient-physician relationship produced [99].

1.4.1.2 – Patient-Centred Healthcare

Patient-centred care is "respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions" [100]. It represented a marked shift in healthcare delivery in the 1990s, a departure from traditional paternalistic medicine towards shared decision-making with patients, their families, and carers [101]. The acknowledgement that the patient is the best judge of their welfare and the most accurate measure of the effectiveness of care underpins this healthcare model[102]. This model places the needs and values of an individual as the primary driving force behind all healthcare decisions, emphasising the need for active collaboration and shared decision-making between providers and patients, including their families and carers.

Epstein et al. (2010) describes several reasons why patient-centred care matters in modern healthcare systems [103,104]:

- The right thing to do: a patient-centred approach is morally right as it promotes patient autonomy and the ability for an individual to control their future. When healthcare providers include their patients in the decision-making process, patients feel an absence of abandonment by the system.

- Improved healthcare outcomes: research has shown that implementing a patient-centric approach increases self-reported quality of life (QoL), improves disease-related outcomes, enhances self-management, and promotes treatment adherence with no additional costs.
- Address disparities in healthcare: By collaborating with patients, there has been a reduction in the disparities in disease-specific treatment and prevention along racial, ethnic, and socioeconomic lines.
- Better value for dollar: when patient-centred care is employed, there is a noticeable increase in patient and physician satisfaction and an overall decrease in the number of diagnostic tests employed.

While a patient-centred approach is described as the ideal form of care, it is often not well-defined, misunderstood, or poorly implemented [105].

1.4.1.3 – Person Centred Healthcare

Throughout the 2000s, person-centred care has increased in popularity and is seen as an evolution of patient-centred care. Where patient-centred care tends to view the individual as a passive receiver of healthcare, person-centred care highlights the importance of knowing the individual behind the patient (i.e. someone with their own needs, wants, desires, and life goals). Knowing the individual is considered necessary to engage the person as an active partner in their care/treatment [105,106]. Person-centred care originated in aged care, with a growing emphasis on fostering relationships and developing care plans through collaboration between healthcare professionals and patients. The core principles of person-centred care also can be seen in dementia care, where the focus is on recognizing and acknowledging the individual as a whole rather than solely focusing on their illness.

While there is considerable overlap between patient-centred and person-centred care, they differ in the outcome sought for the individual. A recent systematic review of already synthesised literature

revealed that the goal of patient-centred care is a functional life for the patient, while the goal of person-centred care is a meaningful life. [107].

1.4.2 – How have Australian healthcare systems implemented person-centred care?

Both federal and state healthcare jurisdictions are committed to implementing person-centred healthcare models.

The Australian Commission on Safety and Quality in Healthcare (ACSQHC) defines person-centred care as foundational to safe, high-quality health care that respects and responds to patients' preferences, needs, and values. Both state and federal healthcare systems have committed to person-centred care and its implementation across the healthcare system using a combination of governance structures, policies, and standards that guide care delivery listed below:

- The ACSQHC developed the National Safety and Quality Health Service (NSQHS) Standards to provide a nationally consistent framework to ensure the provision of high-quality, safe healthcare. The current edition of the NSQHS standards places increased focus on person-centred care, emphasising the importance of engaging patients in shared decision-making, goal-setting, and communication.

- The Australian Health Practitioner Regulation Agency (AHPRA) and National Boards are responsible for registering and regulating healthcare professionals across Australia. It sets professional standards and codes of conduct that emphasise the importance of implementing person-centred care. For example, the Medical Board of Australia's "Good Medical Practice: A Code of Conduct for Doctors in Australia" highlights the need for doctors to treat patients with respect, dignity, and compassion. There does not appear to be a national board specific to sleep or sleep and respiratory medicine.

- In each state and territory, the health department is responsible for the planning, funding, and delivery of healthcare services within their jurisdiction. These departments implement person-centred care initiatives and policies that align with national standards and

frameworks necessary for accreditation through ACSQHC. Each state approaches this differently, with NSW producing guidance for the health department through 'Patient-Centred Care: Improving Quality and Safety through Partnerships with Patients and Consumers', while Victoria has created the 'Better Health Channel' to promote health information and services.

- The ACSQHC has also produced an Australian Charter of Healthcare Rights, which details the standard of care an individual should expect when accessing healthcare services across the country. The current version of the charter reflects an increased focus on person-centred care and consumer empowerment and the right to partnership, information and feedback.

- Various consumer engagement and advocacy organisations, such as the Consumers Health Forum of Australia (CHF) and the Health Issues Centre, promote consumer involvement in planning, designing, delivering, and evaluating healthcare services. Several patient advocacy groups and consumer groups represent the views of persons with narcolepsy living in Australia, including Narcolepsy Support Australia, Narcolepsy and Overwhelming Daytime Sleepiness Society, and the Sleep Health Foundation.

1.5 Frameworks used in this body of work

1.5.1 – Critical realist approach

This body of work uses a critical realist approach to explore the needs, concerns, and barriers to care for those living with narcolepsy in Australia. Critical realism suggests that reality consists of three domains: the ***empirical*** (i.e. trying to understand and analyse reality), the ***actual*** (i.e. that the world exists independently of our own thoughts) and the ***real*** (i.e. unseen causal influences or mechanisms precede and generate events) [108]. The ***real*** is the most important domain and drives us to consider the broader social, economic, political and government structures intersecting when exploring an outcome [109]. Thus, to explore why those with narcolepsy have particular needs, concerns and barriers to care, we need to move beyond the surface level of experiences and observable signs to understand what is happening underneath, at the ***real*** level, that is driving these outcomes[108,110].

1.5.2 – Conceptual Framework for Person-Centred Care

A conceptual framework is necessary to provide orientation when exploring a large entity like the healthcare system by assisting the researcher and reader to understand how any finding fits into the existing knowledgebase and how the different elements of the body of work align [111]. The conceptual framework Santana et al. (2019) created for implementing person-centred was selected for several reasons. First, it enabled consideration of person-centred care from the macro perspective, an essential component often overlooked, where end users/consumers should have a say in creating and revising health policy [112]. Second, it is the product of a narrative review of the background literature on person-centred care and featured co-design elements with healthcare consumers when identifying healthcare priorities [113]. Third, the framework is well established in the literature and used in similar studies exploring the intrinsic relationships between healthcare systems, healthcare providers and patients [113]. Lastly, it accounts for system fragmentation in the Australian healthcare system (i.e. fragmentation between state and federal healthcare).

The framework is summarised in Figure 1, and describes the necessary components for implementing person-centred care within a healthcare system. At the highest level, it identifies three domains needed for person-centred care: ***structure*** (i.e. how is person-centred care delivered through the healthcare system), ***process*** (i.e. how do healthcare providers themselves deliver person-centred care), and ***outcome*** (i.e. how do we capture that person-centred care is working). These three components do not exist in isolation but instead form a road map or tiered, pyramidal system where person-centred care can only be implemented if a solid foundation exists. Hence, embedding the principles of person-centred care within the organizational structure or context of care delivery becomes imperative. Without a strong base, the realisation of person-centred care within the patient-physician relationship is hindered, and accurately measuring the lived experience of navigating healthcare or meeting patients' needs becomes challenging [113].

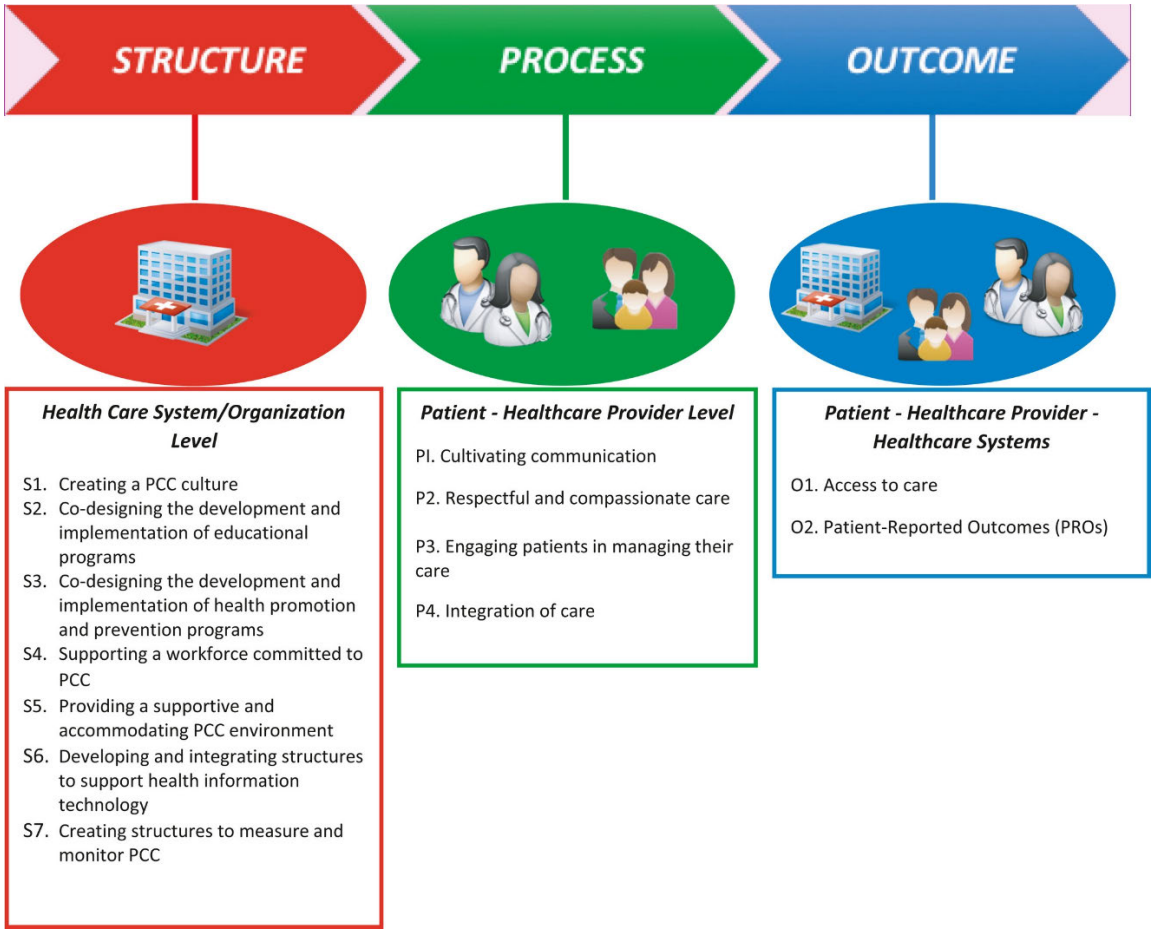

Figure 1: Person-centred care framework (Santana 2019)[113]

1.6 Summary

Narcolepsy carries a substantial burden of disease that affects health-related quality of life, psychosocial health, capacity to work, functional impairment and absenteeism, and health-related stigma. International research studies and sources inform our understanding of the daily impact and management of narcolepsy in Australia. However, these studies likely have diverse prevalence rates, treatment alternatives, and differences in social, welfare, and safety-net structures (e.g. NDIS, PBS) available in Australia. The divergence raises questions about whether the existing evidence base concerning the impact and management of narcolepsy is applicable in the context of the Australian healthcare system.

We also know very little about the healthcare needs and concerns of individuals with narcolepsy and their families and caregivers living in Australia. Our lack of knowledge results from a combination of factors: limited research, available funding, underappreciation of healthcare utilisation associated with narcolepsy and a lack of systematic data collection systems [114,115].

Our lack of knowledge inherently limits the Australian healthcare system's ability to meet the needs and expectations of persons with narcolepsy. Furthermore, it restricts our ability to formulate effective policy that considers different federal and state healthcare responsibilities, provision of supports and services and the increasing need for cross-department collaboration (i.e. health and NDIS). It is important to note that this issue is not specific to narcolepsy; it is true for the entire sleep field. There does not appear to be an effective policy for any aspect of sleep health in Australia, including other far more prevalent sleep disorders (i.e. obstructive sleep apnea, Insomnia).

Both federal and state healthcare systems in Australia are committed to a person-centred approach to healthcare policy and practice. However, there is limited knowledge of how this approach is applied specifically to narcolepsy management and care.

To do so, we must first explore the needs, concerns, and barriers to care for those with narcolepsy and their family and carers' experience. Considering that all levels of the healthcare system in

Australia are committed to implementing person-centred care, it is also important to understand how the healthcare system assesses the needs and concerns of persons with narcolepsy and includes these groups in the decision-making process around healthcare provision. This forms the premise for this body of work.

1.7 Research Questions

There are three questions that this body of work considers:

- What are the needs, concerns, and barriers to care experienced by persons living with narcolepsy and their families and carers in Australia?
- What do persons with narcolepsy and their families and carers perceive well-managed narcolepsy to be?
- How person-centric is the Australian healthcare system, using narcolepsy as an example?

1.8 Definitions

Below are several definitions to aid with understanding the aims of this project.

Barriers to care: The underlying causes or reasons preventing patients from obtaining appropriate healthcare when they need it

Health/healthcare need: we used the Wright et al. (1998) definition of a health need, which *"incorporate the wider social and environmental determinants of health, such as deprivation, housing, diet, education, employment. This wider definition allows us to look beyond the confines of the medical model based on health services to the wider influences on health. The health needs of a population will be constantly changing, and many will not be amenable to medical intervention.*" [116].

Health/healthcare concerns: a health-related matter that provokes interest, importance or worry to an individual, their family/carer or healthcare provider.

Policymakers: a government employee who is involved in the creation, modification, or development of healthcare policy. A policymaker does not necessarily refer to a politician.

Chapter 2: Insight into healthcare policy development Parliamentary Inquiry into Sleep Health Awareness in Australia 2018

In 2018, the federal government established The Parliamentary Inquiry into Sleep Health Awareness in Australia. These inquiries are formal investigations conducted by parliamentary committees comprised of sitting members of parliament. The select committee gathers information around specific issues defined by a 'term of reference', often related to government legislation and administration[117]. In the case of the Sleep Health Awareness in Australia inquiry, the inquiry invited individuals (e.g. private citizens, healthcare professionals) and other stakeholder groups (e.g. for-profit organisations, not-for-profit organisations, peak bodies) to make written submissions in response to the following terms of reference[118]:

1. The potential and known causes, impacts and costs (economic and social) of inadequate sleep and sleep disorders on the community;
2. Access to, support and treatment available for individuals experiencing inadequate sleep and sleep disorders, including those who are children and adolescents, from culturally and linguistically diverse backgrounds, living in rural, regional and remote areas, Aboriginal and Torres Strait Islander;
3. Education, training and professional development available to healthcare workers in the diagnosis, treatment and management of individuals experiencing inadequate sleep and sleep disorders;
4. Workplace awareness, practices and assistance available to those who may be impacted by inadequate sleep or sleep disorders, with a focus on: rostering practices for shift workers, heavy-work requirements, and the transport industry as compared to international best practice; and
5. Current national research and investment into sleep health and sleeping disorders.

The inquiry received many written responses to the terms of reference from non-consumers (e.g. healthcare professionals and not-for-profit organisations) and consumers. Most of the submissions written by persons with a sleep disorder or their family/carers were about narcolepsy, specifically access to treatment, management and impact on day-to-day life[119]. The final report made several policy recommendations to address some of these concerns.

Submissions written to the parliamentary inquiry, final report, and recommendations are part of the public domain. The inquiry process provided a unique opportunity to explore the lived experience of a health condition. Individuals were free to write about any issue, voicing their most pressing concerns about their sleep disorder. Therefore, the inquiry format presented an opportunity to explore how policymakers balance stakeholders' views and translate the needs and concerns of those making submissions. To do this, we thematically analysed submissions written by persons with narcolepsy and their families and carers, identified their main concerns and compared these to the final recommendations for policy change made by the inquiry.

Chapter 3: How patient-centric is health policy development? The Case of the Parliamentary Inquiry into Sleep Health Awareness in Australia

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How patient centric is health policy development? The case of the Parliamentary Inquiry into Sleep Health Awareness in Australia

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ABSTRACT

Objective. Parliamentary inquiries into health-related issues empower everyday Australians to contribute to the development and reform of health policy. We explored how patient and family/carers concerns are translated by this process, using a less well-known disease, narcolepsy, as an example. **Methods.** Written submissions made to the Parliamentary Inquiry into Sleep Health Awareness in Australia 2018 by self-identified patients or family/carers with narcolepsy (n = 13) were extracted and thematically analysed using the Framework Approach. Each submission was systematically coded and abstracted into emergent themes before being evaluated against the final policy recommendations. **Results.** Although patients and their family/carers prioritised issues that affected their daily lives (i.e. mental health sequela, workplace accommodations), the policy recommendations in the report focused mainly on issues of healthcare infrastructure, funding and engagement. Our analysis highlighted several barriers that patients and their family/carers face when contributing to this part of healthcare policy formation. **Conclusions.** Our findings suggest that the parliamentary inquiry process in its current form is not an ideal vehicle by which patients and family/carers can contribute or influence healthcare policy. Despite calling for submissions from patients and their family/carers, the final report and subsequent health policy recommendations made by the inquiry do not appear to be patient-centric or reflective of the submissions written by these stakeholders. Increased transparency, development of processes to balance stakeholder priorities and improved accessibility for stakeholders to participate are needed if health-related parliamentary inquiries are to produce healthcare policy that ultimately meets the needs of patients and family/carers.

Keywords: family and carers, healthcare, health policy, narcolepsy, parliamentary inquiry, patient centred, sleep health awareness, stakeholder engagement.

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Introduction

Policymakers rely on key stakeholder groups (i.e. patients/carers, healthcare professionals, professional organisations) to deliver effective, transparent and trusted healthcare and research policy.[1,2] Balancing the diverse and sometimes divergent priorities of stakeholders can be challenging (i.e. for-profit entities vs patients). Established processes are needed to ensure stakeholders that are more financially powerful, highly vocal, or intellectually conflicted stakeholders do not dominate the policy development process.[3] Seeking diverse opinions between stakeholder groups and within these groups is also important to ensure healthcare policy is both equitable and inclusive. It is widely accepted that participation should be encouraged, with processes needed that facilitate participation from vulnerable groups (e.g. culturally sensitive communication materials), as well as increasing transparency around engagement and policy development process.[3,4]

In Australia, governments employ a form of stakeholder engagement known as parliamentary inquiries. These are used to seek citizen views of policy, government procedure or performance in health, aged care and education, among others.[5] Individuals, organisations, patient advocacy and special interest groups are all given the opportunity to contribute. These inquiries represent one of the few platforms accessible to patients and their families and carers to contribute to health policy development. Each inquiry is limited in scope, where stakeholders are invited to share their perspectives and submit written responses to the terms of reference set forth by the inquiry.[6] Public hearings are also held by the inquiry, with select stakeholders invited to discuss concerns raised in written statements and to answer questions posed by parliamentary members who run the inquiry. On completion, the Committee's findings are summarised in a final report and submitted to parliament, typically recommending government intervention (i.e. introduction of legislature, change of administration processes). Response from the government is required within 6 months of submission, detailing which recommendations will be enacted.[5]

In 2018, the Federal Minister for Health, Aged Care and Sports directed the Standing Committee on Health, Aged Care and Sport to hold a parliamentary inquiry into sleep health awareness in Australia. This was in response to lobbying and advocacy work of peak sleep health professional bodies and support groups (i.e. Sleep Health Foundation and Australasian Sleep Association).[7]

The inquiry terms of reference invited interested individuals and organisations to respond to issues outlined below:

1. The potential and known causes, impacts and costs (economic and social) of inadequate sleep and sleep disorders on the community;
2. Access to, support and treatment available for individuals experiencing inadequate sleep and sleep disorders;
3. Education, training and professional development available to healthcare workers in the diagnosis, treatment and management of individuals experiencing inadequate sleep and sleep disorders;
4. Workplace awareness, practices and assistance available to those who may be impacted by inadequate sleep or sleep disorders;
5. Current national research and investment into sleep health and sleeping disorders.

The final report entitled 'Bedtime Reading' is publicly accessible and has been submitted to parliament for acceptance. However, the final report does not inform the reader how submissions made to the inquiry were prioritised, disregarded, or even considered (be they from patients, family/carers or organisations), nor if they influenced the final reports findings and subsequent policy recommendations.[8] Therefore, the purpose of this paper is to: (1) compare the patients' and family/carers' submissions against the final report and recommendations made by the inquiry; and (2) evaluate to what extent they appear to have been considered and incorporated into this influential health policy process.

We examined this through the lens of narcolepsy, a chronic and rare sleep disorder estimated to affect 1 in every 2000–5000 individuals, usually managed in the community. Little is known of how the condition affects patients and carers in Australia, as routine healthcare data better captures common conditions that incur hospitalisations.[9,10] The disorder arises in childhood or adolescence and affects the brain's ability to stay awake or asleep, causing the individual never to feel rested, fall asleep without warning and have trouble staying asleep at night.[11] Other symptoms include vivid dreams and paralysis brought on by strong emotions such as laughter.[11] Narcolepsy was chosen as it is characterised by a lack of public awareness, with a mean diagnostic delay of 15 years, along with substantial personal and economic burdens.[12–14] Further, as a rare disease, we wanted to examine how the concerns of a relatively small patient population are translated into policy.

Method

Data extraction

All 131 written submissions received by the inquiry are part of the public domain and were downloaded from the inquiry website.[15] Each submission was read by two authors (AS and JC) and included if the writer identified themselves as someone with narcolepsy or written by a family member or carer of someone with narcolepsy.

Analysis

Patient and family/carer submissions were thematically analysed using the Framework Approach (see Supplementary File S1), an applied social policy research framework that results in a thematic framework.[16–18] This approach is a five-step process involving:

1. Familiarisation of the data
2. Identifying a thematic framework
3. Indexing
4. Charting
5. Mapping and interpretation

Relevant submissions were first read iteratively by two authors (AS and JC) to become familiar with emerging ideas and concepts raised. A thematic framework was subsequently developed from integrating the *a priori* terms of reference with emerging concepts from patient/family/carer submissions. Individual submissions were then indexed against the thematic framework and subsequently organised into thematic matrices to map out cross-case and within-case descriptions of the phenomena of interest to identify

emergent themes. A subset of submissions was selected to undergo cross-checking to ensure the reliability of the thematic categories identified for inter-coder reliability ($\kappa = 0.72$, averaged from three coding nodes by authors AS and MA). Any disagreement with the assignment of codes or thematic categories were discussed and resolved with the research team.

Emergent themes that resulted from our analysis were compared against the policy recommendations contained in the final report, 'Bedtime Reading', which was submitted to parliament by the inquiry.[8,19] All analyses were carried out using NVivo (version 12, QSR International).

Ethics approval

Ethics approval for the study was granted by the University of Sydney Human Research Ethics Committee (2019/663).

Results

The inquiry received a total of 131 submissions, of which 67 (51%) were written by organisations, 56 (43%) by individuals, 7 (5%) classified as confidential by the government and redacted and 1 (1%) written by the Department of Health providing information requested by the inquiry. Of the 56 written by individuals, 20 (36%) were written by members of the public regarding issues such as environmental factors on sleep (i.e. wind turbines, electromagnetic radiation), 17 (30%) by self-identified healthcare professionals, 17 (30%) by self-identified patients or family/carers with a sleep disorder and 2 (4%) by self-identified researchers. Of these 17 written by self-identified patients or family/carers, 13 (76%) were specific to narcolepsy, which formed the data for this study, 2 (12%) related to obstructive sleep apnoea and 1 (6%) each related to restless leg syndrome and non-24-h sleep-wake disorder.

The submissions made by patient and family/carers with narcolepsy accounted for 10% of the total submissions received. Our analysis identified nine thematic categories, which were abstracted into three overarching themes: 1) pathways to treatment and care; 2) help-seeking experiences; and 3) patients' and family/carers' lived experience of disease. These, along with illustrative quotes, are contained in Table 1.

Theme 1: pathways to treatment and care

This overarching theme encompassed patient and family/carer concerns around lack of health care and research resource allocation for narcolepsy. Submissions received identified barriers in accessing newer treatment options that are available overseas, but not widely accessible in Australia, and a lack of sleep diagnostic infrastructure (i.e. sleep laboratories, polysomnography equipment), particularly in rural and regional areas. This lack of infrastructure was purportedly worse in Tasmania and South Australia, which caused long wait times and, in some cases ($n = 2$), required interstate travel to receive adequate care. A lack of narcolepsy research conducted within Australia was also identified by patients and family/carers as a concern, with the belief that 'what gets measured, gets managed', leading to oversight of patient and family/carer priorities.

Theme 2: help-seeking experiences

Barriers to help-seeking and accessing care were also frequently described in patient and family/carer submissions. Many perceived that primary and secondary/tertiary healthcare workers lacked knowledge of narcolepsy, which led to them receiving suboptimal care. Areas lacking included symptom recognition, treatment options and management strategies. Several patient and family/carer submissions also highlighted the importance of the therapeutic alliance in narcolepsy; those who had established rapport with their doctor experienced a positive impact on disease trajectory, namely a shorter delay in achieving a diagnosis. Online patient support groups were identified as an important resource for both information and support, particularly during the early phases of the help-seeking process. However, a lack of funding for support groups, specifically around programs associated with building community awareness and overhead costs were identified as a cause for concern.

Theme 3: patients' and family/carers' lived experience of disease

The patients' and family/carers' lived experience of disease theme related to the tangible effects that narcolepsy has on the daily lives of patient and family/carers. Of greatest concern was the sequelae of narcolepsy, in particular mental health concerns (i.e. anxiety, depression, isolation) and psychosocial adversity (i.e. unemployment). This was not just experienced by patients, but also by family members and carers who described dealing with feelings of grief and loss. Another concern that was identified related to difficulties accessing support/welfare services such as Centrelink (i.e. disability support pension) or the National Disability Insurance Scheme (NDIS), as well as limited support offered by workplaces and education institutions for those with narcolepsy to continue their employment and education. Several submissions detailed concerns related to current treatment options, the health impacts associated with long-term use of medications, and the potential for a build-up of tolerance associated with those medications.

When we compared the policy recommendations made by the inquiry to the results of our thematic analysis, four of the nine thematic categories identified by patients were specifically addressed by the report, with two specifically addressed, whereas the other two were only partially addressed[8] (Table 1). These related to the structural and

Table 1. Alignment between the 11 policy recommendations made by the Parliamentary Inquiry into Sleep Health Awareness in Australia 2018 and thematic categories identified using qualitative framework analysis of patients' and family/carers' submissions related to narcolepsy.

Theme 1: pathways to treatment and care				
Sub-theme	**Summary of synthesis**	**Illustrative quotations**	**Policy recommendations**	**Appraisal of recommendations**
Access to newer medications to treat narcolepsy that are available overseas	• Most submissions mentioned the lack of access to newer medications, particularly sodium oxybate. • Participants who described the positive effects of these medications on quality-of-life contrasted it with current/previous treatments. • Regulatory approval and cost of medication identified as main barriers.	• 'The other problem we face with effective treatment is that drugs that are readily available in either the USA or Europe are not quite so readily available here, and if they are, the price is prohibitive for many families.' (Submission 42) • 'Since commencing Xyrem my son has been able to return to full time study and obtain his learners permit and is far more functional than he was on his previous treatments.' (Submission 90)	Recommendation 7: The Committee recommends that if there is no distributor willing to put forward a submission, the Australian Government work with patient advocacy groups such as Narcolepsy Australia or the Sleep Health Foundation to make a submission for the listing or registration of Sodium Oxybate under the Orphan Drug Program.	Recommendation specifically addresses patient and family/carer concerns regarding access to new medications that are not accessible in Australia.
Access to diagnostic healthcare services	• Public patient access to diagnostic sleep studies (polysomnography) varies significantly state-by-state. • Rural access to sleep laboratories is limited, requiring lengthy travel to more urban centres, with significant travel being difficult for someone with narcolepsy. • Perception that the lack of services contributed to lower quality-of-life.	• 'Not all Sleep centres are equipped to test or treat patients with narcolepsy. Instead, I must make an annual trip to Newcastle (2 h drive) to visit my Sleep Specialist for a 12 h maintaining wakefulness and latency test (to keep my drivers license).' (Submission 116) • 'Being in Tasmania offers us little in the way of support groups, medical facilities designed to better understand this condition and treatment options. Yes, it is our choice to live here, but we also shouldn't be penalised because of that choice.' (Submission 42)	Recommendation 4: The Committee recommends that the Department of Health undertake a review of the Medicare Benefits Schedule as it relates to sleep health services in Australia. The review should include, but not be limited to, the following: • Simple diagnostic sleep studies (Level 3 and Level 4) that do not currently attract Medicare rebates. • Ensuring recent changes to enable general practitioners to directly refer patients to diagnostic sleep studies are effective. • Barriers to accessing cognitive behavioural therapy for insomnia via telehealth for patients in regional, rural, and remote areas.	Although the recommendation calls for a review of funding and referral of diagnostic sleep studies, it does not address concerns around inadequate infrastructure (sleep laboratories, equipment needed), and barriers that individuals in rural, regional locations, or in South Australia and Tasmania face.

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Table 1. (*Continued*)

Theme 1: pathways to treatment and care				
Sub-theme	**Summary of synthesis**	**Illustrative quotations**	**Policy recommendations**	**Appraisal of recommendations**
Limited narcolepsy research in Australia	• Participants identified a lack of research into narcolepsy, highlighting that prevalence has not been studied in Australia. • Perception that more research into the disease will lead to a reduction in delay of diagnosis, better treatment options and improved quality-of-life.	• 'To date there has been no study done in Australia to pin-point the actual number of people suffering sleep disorders… Narcolepsy in particular! So far all the information I've read has been based on the statistics provided in the USA.' (Submission 116) • 'Whilst we are fully aware that at this point there is no cure for Narcolepsy, better treatment options should be researched, trying to get that blood/brain barrier crossed to be able to replace the lost orexins, or if gene/stem cell replacement may help.' (Submission 42) • 'Research into the effects of disturbed sleep and how to better manage systems of work to avoid sleep disturbance – or better manage the impacts of sleep disturbance – is essential.' (Submission 67)	Recommendation 11: The Committee recommends that the Australian Government fund research focused on: • The prevalence of sleep disorders, with a particular focus on under-researched population groups such as women and Aboriginal and Torres Strait Islander peoples; • The prevalence, causes, and mechanisms of rare or not well understood sleep disorders, including narcolepsy and idiopathic hypersomnia; • Further analysis of existing population health and longitudinal studies that have collected data relating to sleep. • The impact of long-term shift work on sleep health and potential measures to minimise the associated health risks; and • The effects of digital devices and electronic media on sleep health, especially among children and adolescents.	Recommendation specifically addresses patient concerns around lack of research of narcolepsy, particularly in under-researched populations (i.e. Aboriginal and Torres Strait Islander peoples).

(*Continued on next page*)

Table 1. (*Continued*)

Theme 2: help-seeking experiences				
Sub-theme	**Summary of synthesis**	**Illustrative quotations**	**Policy recommendations**	**Appraisal of recommendations**
Perceived knowledge of narcolepsy in healthcare workers	• Perception that sleep specialists and primary healthcare workers lacked knowledge of narcolepsy, its symptoms and treatments. • Participants felt the lack of recognition of narcolepsy contributed to delay in diagnosis and/or misdiagnosis. • Some participants suggest that a good relationship with their GP had a positive impact on disease trajectory, namely shorter delay to diagnosis.	• 'There is a lack of knowledge and understanding among health professionals, that there is a difference between narcolepsy and cataplexy, what the differences are and as such that they may require different treatment and management.' (Submission 86) • 'Public money had been spent on proving what I don't have. I believe that if general practitioners were more aware of sleep disorders, then less money would be wasted on needless health checks.' (Submission 99) • 'It took many years for my diagnosis, and it certainly wasn't due to a lack of trying, it was a lack of information and knowledge that caused the delay.' (Submission 10) • 'We were lucky that we had an amazing GP who believed in what we said and was prepared to stick his neck out for us.' (Submission 42) • 'My local GP was fabulous in my treatment and organised counselling amongst other small things to help me feel better.' (Submission 116)	Recommendation 10: The Committee recommends that the Australian Government investigate options to separate the existing 'Respiratory and Sleep Medicine' speciality into independent 'Respiratory' and 'Sleep Medicine' specialities under the Australian Health Practitioners Regulation Agency framework.	Recommendation address concerns raised by patients, as an independent sleep speciality would allow for an increased focus on sleep disorders.This approach was also supported by physicians who took part in the inquiry.
The role of support/advocacy groups	• Participants felt online support/advocacy groups were knowledgeable and informative and supportive, helping some come to terms with the condition. • Lack of adequate funding for support groups identified as a concern.	• 'I have found my best support in Facebook groups (such as Narcolepsy Aust, Xyrem support). I still find family, friends, educators, GPs don't fully understand the condition and don't know how to support us best.' (Submission 26) • 'Organisations like Narcolepsy Support Australia have been a major support for us, but like any little not-for-profit organisations, lack the funds to be able to do so much more. Funding should be directed towards these types of things so that that on a professional and community level people are much more aware.' (Submission 42)	No policy recommendations made addressing these concerns.	

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Table 1. (*Continued*)

Theme 3: patients' and family/carers' lived experience of disease				
Sub-theme	**Summary of synthesis**	**Illustrative quotations**	**Policy recommendations**	**Appraisal of recommendations**
Sequelae of narcolepsy	• Participants' submissions suggest significant mental health sequela (particularly feelings of isolation, anxiety and depression) and psychosocial adversity (i.e. daily functionality, unmet aspirations, ability to work) associated with narcolepsy. • Parents described aspirations and unmet goals of their child with narcolepsy and the associated grief both they and the child felt.	• 'Eventually the struggle to keep going can become overwhelming.' (Submission 67) • 'Until I was diagnosed, I was perceived as being lazy, disorganised and a parasite.' (Submission 99) • 'One's personal agency degrades dramatically.' (Submission 14) • 'We have a 16-year-old daughter who has been advised that she will not be getting her licence, like all her friends, who is not allowed to swim on her own, for fear of her having a cataplexy episode and drowning.' (Submission 42)	No policy recommendations made addressing these concerns.	
Disability recognition and social welfare	• Concerns that narcolepsy is not recognised as a disability that can cause issues for patients and family/carers accessing National Disability Insurance Scheme (NDIS) and Centrelink (social security). • Lack of awareness among administrative staff can add to delay in accessing services.	• 'If in the worst-case scenario, she is unable to work, what can the government do to help. Can this sleep disorder readily become part of the NDIS?' (Submission 42) • 'I was informed that my condition is not a recognised disability, and the person I spoke to had never even heard of narcolepsy!' (Submission 10)	No policy recommendations made addressing these concerns.	
Limited workplace and educational support	• Limited accommodations made by workplaces. • Perception that there is not enough educational support to assist children with narcolepsy through schooling.	• 'I love my job, I have a wonderfully supportive employer. But there is no capacity to make accommodations for my disorder, such as having a place to have a nap if needed to during the day.' (Submission 99) • The costs of teachers' time to manage her through additional explanations of what she missed in class etc. is a factor for the school and is limited.' (Submission 26)	No policy recommendations made addressing these concerns.	
Experience with treatment options	• Participants worried about side-effects of medication and the long-term effects it will have. • Concern that stimulant medication will loose effectiveness over time.	• 'My teeth are becoming weak and rotting, and the stimulants are placing excess strain on my heart, which will lead to further complications as well as decrease my lifespan.' (Submission 10) • 'These medications are only masks that hide symptoms and become less effective over time.' (Submission 17)	No policy recommendations made addressing these concerns.	

logistical issues of health care (i.e. funding, access to new medications) rather than addressing concerns of patients and their family/carers that have a tangible effect on their daily life (i.e. mental health support, employment accommodations). This is despite the inquiry asking for the impact of sleep disorders on the community in the first term of reference.

Discussion

The analysis of public submissions to a parliamentary inquiry into health highlights several issues regarding the involvement of patients and family/carers as part of the stakeholder engagement process in shaping policy:

Avenues available for patients and family/carers to voice healthcare concerns

Despite narcolepsy being a rare sleep disorder with a prevalence of approximately 1/2000–1/5000,[20] patients and their family and carers with narcolepsy were disproportionately represented in the inquiry submissions, accounting for 10% (13/131) of total submissions and 76% (13/17) of all patient and family/carer submissions received. Furthermore, 18% (2/11) of the recommendations made by the inquiry specifically relate to narcolepsy. This over-representation may be because patients with more common sleep disorders (i.e. obstructive sleep apnoea, insomnia) have fewer concerns about their care, are less organised and engaged, or alternatively, have access to pre-existing pathways to raise these concerns. Perhaps the small population size of rare (sleep) disorders makes it difficult for these patients to have their voices heard when accessing these same pathways. It may also be attributed to the lack of systematic data collection of rare diseases in Australia and simply be a case of 'what gets measured, gets managed'.[9,21] Our findings raise an important question: What are the avenues available for patients and their family/carers, particularly with those from disparate groups (i.e. chronic/rare diseases), to voice their concerns in a way that results in a meaningful contribution to healthcare policy?

Apparent discordance between the scope of the terms of reference, priorities of patients' families, and recommendations identified in the final report/submissions received

The first term of reference of the inquiry specifically calls for information on the 'causes, impacts and costs (economic and social)' of sleep disorders on the community. Our analysis showed that although patient and family/carers responded to this, with emphasis placed on mental health and daily functionality, no policy recommendations were made in these domains (Table 1). Rather, policy recommendations in the final report focused on healthcare engagement, infrastructure, and funding (i.e. sleep laboratories, medication access). Although these recommendations represent a positive outcome of the inquiry for improving access to care, clear recommendations addressing daily living priorities such as employment support and welfare access remain lacking in the final report. This suggests some discordance between priorities identified in the recommendations made by policymakers and those held by patients and their family and carers with narcolepsy (Table 1).

Overall, there is a lack of transparency around how stakeholder submissions were translated and competing stakeholder priorities balanced. In the absence of a transparent process and inclusion of patient/family/carer groups in the decision-making process, what matters most to patients has been decided for patients rather than with patients. This is of concern given that dissonance between patient and health system priorities has been shown to lead to reduced engagement, lower satisfaction with treatment and poorer patient outcomes.[22] Perhaps the process of the inquiry needs to be modified to allow patient, family and carer groups the opportunity to give feedback prior to submission of the final report, similar to patient co-design in research.[23]

Another issue identified was the limited disclosure of (potential) conflicts of interest by stakeholders who participated in the inquiry or those that facilitated it. The inquiry received submissions from for-profit businesses and primary care providers writing in the capacity of owners of private clinics. Care needs to be taken to ensure any party with financial ties to industry not exert undue influence on the process of policy development. This extends to managing the perception of conflict of interests and may be achieved by increasing transparency of stakeholder engagement and requiring conflict of interests declarations from all parties involved in the policy development process.[24]

Significant barriers for the community to participate in healthcare policy

The terms of reference specifically call for submissions regarding disadvantaged and under-represented groups such as children and adolescents, those from culturally and linguistically diverse backgrounds, those living in rural, regional, and remote areas and Aboriginal and Torres Strait Islander peoples; however, we identified several barriers to participate in the inquiry that these groups would have encountered:

- Submissions could only be made via online submission or by posting a hand-written response, precluding individuals that lack access to computer facilities or who may have inadequate writing skills. Although individuals were invited to attend the hearing, these were selected by the inquiry from the pool of those that wrote submissions.
- Terms of reference were written only in English.
- The terms of reference of the inquiry require a university graduate reading level (Flesch-Kincaid readability score of 2.4 – scored by author AS).[25]

These barriers suggest that the inquiry process will result in only a self-selected sample of the population being represented. This may result in patients and family/carers from different backgrounds (i.e. cultural, socioeconomic) missing opportunity to voice concerns they may have. There is a need to improve stakeholder engagement through adopting more inclusive approaches that can facilitate access and participation. For example, translation of the terms of reference into different languages or involving Aboriginal and Torres Strait Islander leaders in the developmental phase of parliamentary inquiries. Such approaches foster a true collaborative partnership with patients to genuinely influence the decision-making process and drive meaningful changes in policy.[26]

Role of government and parliamentary inquiries in healthcare and policy generation

The inquiry produced 11 policy recommendations that were informed through the collaborative process between patients, physicians, and other stakeholders.[8] The report was submitted to parliament in early 2019; however, it is yet to be accepted or responded to. The government is required to respond within 6 months of submission; however, this is rarely adhered to, with delays of up to 2 years common.[5] Although recent delays may be attributed to COVID-19, inquiries such as the 'Inquiry into Chronic Disease Prevention and Management in Primary Health Care' was submitted in May 2016 and is yet to receive a response. To ensure recommendations are implemented, allocation of additional resources (i.e. funding, staff) may be needed to ensure a quick response, given they contain the most salient recommended policy changes that have resulted from collaboration among key stakeholders.

The delayed response from government speaks to the wider question of whether parliamentary inquiries are appropriate vehicles for health policy development and reform. A key limitation of these inquiries is that there is no clear path for policy change. The decision to implement recommendations of a parliamentary inquiry is contingent on its alignment with the policy agenda of government and its perceived importance by cabinet ministers.[27] Ethically, is it fair to ask patients and their family and carers to publicly share their lived experience with no guarantee that the recommendations will be accepted, let alone addressed? Typically, stakeholder engagement is increasingly driven by more powerful stakeholders (i.e. doctors, non-government organisations, funding bodies). Of the patient and family/carers stakeholders that do participate, they may only represent a small subsect of wider society (i.e. more health literate, affluent, monocultural). In combination with issues around transparency, balancing stakeholder bias, and accessibility, it suggests that parliamentary inquiries are not ideal policy-shaping tools. However, these inquiries represent a unique form of stakeholder engagement that is rarely seen in health care. The call for public submissions in response to the terms of reference allows any Australian the opportunity to have their voice heard, empowering ordinary citizens to get involved in shaping the healthcare system. This differs from other models of patient and family/carer contribution to health policy development (e.g. Health Consumers Australia), which instead advocate on behalf of their members. As seen in the example of narcolepsy, niche health care issues that may not necessarily be on the agenda when considering population-wide health care needs are given both a platform and the opportunity to be heard. Although far from perfect, these parliamentary inquiries are representative of a bottom-up approach to stakeholder engagement and perhaps should be used as a basis to expand future stakeholder engagement initiatives.

Strengths and limitations

Author AS is a person with narcolepsy, which enabled greater insight into how patients and carers experience the system; however, this may have led to researcher bias. This was reduced by including experienced qualitative researchers with no such lived experience in the thematic analysis. The study was limited by the number of patient/family/carer submissions received by the inquiry that related to narcolepsy. In addition, participants represent a self-selected sample of the population with a higher level of literacy, education, and interest in sleep disorders than the general community.

Conclusion

Parliamentary inquiries represent one of few opportunities for patients and their family and carers to contribute directly to the development and reform of healthcare policy. Although our study highlights some of the significant, practical barriers that patients and their family and carers encounter when trying to shape healthcare policy, at its core is a process that empowers everyday Australians to shape the healthcare system. This is particularly important in the context of rare diseases like narcolepsy, as limited population data, systems for patient data collection, and less research places greater emphasis on the lived experience of the patient in determining satisfaction, treatment success, as well as identifying any potential concerns that may arise.[9,28] Where the parliamentary inquiry does falter is in its lack of transparency when translating submissions, limited disclosure of potential conflicts of interest among stakeholders and barriers that stakeholders may face when contributing to the inquiry. Although the underlying premise of an open, public domain is sound, reform addressing these concerns is needed to ensure healthcare policy remains targeted and trusted.[3] As health policy forms the bedrock of health care, more needs to be done to incorporate patients' and their family/carers'

concerns and priorities into its development. Only then can we cultivate truly patient-centred healthcare systems.

Supplementary material

Supplementary material is available online.

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Data availability. The data that support this study was obtained from the Federal Parliament of Australia website. All submissions made are part of the public domain and are accessible at: https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/SleepHealthAwareness/Submissions.

Conflicts of interest. Aaron Schokman declares that he is a member of two narcolepsy patient support groups. This relationship did not influence or affect any part of the study or the decision to submit the manuscript for publication. Aaron Schokman also declares that he made a submission to the parliamentary inquiry. This submission was analysed and coded by other authors (JC and MA) and did not influence or affect any part of the study. The remaining authors declare no conflicts of interest.

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Chapter 4: How do we determine if narcolepsy is 'well-managed' or treated?

In Chapter 3, we found that persons with narcolepsy and their families and carers perceived the daily impact of narcolepsy encompassed several psychosocial domains, including mental health and daily functionality. Healthcare professionals were also perceived to lack knowledge and understanding specific to narcolepsy. Although persons with narcolepsy and their family and carers prioritised issues that affected their daily lives (i.e. mental health sequela, workplace accommodations), the policy recommendations in the report focused mainly on issues of healthcare infrastructure, funding and engagement.

While these results are not representative of all persons with narcolepsy, they led me to hypothesise that there may be a misalignment between stakeholders around the healthcare needs and priorities of those with narcolepsy. The management of narcolepsy is almost exclusively pharmacological. As such, I wanted to know the measures and outcomes used to determine whether narcolepsy is 'well-managed'.

To address this, I explored the outcome measures frequently used in narcolepsy randomised controlled trials (RCTs) and whether they aligned with any psychosocial domains identified in Chapter 3. Considering some symptoms of narcolepsy are non-specific to the disorder, I also wanted to explore whether the patient-reported outcome measures used to assess treatment efficacy had been validated in a narcolepsy population.

Chapter 5: Evaluation of psychometric properties of patient-reported outcome measures frequently used in narcolepsy randomized controlled trials: a systematic review

The following chapter has been published in a peer-reviewed journal:

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ORIGINAL ARTICLE

Evaluation of psychometric properties of patient-reported outcome measures frequently used in narcolepsy randomized controlled trials: a systematic review

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Abstract

Study Objectives: To systematically determine subjective and objective outcome measures used to measure the efficacy of narcolepsy interventions in randomized controlled trials (RCTs) in adults and children and assess psychometric properties of patient-reported outcome measures (PROMs) used.

Methods: We searched bibliographical databases and clinical trial registries for narcolepsy RCTs and extracted objective and subjective outcome measures. If PROMs were used, we searched for psychometric studies conducted in a narcolepsy population using bibliographical databases and appraised using Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines.

Results: In total, 80 different outcome measures were used across 100 RCTs. Epworth Sleepiness Scale (ESS) (n = 49) and Maintenance of Wakefulness Test (n = 47) were the most frequently used outcome measures. We found 19 validation studies of 10 PROMs in narcolepsy populations. There was limited evidence for validity or responsiveness of the ESS; yet sufficient reliability (pooled ICC: 0.81–0.87). Narcolepsy Severity Scale (NSS) had sufficient reliability (pooled ICC: 0.71–0.92) and both adult and pediatric versions had sufficient discriminant validity (treated/untreated). Content validity was only evaluated in pediatric populations for ESS-CHAD and NSS-P and rated inconclusive. Quality of evidence of the psychometric studies for all scales ranged from very low to low.

Conclusions: Although recognized by regulatory bodies and widely used as primary outcome measures in trials, there is surprisingly little evidence for the validity, reliability, and responsiveness of PROMs frequently used to assess treatment efficacy in narcolepsy. The field needs to establish patient-centered minimal clinically important differences for the PROMs used in these trials.

Statement of Significance

This is the first systematic review that explores both the outcome measures used in randomized controlled trials (RCTs) of people with narcolepsy and the psychometric properties of frequently used patient-reported outcome measures (PROMs). Narcolepsy interventions focus exclusively on treating symptoms; thus, knowing what outcome measures are used in efficacy studies is important if patients' expectation of treatment is to be met. Patient-reported outcome measures are frequently used in narcolepsy RCTs; however, there is limited evidence showing their appropriateness for use (i.e. validity, reliability, responsiveness). Furthermore, psychometric studies on existing PROMs or the development of ones that are narcolepsy-specific are needed before we can be confident that interventions are efficacious.

Key words: narcolepsy; cataplexy; psychometric properties; patient-reported outcome measures; randomized controlled trials; cosmin; systematic review; reliability; responsiveness; validity

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Introduction

Five symptoms characterize narcolepsy: excessive daytime sleepiness (EDS), cataplexy, hypnogogic/hypnopompic hallucinations, sleep paralysis, and disrupted nocturnal sleep [1]. The presence of cataplexy (sudden loss of skeletal muscle tone triggered by a strong emotion such as laughter) differentiates between the two subtypes of narcolepsy: narcolepsy with cataplexy—narcolepsy type 1 (N1); and narcolepsy without cataplexy—narcolepsy type 2 (N2) [2]. The most common approach to treating narcolepsy is pharmacological intervention, with current medications focused entirely on treating symptoms [3]. Nevertheless, those with narcolepsy continue to experience negative impacts on quality of life and daily function from symptoms, despite receiving standard treatment [3, 4].

Randomized controlled trials (RCTs) are the gold standard for establishing treatment efficacy [5]. Choosing outcome measures that accurately capture symptoms of narcolepsy is important not only to interpret the effects of treatment correctly but also to ensure the results are valuable to clinicians, people with narcolepsy, and other decision makers [6]. Outcome measures are generally categorized as either objective or subjective. Objective measures are quantifiable and independent of an individual's opinion or experience (e.g. Maintenance of Wakefulness Test [MWT]), whereas subjective measures are based on personal experience (e.g. Epworth Sleepiness Scale [ESS]). An important subset of subjective measures are patient-reported outcome measures (PROMs). These are typically short, easy-to-answer questionnaires completed by patients and are designed to capture the patient experience of specific concepts/constructs such as symptoms and the impact of a health condition in a way that is considered meaningful to patients.

The ESS has been used as the primary endpoint for EDS in efficacy trials and is considered sufficient evidence for regulatory approval of narcolepsy treatments [7–9]. PROMs are often created to measure complex and often unobservable constructs based on individual perspectives. Care must be taken to ensure a PROM actually measures the construct of interest, particularly if used in another population or for a different purpose than the one it was designed for [10]. The FDA has published guidelines on PROM use in therapeutic development, requiring evidence of the validity of PROMs to support medical product labelling claims [11]. Documented characteristics of the PROM are required (e.g. the number of items, and the population for intended use), including evidence showing its adequacy in terms of measurement properties, commonly referred to as psychometric properties (e.g. content validity, internal consistency). A PROMs usefulness can be determined by assessing its validity (i.e. the construct the PROM purports to measure is truly what is being measured), reliability (i.e. the PROM is free from measurement error), and responsiveness (i.e. the PROM is able to detect meaningful change) [12]. The Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) guidelines provide uniform terminology of psychometric properties and standards/criteria by which psychometric properties of a PROM can be assessed [10].

The importance of showing adequate content validity of a PROM is stressed by the FDA, EMA, and COSMIN over other psychometric properties [11, 12]. Content validity is "the degree to which the content of an instrument is an adequate reflection of the construct to be measured" [10]. Using a PROM in another population than the one it was designed for and validated in requires evidence that the two populations' perception of the construct being measured is the same. Individual questions that make up a PROM need to be relevant to the specific construct that is being measured (specific to each population and context of use) and comprehensive enough that the PROM thoroughly reflects a respondent's perception of the construct [10]. Conversely, insufficient content validity can affect how other psychometric properties are interpreted [10]. For example, while a high Cronbach's α demonstrates high internal consistency, it does not guarantee that the construct of interest is accurately captured or that all-important concepts are included. Similarly, high test–retest reliability or high responsiveness does not guarantee construct validity [10].

Our aim was to evaluate the extent to which PROMs are used in RCTs to measure treatment success in a narcolepsy population and the adequacy of the PROMs used in a two-staged systematic review:

Stage 1: To identify the objective and subjective outcome measures used to measure narcolepsy treatment in RCTs involving adults and children.

Stage 2: To evaluate the published evidence of psychometric properties of PROMs frequently used in narcolepsy RCTs.

Methods

This two-stage systematic review was prospectively registered with the PROSPERO International Prospective Register of Systematic Reviews (CRD42020209827) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and checklist [13]. This review also utilized the COSMIN initiatives guidelines for conducting a systematic review of PROMs in a target population [10, 14]. This includes guidance on searching for studies of each measurement property of PROMs and criteria by which the methodological quality of each study and the results are assessed.

Stage 1: To identify the objective and subjective outcome measures used to measure narcolepsy treatment in RCTs involving adults and children

Eligibility criteria Publications and clinical trial protocols describing RCTs investigating the efficacy of treatment intervention in people with narcolepsy were eligible for review. Participants of eligible studies were either adults or children diagnosed with narcolepsy (either type 1 or 2) using either the International Classification of Sleep Disorders (ICSD) or the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5). No criteria were placed on the type of intervention used in RCTs, nor was any restriction placed on the date of publication. Publications or protocols written in a language other than English were excluded. If a publication cited a clinical trial protocol, the publication was excluded in favor of the clinical trial protocol.

Information sources and search strategy Medline (Ovid), Embase (Ovid), PsycINFO (Ovid), CINAHL, and Scopus and clinical trial registries (www.clinicaltrials.gov, www.clinicaltrialsregister.eu, and www.anzctr.org.au) were searched on the 24th of May 2022.

The search strategy for published RCTs combined a Cochrane filter used to identify RCTs (sensitivity-maximizing version) and keywords/MeSH terms specific to narcolepsy [15]. Clinical trial records were searched for intervention studies that involved narcolepsy or cataplexy-specific populations. Our search strategy can be found in Supplementary A.

Study selection Title, abstract, and full-text screening of eligible articles were independently performed by two reviewers (A.S. and D.N.) using Covidence, an online systematic review tool [16]. Disagreements were discussed among reviewers, and consensus was reached, with a third reviewer (N.G.) adjudicating. Studies with both a Clinicaltrials.gov record and published articles were only included once by comparing clinicaltrials.gov identifiers. Multiple publications from a single RCT were limited to the primary paper describing the trial results and main outcome measures used.

Data items Outcome measures that were used to measure treatment efficacy were extracted from eligible studies and categorized as primary or secondary outcome measures independently by two authors (A.S. and D.N.) using information contained in study records. In the event published journal articles did not explicitly identify a measure as primary or secondary, the paper's content and aims were reviewed (A.S., D.N., and N.G.) until a consensus was reached. Coprimary outcome measures were each counted as a primary outcome measure.

Classification of outcome measures Outcome measures identified were classified as either objective or self-reported measurements (authors A.S. and N.G.). Self-reported measures were further classified as either (1) PROMs if it assessed the status of a patient's health condition using a standardized bank of items and responses were made directly by the patient, without interpretation by another person, or proxy report (except if the patient was a child) or (2) used another method such as a visual analog scale, diary, or answered by another person (i.e. physician completing the Clinical Global Impressions Scales) [11].

Stage 2: To evaluate the published evidence of psychometric properties of PROMs frequently used in narcolepsy RCTs

Eligibility criteria

PATIENT-REPORTED OUTCOME MEASURES PROMs identified in stage 1 of this review that either assessed narcolepsy symptoms and/or associated disability and function were eligible for inclusion in stage 2. PROMs were included if used as an outcome measure in (1) at least two narcolepsy RCTs or (2) at least one narcolepsy RCT and were developed specifically for use in a narcolepsy population. Instances where a PROM may have been used (e.g. sleep diary) but no explicit PROM mentioned (e.g. consensus sleep diary) were not eligible. PROMs assessing constructs not specific to narcolepsy symptoms or associated disability (e.g. quality-of-life, function, mental health, etc.) were also excluded. Characteristics of identified PROMs were extracted from original development studies and presented using the recommended COSMIN tabular format (Table 1).

TYPES OF STUDIES Psychometric studies of eligible PROMs were required to have been published in a peer-reviewed journal, with the full-text available in English. Cross-cultural adaptation studies were also included. Studies that investigated the psychometric properties of a PROM in the context of diagnosing narcolepsy (i.e. discriminative validity) were excluded.

PARTICIPANTS To be eligible, psychometric studies had to be conducted in a population diagnosed with narcolepsy (N1 or N2) using ICSD-1–3 or DSM criteria. Studies conducted in a mixed population (i.e. participants with various sleep disorders) were included if an analysis of the psychometric properties using a narcolepsy subsample was described. Studies utilizing both adult and children/adolescent populations were included

Information sources and search strategy for validation studies of included PROMs Published studies investigating content validity or other measurement properties of included PROMs were searched for on the 24th of May 2022. Studies were searched for using Medline (Ovid), Embase (Ovid), PsycINFO (Ovid), CINAHL, and Scopus bibliographical databases using an amalgamation of COSMIN recommended search strategies and Cochrane narcolepsy-specific search strategy (Supplementary A).

Data extraction and analysis of psychometric properties of PROMs using the COSMIN checklist One reviewer (A.S.) screened all title/abstract and full-text articles to determine eligibility. The full-text evaluation of the screened articles and data extraction were conducted independently by two authors (A.S. and Y.S.B.) using the COSMIN checklist. The checklist consists of questions that assess content validity and eight other measurement properties: (1) structural validity, (2) internal consistency, (3) cross-cultural validity/measurement invariance, (4) reliability, (5) measurement error, (6) criterion validity, (7) hypotheses testing for construct validity (convergence and discriminative), and (8) responsiveness to change (in response to intervention) [10]. The COSMIN checklist was completed in three stages. The study design (methodology used) and potential risk of bias of each study exploring measurement properties of PROMs were rated using a four-point scale (excellent, good, fair, poor), with the lowest rating of any of the questions used as the overall rating.

Second, the results from each study of any one measurement property of a PROM are rated against the criteria for what is considered a "good measurement property" (Supplementary Table S1). The criteria assess both the framework used to assess the measurement property and the result obtained against a specific standard (e.g. was Cronbach's α used to assess internal consistency AND was the result ≥ 0.70). A three-point rating scale is used for each result (sufficient, indeterminant, insufficient), with the ratings pooled together to give an overall score for the quality of the measurement property for each PROM (Supplementary Table S4).

Finally, an overall score of the quality of evidence for each pooled result of a measurement property is determined (Supplementary Table S3) using a modified version of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [17]. A four-point scale is used (high, moderate, low, very low), with each study starting with a "high" rating. The rating combines the first two components of the COSMIN checklist, and each study is subsequently downgraded

Table 1. Characteristics of the patient-reported outcome measures that are used in atleast two RCTs investigating treatment efficacy in people with narcolepsy or used in atleast one narcolepsy RCT and developed specifically for narcolepsy

PROM (reference to first article)	Construct(s)	Target population	Recall period	(Sub) scale(s) (number of items)	Response options	Range of scores	Original language
Stanford Sleepiness Scale (SSS)	Situational sleepiness, sleepiness at a given time	Any adult	At time of measure	1 (1)	(1) Feeling active and vital, (2) Functioning at a high level, (3) Relaxed; awake, (4) A little foggy, (5) Fogginess, (6) Sleepiness, (7) Almost in Reverie	1–7 (response option is score)	English
Epworth Sleepiness Scale (ESS) [18]	Average sleep propensity in daily life	Adults with EDS or suspected EDS	Prior month	1 (8)	(0) Would never doze, (1) Slight chance of dozing, (2) Moderate chance of dosing, (3) High chance of dosing	0–24; (higher scores indicate higher likelihood the scorer will fall asleep during the day)	English
Epworth Sleepiness Scale—Children and adolescent (ESS-CHAD) [19]	Average sleep propensity in daily life	Children and adolescents with EDS or suspected EDS			(0) Would never fall asleep, (1) Slight chance of falling asleep, (2) Moderate chance of falling asleep, (3) High chance of falling asleep		
Karolinska Sleepiness Scale (KSS) [20]	Situational sleepiness, sleepiness at a given time	Any adult	At time of measure	1 (1)	(1) Extremely alert, (2) Very alert, (3) Alert, (4) Rather alert, (5) Neither alert nor sleepy, (6) Some signs of sleepiness, (7) Sleepy—but no effort remaining awake, (8) Sleepy, but some effort to stay awake (9) Very sleepy, great effort to stay awake, (10) Extremely sleepy, can't keep awake	1–10 (score represents sleepiness at given time)	English
Pittsburgh Sleep Quality Index (PSQI) [21]	Sleep quality, habits, and disturbances	Any adult	Prior month	7 (19)	(0) Very good, (1) Fairly good, (2) Fairly bad, (3) Very bad	0–21 (subscales scored 0–3). Higher scores indicates worse sleep quality	English
Brief Fatigue Inventory (BFI) [22]	Severity and impact of cancer-related fatigue	Patients with fatigue due to cancer and cancer treatment	Prior 24 h	1 (9)	11-Point numeric scale, with higher scores indicating higher levels of fatigue and interference with daily life	0–10 (global fatigue score obtained by averaging items. Higher scores indicate more fatigue)	English
Pediatric Daytime Sleepiness Scale (PDSS) [23]	Daytime sleepiness	Students aged 5–17 years old	No time frame	1 (8)	(0) Never, (1) Seldom, (2) Sometimes, (3) Frequently, (4) Always	Higher scores indicate increased sleepiness and are associated with poorer educational outcomes	English
Narcolepsy Symptom Assessment Questionnaire (NSAQ) [24]	Changes in narcolepsy status and symptoms	Individuals with narcolepsy*	Prior 24 h	26 questions across various domains	Varying (questions ask scorer to rate symptoms as increased, decreased, or remains the same, 5-point Likert scales)	—	English
Narcolepsy Severity Scale (NSS) [25]	The severity of main narcolepsy symptoms	Adults diagnosed with narcolepsy type 1	Prior month	1 (15)	Varying (4 and 6 Likert scale)	Mild (0–14), moderate (15–28), severe (29–42), and very severe (43–57)	French
Narcolepsy Severity Scale—Paediatric (NSS-P) [26]	The severity of main narcolepsy symptoms	Children diagnosed with narcolepsy type 1		1 (14)		Mild (0–14), moderate (15–28), severe (29–42), and very severe (43–54)	

PROM: Patient Reported Outcome Measure, ESS: Epworth Sleepiness Scale, ESS-CHAD: Epworth Sleepiness Scale—Children and Adolescent, PSQI: Pittsburgh Sleep Quality Index, NSS: Narcolepsy Severity Scale, NSS-P: Narcolepsy Severity Scale-Pediatric, SSS: Stanford Sleepiness Scale.

based on the potential risk of bias in the studies, inconsistencies in the pooling of results, imprecision (i.e. total sample size), and indirectness (i.e. used partly in other populations or settings) (Supplementary Table S2).

Results

Stage 1: To identify the objective and subjective outcome measures used to measure narcolepsy treatment in RCTs involving adults and children

The systematic search identified 5511 records, of which 5357 were sourced from bibliography databases and 154 from clinical trial records (Figure 1). Following the removal of duplicates, 3340 records underwent title and abstract screening. A total of 343 records were selected for full-text screening, from which 100 RCTs conducted in a narcolepsy population were identified and included.

Across these 100 RCTs, we identified 80 unique outcome measures used to assess treatment efficacy. Outcome measures used in at least two RCTs can be found in Figure 2, stratified by their use as a primary or secondary outcome measure. Thirty-eight (48%) of the measures used were objective, and 42 (52%) were subjective. A PROM, the ESS (n = 49), was the most frequently used of all outcome measures in these RCTs [18]. The most common objective outcome measures used were the MWT (n = 47, and also the most common primary outcome measure n = 33 studies), polysomnography (PSG) (n = 34) and multiple sleep latency test (MSLT) (n = 21), while the most common subjective measures were the ESS (n = 49), clinical global impressions scale (n = 33) and sleep/wake/activity diaries (n = 31) (Figure 2). Nonstandardized weekly diaries (where the patient or parent records the number and severity of cataplexy attacks) were the most used subjective outcome measure for the symptom of cataplexy (n = 28).

Of the 100 RCTs identified, four were conducted in a pediatric population (age < 18 years). A cataplexy diary was the most common primary outcome measure (n = 2) used, followed by the MSLT (n = 1), CGI-C (n = 1), and PDSS (n = 1). The ESS-CHAD was used once as a secondary outcome measure.

We identified 10 PROMs as having either been used in two or more RCTs or used in at least one RCT and developed to assess symptoms/associated disability of narcolepsy (Table 1). Of these, the ESS was the only PROM to be used in two or more RCTs, having been used a total of 20 times as a primary outcome measure to assess narcolepsy symptoms and/or associated disability. Only one other PROM was used as the primary outcome measure: the Pediatric Daytime Sleepiness Scale (PDSS) [27].

Stage 2: to evaluate the published evidence of psychometric properties of PROMs frequently used in narcolepsy RCTs

We systematically searched for psychometric validation studies of the 10 PROMs frequently used in RCTs and identified 952 records sourced from bibliography databases (Figure 3). Most of the articles found were related to the ESS (62%). Following the removal of duplicates, 603 records underwent title and abstract screening. A total of 38 records were selected for full-text screening. Nineteen validation studies of the 10 PROMs were found. Most studies (n = 9) related to the ESS, with six being retrospective analyses of RCT data and two being validation studies of a modified version of the ESS specific for children and adolescents (ESS-CHAD).

Characteristics of the ten PROMs frequently used in narcolepsy RCTs and included in stage 2 of this review can be found in Table 1. A summary of the 19 studies that explore the psychometric properties of these PROMs can be found in Table 2.

Evaluating the evidence base supporting the use of PROMs in a narcolepsy population using the COSMIN methodology

A pooled summary of the findings from psychometric studies included in this analysis can be found in Supplementary C, Table S4.

1) Content validity

We found only one study that explored content validity; an evaluation of the Epworth Sleepiness Scale—Children and Adolescence (ESS-CHAD) [19]. Another briefly described the development process of the Narcolepsy Severity Scale (NSS) [25]. No other PROMs, including the widely used ESS, had a published study evaluating the content validity in an adult narcolepsy population. Table 3 summarizes the appraisal of content validity using the COSMIN guidelines.

ESS-CHAD No development study was found for the ESS-CHAD (or for the ESS upon which it was based). The content validity study of the ESS-CHAD explored the relevance and comprehensibility of the items but not comprehensiveness [19]. Relevance, comprehensiveness, and comprehensibility are equally important, and all three are required; thus, the ESS-CHAD received an overall content validity rating of "inconclusive." Quality of evidence was found to be low due to the small size of the study population (n = 13 children, n = 19 adolescents), concerns that changes made to the ESS-CHAD following this study were not assessed, and the number of researchers involved in analyzing the qualitative interviews not described.

NSS No content validity studies were found for the NSS; however, one publication briefly described the development process [25]. While the paper briefly discussed the relevance and comprehensibility of the items, comprehensiveness was not mentioned. Overall, the quality of evidence was rated very low (due to the brief description), and overall content validity was rated inconclusive.

2) Structural validity

COSMIN defines structural validity as a measure of the degree to which the scores of a PROM are an adequate reflection of the dimensionality of the construct being measured. If a PROM has sufficient structural validity, the whole PROM should be unidimensional (i.e. all items measure a single construct), or the PROM should contain subscales (where all items in a subscale measure a unidimensional construct).

The requirement for sufficient structural validity only applies to PROMs that are based on a reflective questionnaire model. In a reflective model, all questions are manifestations of the same construct (i.e. the questions reflect aspects of a single construct) (Figure 4). Conversely, a formative model is where the construct does not exist naturally on its own and

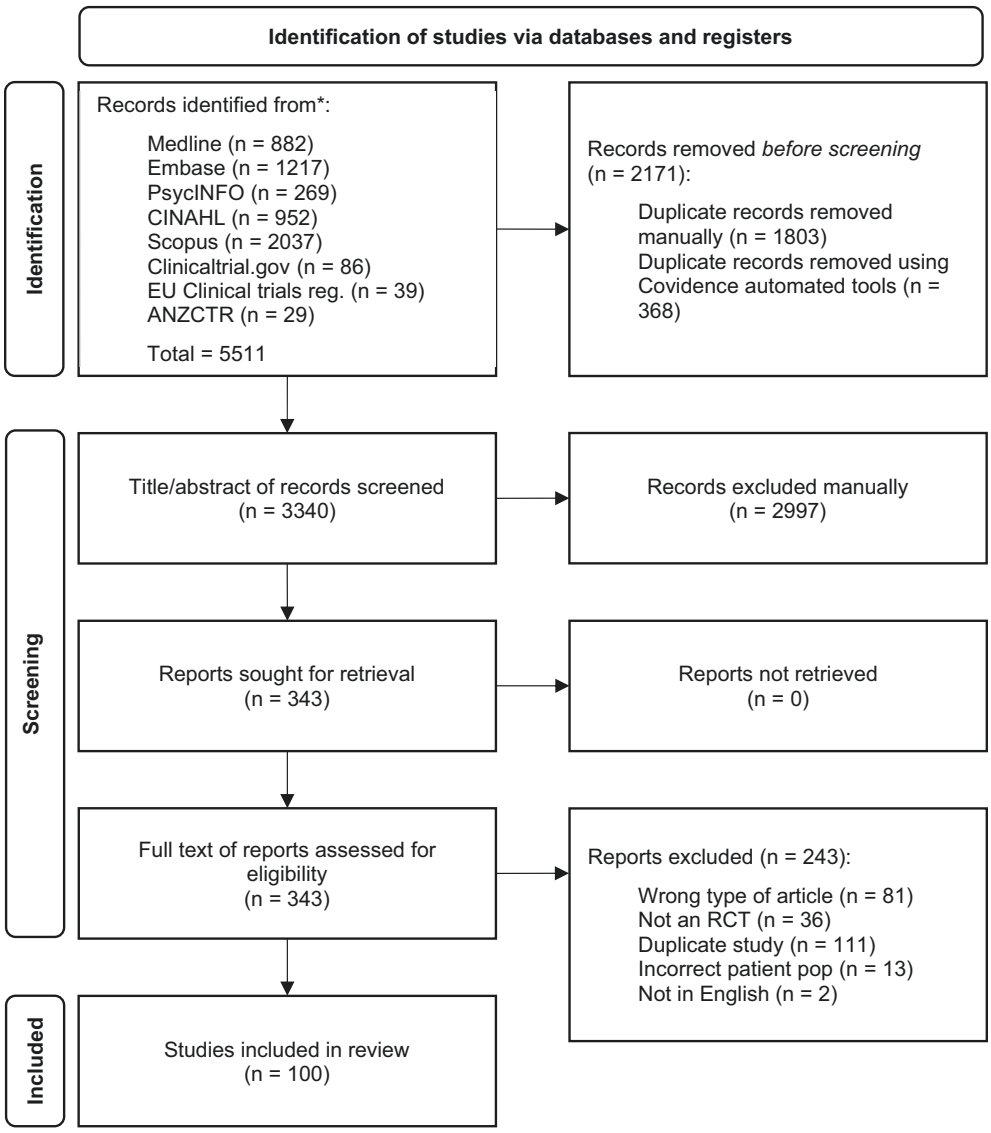

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram for identifying eligible randomized controlled trials in a narcolepsy population. RCT: Randomized controlled trial.

is instead "formed" from different constructs (Figure 4). The General Anxiety Disorder-7 (GAD-7) is an example of a reflective model, as all questions measure manifestations of anxiety (a single construct). Conversely, the Pittsburgh Sleep Quality Index (PSQI) is an example of a formative model, as it contains subscales measuring different aspects of sleep (e.g. sleep duration, sleep disturbances) that are combined into a single construct of sleep quality. Structural validity is an important measurement property for reflective models as we expect questions measuring a single construct to be related, whereas it has no meaning in a formative model as there is no requirement for questions or constructs measured to be related to one another [10, 14, 28].

NSS and NSS-P The structural validity of the NSS and NSS-P was explored in several studies [25, 29–31]. However, these PROMs are designed as a single scale that purports to measure a construct of symptom severity that does not naturally exist (i.e. they are "formative" models that assess the five different symptoms of narcolepsy (e.g. severity of EDS, severity of cataplexy) and combined into a single dimension).

3) Internal consistency

Internal consistency refers to the interrelatedness of items within a unidimensional scale or subscale, measured using Cronbach's α. For internal consistency to be correctly understood and interpreted, sufficient evidence of structural validity is required as a prerequisite (i.e. scale is unidimensional or has subscales) [14]. Subscale internal consistency can be shown for PROMs based on formative models if the PROM subscale is unidimensional and all items within a subscale measure the one construct) [14].

ESS-CHAD Internal consistency of the ESS-CHAD was assessed in a single study using retrospective clinical trial data [32]. Using an N1 population (n = 100), Cronbach's α was 0.76 (95% CI: 0.68–0.82). This score was rated indeterminant for internal consistency as no evidence of structural validity of the ESS-CHAD (or

Figure 2. Outcome measures used in two or more RCTs in people with narcolepsy (as identified in the first stage of this systematic review) stratified by use as either a primary or secondary outcome measure.

ESS) in a narcolepsy population was found (considered a prerequisite for proper interpretation of the score) [14]. While structural validity has been explored in other cohorts, other reviews did find consensus on this psychometric property of the ESS [33].

NSS and NSS-P Internal consistency of the NSS and NSS-P was evaluated in the same papers as the construct validity [25, 29–31] and assessed either between all questions or between questions grouped by the results of factor analysis. As neither the NSS and NSS-P measure a unidimensional construct nor contain subscales, the measurement property of internal consistency was considered irrelevant (Table 4 and Supplementary Table S4). As per the COSMIN checklist, the findings were summarized but not scrutinized [14].

PDSS Internal consistency of the PDSS was explored in one study using a narcolepsy population [27]. While internal consistency was found to be sufficient (Cronbach's α = 0.81), it lacked evidence of structural validity in a narcolepsy population and thus rated indeterminant (Table 4 and Supplementary Table S4). The quality of evidence was graded very low due to the small population size (n = 31).

4) Test–retest reliability

Test–retest reliability refers to the proportion of total variance in a respondent's PROM scores that is due to "true" differences between patients. It is a measure of the consistency of the score rather than its accuracy, and its proper interpretation of the statistic relies on the assumption that the respondent's symptoms are stable across time points [34].

ESS The test–retest reliability of the ESS was measured in two studies that retrospectively analyzed RCT studies [35, 36]. Scores were compared across different time points in the RCT, with the population size of each analysis varying (lowest n = 52, highest n = 199). A pooled result of ICC: 0.81–0.87 was reported and rated sufficient against the criteria for good measurement properties (Table 4 and Supplementary Table S4). The quality of the evidence was graded "very low" due to the RCT setting, as proper interpretation requires patients to be stable across time points (stability was assumed, no evidence reported), concerning RCT participants not being representative of the narcolepsy population (due to clinical trial inclusion/exclusion criteria with one study requiring ESS score of >14) and potential incorporation bias [37].

ESS-CHAD Test–retest reliability of the ESS-CHAD was explored using retrospective analysis of clinical trial data [32]. Children and adolescents (n = 64) were assessed, with an ICC: 0.76 reported. When separated by age, sufficient test–retest reliability was reported in children of 7–11 years (n = 21) (ICC: 0.86), yet found to be insufficient in children of 12–17 years (n = 43) (ICC: 0.66). Like the ESS, evidence was rated very low due to the RCT setting, clinical trial population not necessarily representative of the wider population, and small population size.

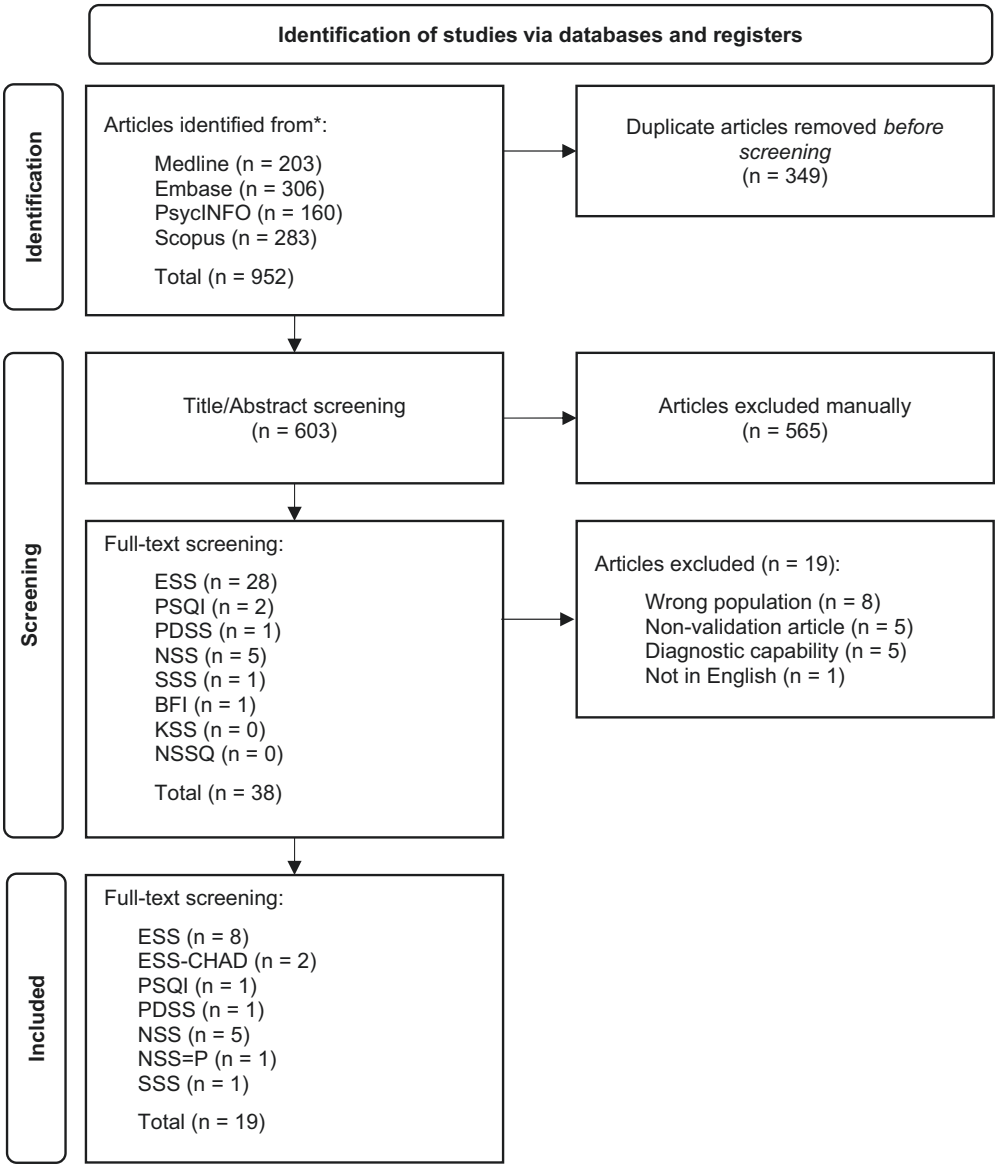

Figure 3. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram for identifying eligible psychometric studies of frequently used patient-reported outcome measures in narcolepsy randomized controlled trials. RCT: randomized controlled trial, ESS: Epworth Sleepiness Scale, ESS-CHAD: Epworth Sleepiness Scale—Children and Adolescent, PSQI: Pittsburgh Sleep Quality Index, NSS: Narcolepsy Severity Scale, NSS-P: Narcolepsy Severity Scale-Pediatric, SSS: Stanford Sleepiness Scale, BFI: Brief Fatigue Inventory, KSS: Karolinska Sleepiness Scale, NSSQ: Narcolepsy Sleep Status Questionnaire.

NSS Test–retest reliability of the NSS was explored across four studies using a narcolepsy population [25, 29–31]. A total population of 86 persons diagnosed with N1 participated, and the pooled ICC: 0.71–0.92 was rated as sufficient against the criteria for good measurement properties (Table 4 and Supplementary Table S4). The quality of evidence was overall graded low due to the small population size and the long time interval between measurements (up to several months where there may have been a considerable change).

NSS-P Test–retest reliability of the NSS-P was explored in a single study of 32 participants diagnosed with N1 [26]. The result showed no significant difference between time points; however, this was rated indeterminant as a dependent *t*-test was used for statistical analysis between time points rather than interclass coefficient or weighted kappa (Table 4 and Supplementary Table S4) [14]. The quality of evidence was graded very low due to the small population size (n = 32) and unknown time interval used in the study.

5) Hypothesis for testing construct validity—discriminant validity

Discriminant validity or known-group validity is a measure of the ability of a PROM to distinguish between groups, where the measurement of a specific construct is *a priori* assumed to differ between them (i.e. participants treated for sleepiness should be less sleepy than those who are untreated) [14]. This type of validity relies on the assumption that the PROM validly measures a specific construct.

ESS-CHAD The capacity of the ESS-CHAD to discriminate between treated/non-treated cohorts and between sex in children

Table 2. Validation studies of commonly used patient-reported outcome measures in RCTs investigating treatment efficacy in people with narcolepsy

			Population with narcolepsy				Instrument administration		
PROM	Ref	Setting	*n*	Age, mean (SD, range), yr	Gender % female	Disease	Inclusion criteria	Country	Language
ESS	[35] [38]	Retrospective analysis of clinical trial	231	36.2 (13.2, —)	65%	N1, N2	Diagnosis using ICSD-3 or DSM-5, required to have baseline mean sleep latency <25 min on the MWT and usual nightly total sleep time ≥6 h. Key exclusion criteria included usual bedtime later than 1:00 am, an occupation requiring nighttime or variable shift work, or any other clinically relevant medical, behavioral, or psychiatric disorder associated with EDS	United States	English
	[36]	Retrospective analysis of clinical trial	95	Intervention group A = 38.2 (14.1, —), Intervention group B = 39.3 (15.4, —)	45%	N1, N2	ICSD-2 and a baseline score of ≥14 on the ESS	Switzerland	—
	[39]	Retrospective analysis of two clinical trials	228	Trial 1: 38.6 (—) Trial 2: 40.5 (—) Range of both (16–75)	Trial 1: 65.4% Trial 2: 51.8%,	N1, N2	Diagnosis of narcolepsy based on PSG and MSLT performed ˂5 years; Currently experience EDS, cataplexy, and recurrent sleep attacks almost daily for at least 3 months. Women of child-bearing potential were required to use a medically accepted method of birth control unless surgically sterile or 2 years postmenopausal	44 sites internationally	—
	[40]	Retrospective analysis of clinical trial	522	41.7 (13.3,17–68)	—	N1	Diagnosis using ICSD-1, daily lapses into sleep ≥3 months, cataplexy, and mean sleep latency ˂8 min on MSLT	United States	English
	[41]	Retrospective analysis of clinical trial	93	38.7 (12.1, 18–70)	65%	N1, N2	ICSD-2 and ≥10 score on the ESS and a mean baseline MWT sleep latency score of ≤10 min	United States	English
	[42]	Sleep disorders clinic	23	32.0 (10.1, 18–57)	83%	N1, N2	ICSD-1	Mexico	English
	[43]	Sleep disorders clinic	10	15.6 (4.5, —)	20%	N1	ICSD-2 including EDS, cataplexy, confirmation using PSG, and MSLT ≤8 min, with two or more SOREM	Taiwan	Chinese
ESS-CHAD	[19]	Sleep clinics	29	11.6 (3.5, 7–17)	48%	N1	Diagnosed with N1, with ICSD criteria cited	United States	English
	[32]	Retrospective analysis of clinical trial	106	11.9 (2.39, 7–16)	40%	N1	ICSD-2 or 3, depending on when participant was diagnosed or undergoes an MSLT to confirm type 1 using ICSD-3 criteria. Exclusion: various (e.g. unstable medical condition, inability to follow instructions)	United States (inc. several internationally)	English

Table 2. Continued

			Population with narcolepsy				Instrument administration		
PROM	Ref	Setting	*n*	Age, mean (SD, range), yr	Gender % female	Disease	Inclusion criteria	Country	Language
NSS	[25]	Sleep clinic/ university	175	41.5 (17.4)	41%	N1	ICSD-3, cataplexy, mean sleep latency on MSLT ≤8 min with ≤2 sleep-onset REM periods and CSF hypocretin-1 level <110 pg/mL	France	French
	[29]	Sleep clinic	122	26.1 (15.4)	34%	—	ICSD-3 criteria (N1)	China	Chinese
	[44]	Sleep clinic/ university	381	38.9 (17.1, —)	47%	N11	ICSD-3, cataplexy, mean sleep latency on MSLT ≤8 min with ≤2 sleep-onset REM periods and CSF hypocretin-1 level <110 pg/mL	France	French
	[30]	Outpatient clinic	52	37.6 (12.0, 18–70)	60%	N1	ICSD-3	Brazil	Spanish
	[31]	Sleep clinic	151	31.4 (11.5, —)	28%	N1	Diagnosis using ICSD-3, complaints of sleepiness for atleast 3 months, mean sleep latency of MSLT <8 min with ≥2 SOREMPs, hypocretin-1 deficiency (<110 pg/mL, *n* ¼ 37) or, if CSF hypocretin-1 unavailable, clear-cut cataplexy, and positive HLADQB1*0602	China	Chinese
NSS-P	[26]	Sleep clinic	209	13.3 (2.6, 6–17)	41%	N1	Diagnosis using ICSD-3, presence of EDS for at least 3 months, mean sleep latency ≤8 min MSLT with at least 2 sleep-onset REM periods, and typical cataplexy, or low CSF levels of orexin-A (<110 pg/mL).	France	French
PDSS-C	[27]	Sleep disorders clinic	31	12.6 (3.4, —)	32%	N1	Diagnosis using the ICSD-2, diagnosis of narcolepsy with cataplexy using clinical interviews (confirmed by MSLT and PSG scores and human leukocyte antigen [HLA] typing of DQB1*0602 positive)	China	Chinese
PSQI-K	[45]	Regional sleep disorder clinic	50	26.7 (12.7, —)	44%	N1, N2	ICSD-2	Korea	Korean
SSS	[46]	Sleep disorder clinic	10	42 (—, 19–65)	70%	N1	Sleep attacks and cataplexy	—	—

Table 3. Content validity of PROMs used in RCTs of people with narcolepsy

PROM	Relevance	Comprehensiveness	Comprehensibility	Overall content validity score
Epworth Sleepiness Scale	—	—	—	—
Epworth Sleepiness Scale—Children and Adolescence[19]	Sufficient	Indeterminant	Sufficient	Inconclusive
Narcolepsy Severity Scale [25]	Sufficient	Indeterminant	Sufficient	Inconclusive
Narcolepsy Severity Scale—Pediatric	—	—	—	—
Pediatric Daytime Sleepiness Scale	—	—	—	—
Pittsburgh Sleep Quality Index	—	—	—	—
Narcolepsy Symptom Assessment Questionnaire	—	—	—	—
Brief Fatigue Inventory	—	—	—	—
Karolinska Sleepiness Scale	—	—	—	—
Stanford Sleepiness Scale	—	—	—	—

Content validity results obtained in these studies were rated against COSMIN criteria for what is considered evidence of good content validity (sufficient, insufficient, inconclusive). The background color of each cell represents our confidence that the results obtained in these studies reflect the true content validity of the PROM, as assessed using the COSMIN GRADE approach (green = high, yellow = moderate, orange = low, red = very low). — A dash indicates no evidence was found assessing this measurement property.

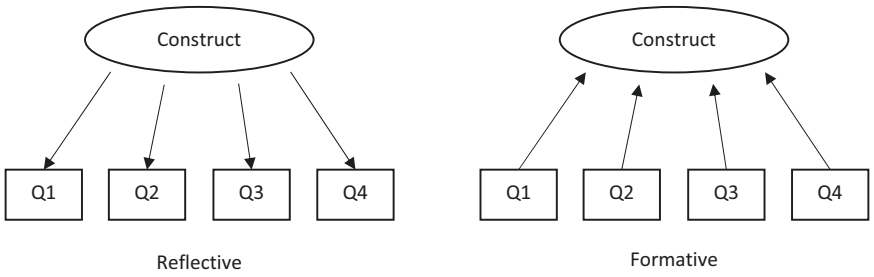

Figure 4. Conceptual diagram representing the relationship between questions and the construct measured in reflective and formative question models.

Table 4. Summary of other measurement properties of PROMs used in narcolepsy RCTs

PROM	Structural validity	Internal consistency	Reliability	Discriminant validity (treated vs. untreated)	Responsiveness
Epworth Sleepiness Scale	—	—	Sufficient	—	Indeterminant
Epworth Sleepiness Scale—Children and Aadolescence	—	Indeterminant	Sufficient (children 7–11 years) Insufficient (children 12–17 years)	Insufficient (children 7–11 years) Sufficient (children 12–17 years)	Indeterminant
Narcolepsy Severity Scale	N/A*	N/A*	Sufficient	Sufficient	Indeterminant
Narcolepsy Severity Scale—Pediatric	N/A*	N/A*	Indeterminant	Sufficient	Indeterminant
Pediatric Daytime Sleepiness Scale	—	Indeterminant	—	—	Indeterminant
Pittsburgh Sleep Quality Index	—	—	—	—	—
Narcolepsy Symptom Assessment Questionnaire	—	—	—	—	—
Brief Fatigue Inventory	—	—	—	—	—
Karolinska Sleepiness Scale	—	—	—	—	—
Stanford Sleepiness Scale	—	—	—	—	—

Pooled results from each measurement property of each PROM were rated against COSMIN criteria for what is considered evidence of good measurement property (sufficient, insufficient, inconclusive). The background color of each cell represents our confidence that the results obtained in these studies reflect the true content validity of the PROM, as assessed using the COSMIN GRADE approach (green = high, yellow = moderate, orange = low, red = very low). — A dash indicates no evidence was found assessing this measurement property.
*An N/A rating was given where a measurement property was assessed in a study, but the measurement property was found to not be relevant. As per the COSMIN checklist, structural validity and internal consistency are irrelevant to PROMs that are based on formative question models.

was assessed through retrospective analysis of clinical trial data (n = 100) [32]. A two-tailed t-test was used to calculate the mean difference between female/male (–0.68) and nontreated/treated (2.84) participants. Furthermore, analysis showed that in participants aged 7–11 years (n = 36), mean difference was assessed between female/male (–1.59) and non-treated/treated (1.30). Similarly, participants aged 12–16 years (n = 64), mean difference was also reported between female/male (–0.27) and non-treated/treated (3.39). We found the ESS insufficient for discriminative validity in children under 12 and sufficient for those aged 12–17 years. Quality of evidence was rated very low due to the population used (clinical trial participants who may not be representative of the entire population), incorporation bias, and small cohort size.

NSS Discriminant validity of the NSS was explored in three studies using 637 people with N1 [25, 29, 44]. A t-test was used to determine the mean difference between treated/non-treated adults (mean difference: 9.08, 7.70, and 4.60). The NSS was able to distinguish between medicated and non-medicated individuals ($p < 0.05$), however quality of evidence was graded low due to the mix of interventions used and the structure of the PROM weighted towards the symptom EDS (i.e. we are unable to tell if the PROM can discriminate between people treated/untreated for single symptom domains like cataplexy) (Supplementary Table 4, S4).

NSS-P Discriminant validity of the NSS-P was explored in a single study of 160 participants diagnosed with N1 [26]. The NSS-P was able to distinguish between non-treated/treated individuals (mean difference = 3.71). ($p < 0.05$), with quality of evidence was graded low due to similar concerns raised in NSS (Supplementary Table 4, S4).

6) Responsiveness to change (in response to intervention)

Responsiveness is the ability of a PROM to detect a change in a construct before and after an intervention. The result for this measurement property is rated using hypothesis testing, where authors determined a priori the size and direction of the effect a treatment would have on a PROM score [14]. This is typically informed by a minimal clinically important difference (MCID), the minimum threshold for an outcome score that a patient or physician would consider a given change to be meaningful or worthwhile [47]. This is typically calculated using anchor points

(other reference points or outcomes such as QoL measures) that show that an intervention has clinical significance. An MCID for any PROM is needed to adequately assess its responsiveness psychometric. It is common for psychometric studies to use a paired *t*-test to show the responsiveness, however, this is considered inappropriate. A paired *t*-test shows that a statistically significant difference exists between the mean scores of a PROM pre- and post-intervention (i.e. H_0 = PROM score pre- and post-intervention is the same). Showing significance using a paired *t*-test does not assess if the magnitude of the difference in scores is clinically significant (informed by the MCID) [14, 48].

ESS Responsiveness of the ESS was explored in a single study consisting of 10 adults and children diagnosed with N1 [43]. The study found the ESS was able to show a statistically significant difference in means pre- and post-treatment; however, this was rated indeterminant due to the use of a paired *t*-test and no evidence of an MCID used in the study. Quality of evidence was rated as very low due to the small population size and participants being a mix of adults/children, which is considered inappropriate due to differences in the presentation of narcolepsy in these two groups [49–51].

ESS-CHAD A retrospective analysis of clinical trial data was used to explore the responsiveness of the ESS-CHAD in children (<18 years) diagnosed with N1 (n = 59) [32]. The study found the ESS-CHAD was able to show a statistically significant difference in means pre- and post-treatment; however, this was rated indeterminant due to the use of a paired *t*-test and no evidence of an MCID used in the study. This contributed to a quality of evidence rating of very low, along with the small population size (7–10 cohort, n = 21).

NSS Four studies explored the responsiveness of the NSS using 160 participants diagnosed with N1 [25, 30, 31, 44]. Pooled results showed a statistically significant difference of means between pre- and post-treatment scores using the NSS; however, this was calculated using paired *t*-test. Confidence intervals for the difference of means nor ΔSD were provided in any of these studies. No MCID for the NSS was found; thus, responsiveness was rated indeterminant. The quality of evidence was rated low due to a mix of interventions given to participants and the small population size of each study. This is because the NSS does not contain subscales and is weighted more towards measuring EDS symptoms (75% of questions relate to EDS). It is unknown if the NSS is responsive to change when measuring interventions targeting symptoms other than EDS.

NSS-P A single study explored the responsiveness of the NSS-P using 33 participants diagnosed with N1 [26]. Pooled results showed sufficient responsiveness of the NSS, with a mean difference in score of 3.12 ± 7.12 reported between treated/ untreated cohorts. The study did suggest an MCID of 3.60–3.76; however, this was calculated using effect sizes (e.g. 0.5 × ΔSD), not in combination with any anchor points. This is not considered an appropriate calculation of MCID and thus is not a reflection of what people with narcolepsy would consider clinically significant [52]. This, along with the use of a paired *t*-test, informed our rating of indeterminate. The quality of evidence was rated low due to the small population size and the mix of interventions given to participants, similarly seen in studies of responsiveness of the NSS (Supplementary Table 4, S4).

PDSS A single study explored the responsiveness of the PDSS using 31 participants diagnosed with N1 [27]. The study indicated that the PDSS could detect change over time, but no results were published, thus rated as indeterminant. The quality of evidence was rated as very low due to the small population size and lack of information published in the study (Supplementary Table 4, S4)

7) Hypothesis for testing construct validity—convergent validity

Convergent validity refers to how closely the PROM relates to other variables and measured constructs. In the context of narcolepsy, convergent validity can be difficult to interpret as some constructs are not well defined (i.e. ESS and MSLT measuring different aspects of sleepiness). Thus convergent validity was not assessed using the COSMIN (as per checklist), instead summarized qualitatively (Supplementary Table S4).

ESS The ESS measures a different construct than its objective counterparts (i.e. MSLT and MWT) (Supplementary Table S5) [53]. We hypothesized *a priori* that there should be a strong negative correlation with the MWT and a strong positive correlation with the MSLT (considering all used as measures of sleepiness in EDS). Pooling the results of validation studies together, we found the correlation was smaller than expected (MWT r = –0.42 to –0.18, MSLT r = 0.41 to 0.27).

NSS The NSS was compared against the ESS, MWT, MSLT, and PSQI. While these outcome measures capture different constructs, a moderate, positive correlation with the ESS was expected and reflects that approximately 50% of the NSS questions relate to sleepiness/vigilance.

8) Cultural validity, measurement error, and measurement invariance

No validation studies exploring cultural validity/measurement invariance and measurement error in a narcolepsy population were found. Criterion validity was not included in this study as no there is no gold standard of narcolepsy that PROMs could be compared against.

Discussion

The first stage of this systematic review identified the ESS (a PROM) as the most frequent outcome measure used in narcolepsy RCTs, followed in frequency by objective measures: the MWT and PSG. When assessing outcome measures used in narcolepsy child/adolescent RCTs, only four RCTs were found to have used a specific pediatric population. The clinical global impressions (change) were used four times, while cataplexy diaries, the MSLT, and the PDSS were all used twice. The modified version of the ESS designed for children and adolescents (ESS-CHAD) was used once as a secondary measure.

Overall, we identified ten PROMs used in either two or more RCTs or developed specifically to measure symptom/disability in people with narcolepsy. In the second stage of this review, we found very little evidence supporting the use of these 10 PROMs in RCTs measuring treatment efficacy in people with narcolepsy. Most PROMs assessed excessive daytime sleepiness (EDS), with few assessing other symptoms associated with narcolepsy [4]. Few high-quality psychometric studies were found assessing

these PROMs, with concerns around sample size, incorporation bias, and inappropriate statistical tests identified.

Content validity and the construct EDS

Content validity is considered the most important psychometric property as it refers to how well a PROM measures all aspects of a given construct. Our analysis showed that PROMs used to capture excessive daytime sleepiness in narcolepsy trials lacked evidence of content validity. This may be because of the way they construct of EDS is conceived. The definition of EDS varies across the literature (including academic and regulatory approval documentation), with "EDS" and "excessive sleepiness" often used interchangeably. A recent review describes EDS presenting clinically as several sleep-related symptoms (e.g. excessive sleepiness, sleep attacks, sleep inertia, etc.), while people with narcolepsy have stressed their experience of EDS extends beyond just sleepiness to include autonomic functions and cognition [53]. If EDS is a multidimensional construct, clarity is needed around how best to capture these dimensions. Our review found that both objective and subjective outcome measures purporting to assess EDS as the primary endpoint in RCTs (i.e. MWT, ESS, and MSLT) assessed dimensions of actual sleepiness. Perhaps other dimensions of EDS should be used as the outcome in RCTs to better reflect patient concerns, as treatment may only be efficacious for excessive sleepiness but not sleep attacks or potentially less efficacious for this aspect of EDS than others. Variability in the items assessing EDS makes it difficult to compare treatment efficacies, as frequently used PROMs and objective measures in RCTs capture different aspects of sleepiness.

There was little variation in outcome measures used to capture cataplexy, with weekly cataplexy diaries commonly used. However, these diaries preclude the assessment of many measurement properties due to the lack of standardization of items and responses and fail to capture nuances of the symptom (i.e. partial/full cataplexy attacks, whether residual cataplexy is tolerable) [4].

No specific outcome measures were identified for the other symptoms of narcolepsy.

Patient-reported outcome measures

ESS and ESS-CHAD The ESS was the most frequently used outcome measure in RCTs in people with narcolepsy and the second-most frequently used primary outcome measure. Despite its frequency of use and acceptance by regulatory authorities, we found surprisingly little evidence supporting its use in people with narcolepsy. No content validity studies were found for the ESS in adults, nor were studies found exploring structural validity and internal consistency using an adult narcolepsy population. There was evidence (from low-quality studies) for the convergent validity between the ESS and MSLT/MWT, which demonstrated a weaker-than-expected correlation, yet all three outcome measures have been used as the primary endpoint for EDS in narcolepsy RCTs. Validity is the degree to which a PROM measures the construct it purports to measure, and given the frequency of use of the ESS in clinical trials (n = 49), it's remarkable that limited quality studies have been completed. Only one study showed sufficient evidence of responsiveness to change; however, this was graded "very low" quality as the study population used was small (n = 10) and comprised of a mix of adults and children (considered inappropriate as an adult and pediatric narcolepsy differ in clinical presentation and severity) [43, 50, 51].

Most studies on measurement properties of the ESS in people with narcolepsy were retrospective analyses of RCTs. This includes two studies that showed sufficient test–retest reliability of the ESS; however, the quality of this evidence was rated very low. Inclusion/exclusion criteria of clinical trials are selective, and this needs to be taken into consideration when appraising validation studies that use this data. The cohort used should be representative of all those with narcolepsy, not an ideal clinical trial population (e.g. inclusion criteria of one RCTs used in a validation study required an ESS score of ≥14, mean sleep latency of MWT <10 min, and women required to be on birth control, while also excluding many comorbidities [18]). Incorporation bias is also introduced when using RCTs for such studies, whereby the outcome measures are also used as the screening criteria, which may falsely lead to elevated sensitivity [37].

ESS-CHAD The ESS-CHAD was one of two PROMs used in child/adolescent narcolepsy RCTs. Content validity was explored in one study, with sufficient relevance and comprehensibility shown, but comprehensiveness was not explored. Assessment of discriminatory validity in children 7–11 years found a mean difference of 1.30 between untreated/treated cohorts, whereas, in children 12–17 years, the mean difference was 3.39 between untreated/treated. It is unclear if a score of 1.30 is a MCID, with the result perhaps attributed to the advanced reading skill needed to interpret the items of the PROM; we calculated that a seventh-grade reading level is required (Flesch Reading Ease Score: 73.5) [54]. It may be that most children under 12 do not understand the difference between a "high chance of falling asleep" and a "moderate chance of falling asleep." Sufficient test–retest reliability was shown in children under 12 (ICC: 0.856), with insufficient test–retest reliability in children 12–17 years (ICC: 0.656). Given concerns around the interpretability of the ESS-CHAD, it is reasonable to assume older children would have a higher test–retest score than the younger cohort; however, this was not observed. This may be attributed to the small population size used in under 12 years (n = 8 untreated/n = 13 treated) and calls for further validation studies to be undertaken.

NSS (adult and pediatric) Conversely, we found several validation studies of the NSS. Development was briefly detailed in Dauvilliers et al. and validated for use in an N1 population [25, 26], but no content validity studies were found for either the NSS or the NSS-P. There are some concerns around the comprehension of the NSS-P, as one study stated that responses from 20% of participants were excluded from the study as they misunderstood the question/symptoms [26]. The NSS was created to assess the traditional "five symptoms" of narcolepsy, with a final combined score reflective of overall symptom severity. Yet the NSS/NSS-P does not contain subscales, thus limiting its ability to evaluate change in the different symptoms of narcolepsy and limiting its applicability to N1 when it could also be used in an N2 population. Allowing the five symptom domains to be scored as individual scales would allow the assessment of individual symptoms whilst allowing for subscales to be assessed for appropriate measurement properties and combined into an overall

final score. Further validation studies could be conducted using this format and across the five symptom domains (e.g. assessing responsiveness to EDS treatment, responsiveness to cataplexy treatment).

Other PROMs The evidence base for psychometric properties of other PROMs used in narcolepsy trials was either very limited or completely lacking.

Summary Based on the results of this review, no PROM can be recommended as a measure of treatment efficacy in a narcolepsy population. The ESS and ESS-CHAD purport to measure "average sleep propensity." However, evidence suggests they may not be appropriate for use as an endpoint for EDS, as patients have reported EDS extends beyond sleepiness [4, 53]. High-quality psychometric property studies that are not retrospective analyses of clinical trials are needed to inform several psychometric aspects, particularly construct validity. To inform the property of responsiveness, identification of a MCID using anchor points (e.g. patient and/or clinician-based determinants of "change" or improvement) are required, as has been done with other conditions (e.g. depression) [52]. Conversely, the NSS and NSS-P contain questions related to EDS that extend beyond sleepiness, with "daytime sleep attacks" and "worry" around falling asleep throughout the day assessed. Neither the NSS nor NSS-P can be recommended for assessing treatment efficacy in RCTs as the PROM results in a final score comprised of five narcolepsy symptom domains combined. This raises questions about its appropriateness for assessing an intervention that only targets one symptom. The addition of subscales for each symptom and further psychometric testing are recommended.

Research agenda/future prospective

To accurately assess treatment efficacy in narcolepsy, EDS and other symptoms first need to be clearly defined in narcolepsy phenotypes (i.e. N1/N2, adult/child). Persons with narcolepsy have indicated in several forums that EDS extends beyond the feeling of sleepiness [4, 53]. Furthermore, work is needed to clarify these dimensions through qualitative study and extends to other symptom domains such as cataplexy. Only then can appropriate outcome measures be chosen or developed to accurately capture change in these domains.

To ensure PROMs used in narcolepsy RCTs are appropriate for use, both quality psychometric studies of existing PROMs and perhaps the development of PROMs specific to narcolepsy are needed. This includes validated measures for assessing cataplexy as diaries may not be able to distinguish from similar phenomena (e.g. cataplexy mimicries such as epilepsy) [4]. Given the context of treatment efficacy in RCTs, priority should be given to the development of MCIDs using anchor points that are meaningful to people with narcolepsy (e.g. HR-QoL, ability to work, etc). This would allow for a better understanding of the responsiveness of each PROM in use.

Conclusion

This systematic review identified the most common outcome measures used in RCTs in narcolepsy populations and assessed the psychometric properties of PROMs used. While the ESS is the most common outcome measure used in RCTs of narcolepsy treatments, there seems to be remarkably little evidence of its psychometric properties. Given the primacy of the ESS, a thorough validation study of its measurement properties seems overdue. Further study is needed around what aspects of EDS and other symptoms are important to people with narcolepsy before we determine how best to measure these. Our study points to the need for comprehensive PROMs to be developed for narcolepsy (tailored for subtypes and adults/children), as well as further high-quality validation studies of existing PROMs. Furthermore, identification of a minimal clinically important difference is needed from the patient perspective for each PROM before we can be confident that we are accurately measuring the symptoms experienced by persons with narcolepsy and to what extent interventions are efficacious.

Supplementary Material

Supplementary material is available at *SLEEP* online.

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Disclosure Statement

None declared.

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Chapter 6: What do persons with narcolepsy and their family/carers perceive 'well-managed' narcolepsy to be?

The results from Chapter 5 suggest that 'well-managed' narcolepsy is primarily based on symptom control, at least in a clinical trial setting. The ESS was the most common outcome measure assessing EDS in narcolepsy RCTs. However, persons with narcolepsy have described EDS as more than feeling sleepy or 'falling asleep' [22]. The ESS has not been adequately validated in a narcolepsy population and appears to lack concordance with the second most frequently used outcome measure, the MSLT. The two most frequently used outcome measures in narcolepsy RCTs lacking concordance makes it more difficult for regulators and healthcare professionals to compare results and navigate treatments best suited for their patients. Few studies included measures of impact on quality of life or other areas that persons with narcolepsy prioritise (e.g. ability to work and perform self-care). These outcomes do not appear to align with the perceived needs and priorities that persons with narcolepsy have. There also appears to be a lack of clarity around what EDS encompasses (partly due to a lack of content validity), with little known about how those with narcolepsy perceive this symptom. These findings led me to hypothesise that the concept of 'well-managed' narcolepsy is perhaps not known or well-defined, at least from the perspective of those living with narcolepsy.

The results from chapters 3 and 5 inform the direction of the subsequent two studies I conducted. I wanted to explore the needs, concerns, and barriers to care of those living with narcolepsy in further detail, using a more extensive and diverse sample. I also wanted to explore how persons with narcolepsy and their family/carers perceive 'well-managed' narcolepsy to be. To do this, I conducted 1:1 semi-structured interviews, guided by the results from Chapter 3, where we previously identified the domains persons with narcolepsy and their families and carers consider important.

Several submissions by persons with narcolepsy to the parliamentary inquiry described their spouses and family members misunderstanding narcolepsy and trivialising symptoms. This informed the decision to interview each group separately to explore their experiences and perspectives, which

may sometimes diverge. Further, narcolepsy onset typically occurs in adolescence, allowing the unique opportunity to explore the parent/carer perspective of living with narcolepsy.

Chapter 7: A Qualitative Exploration of the Lived Experience of Mothers' Caring for a Child with Narcolepsy

The following chapter has been submitted for publication in a peer-reviewed journal:

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Title: A Qualitative Exploration of the Lived Experience of Mothers' Caring for a Child with Narcolepsy

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Abstract

Introduction: Parents/carers of a child with narcolepsy (CwN) are often required to become an expert in narcolepsy and navigate healthcare, education, and welfare systems on behalf of their child. Managing paediatric narcolepsy is complex and challenges the child and the entire family, yet few studies have explored carers' experiences.

Methods: Twenty mothers (50% had a CwN <18 years at the time of interview; 85% NT1) participated in a 1:1 semi-structured interview. Participation from fathers was sought; however, none were recruited. A multidisciplinary team of researchers/clinicians analyzed interview transcripts using thematic analysis.

Results: Mothers perceived that most people misunderstood the whole-person impact of narcolepsy, including their child's peers, teachers, and support networks. Narcolepsy had a substantial psychological impact on both the child and the whole family, yet was largely unaddressed by healthcare professionals, leaving mothers unsure of where to turn for help. Most parents described negative experiences with their child's specialist, often perceiving the specialists to lack knowledge specific to narcolepsy. Information about illness trajectory and support services was limited or inaccessible, fuelling many mothers' hopes and fears for their child's future.

Conclusion: Our results contextualize the whole-person impact of narcolepsy from the perspective of parents and carers, highlighting the need for proactive inclusion of parents/carers in developing healthcare policy and practice. It calls for developing tools and resources to capture 'well-managed' narcolepsy from the perspective of parents/carers for use in research and clinical practice.

Introduction

Narcolepsy is a rare neurological sleep disorder affecting the ability to control regular sleep-wake cycles. Narcolepsy is often characterized by Excessive Daytime Sleepiness (EDS), a term used to describe a collection of symptoms associated with feeling sleepy throughout the day. Another is cataplexy – muscle paralysis triggered by emotion that is usually positive (e.g. laughter)[1]. Cataplexy is the only symptom specific to narcolepsy and is used to differentiate between subtypes of narcolepsy, narcolepsy with cataplexy (NT1) and narcolepsy without cataplexy (NT2) [1,2].

Like other rare disorders, a lack of knowledge and awareness of narcolepsy has been observed amongst the public and healthcare professionals [3]. Narcolepsy has been shown to carry substantial psychosocial and economic burdens and is associated with health-related stigma[4-7]. As such, a person living with the disorder is often required to become an expert and advocate for their illness[8]. With the onset of narcolepsy typically occurring during adolescence [9], the role of illness expert usually falls to parents/carers, in addition to coordinating care, navigating education and healthcare systems, treatment adherence and applying for reasonable accommodations in the workplace/school [10].

Managing a complex disorder like narcolepsy can be challenging for the child and the whole family. Previous studies show adolescents with narcolepsy have impaired family function, have a higher risk of depression, social and emotional distress, aggressive behaviour, and poorer education outcomes [11-14]. However, few studies have explored these issues from the perspective of parents/carers caring for a child with narcolepsy (CwN). This study explores the needs, concerns, and barriers to care experienced by parents/carers of adult and adolescent CwN.

Methods

Ethics and design

We carried out 1:1 semi-structured interviews that were analyzed thematically [15]. Ethics approval was granted by The University of Sydney Human Research Ethics Committee (reference 2021/110). The consolidated criteria for reporting qualitative research (COREQ) checklist was also used [16] (Appendix A). The interview schedule was developed by AS and JC (Appendix B), informed by the findings of a previous thematic analysis of narcolepsy patient and family/carer submissions made to a public stakeholder meeting in Australia [17].

Recruitment and consent

Flyers, emails, and social media posts were used to recruit potential participants. Patient advocacy group 'Narcolepsy Support Australia' assisted by distributing recruitment materials via social media accounts. To be included, potential participants needed to live in Australia and be a parent (mother/father) or carers of someone diagnosed with narcolepsy by a registered sleep specialist. Participants reviewed the participant information and were given the opportunity to ask questions before giving informed consent. Interviews were conducted using a consecutive and iterative approach, with purposive sampling[18] used to recruit a diverse sample of parents/carers from different Australian states/territories due to differences in healthcare systems across jurisdictions.

Interview procedure

One interviewer (AS) conducted semi-structured interviews from 30/06/2021 – 14/10/2021 using Zoom, an online meeting platform. Both audio and video recordings were collected, and field notes were written throughout all interviews. Data saturation was determined to have occurred when no new needs, concerns, or barriers to care were mentioned, or different perspectives were given on existing topics across three consecutive interviews. This decision was based on field notes and decided by three authors (AS, JC, NG) fortnightly.

Data analysis

Interview recordings were transcribed using the NVivo Transcription Service, anonymized and checked for accuracy (AS and CK). Data were interpreted thematically using the established six-step qualitative analysis process [15], as it provides a flexible method of analyzing and interpreting substantial amounts of qualitative data (additional information – see Appendix C). Six authors from diverse backgrounds (e.g. qualitative research, medicine, pharmacy and lived experience) participated in the analysis (AS, JC, NT, DN, AM, CK).

Results

Participant characteristics

Twenty-three participants were recruited, all of whom were primary carers of a CwN. Despite attempting to recruit mothers and fathers for this study, only mothers expressed interest in participating. Data saturation occurred after twenty interviews, averaging 52 minutes and ranging from 31 to 100 minutes. Half of the mothers indicated their child was under 18 years (mean age 15.9 years, SD 2.6), while the remainder were mothers of an adult CwN (mean age 25.9 years, SD 5.2).

Qualitative data synthesis

Three overarching themes were identified in our analysis: 1) Changing Identities – Families learning to live with narcolepsy, 2) Seeking, reaching, utilizing – The Help-Seeking Journey of Narcolepsy, and 3) 'Is she going to be at home forever?' – Hopes and fears for the future. Each theme is summarised below, along with exemplar quotations from mothers (tables 1-3).

Theme 1: Changing Identities – Families Learning to Live with Narcolepsy

Subtheme 1: "[he told me] it would be easier if I had cancer because they'd understand that" – Misperceptions and misunderstanding of narcolepsy

Mothers perceived widespread misunderstanding of narcolepsy among their CwN's siblings, peers, and educators. The misunderstanding was also described among mothers' own social groups, where symptoms were often trivialized as simply *"sleeping too much"* **[Mother 11]**. Most were perceived to lack awareness of narcolepsy symptoms, daily impact and behaviours (e.g. aggression, lack of focus). In a high school context, one mother recounted being told by a teacher that her child *"didn't actually have a medical condition"* **[Mother11]** and was 'attention seeking'. Others said their child was singled out in front of the class or forced to stand or exercise mid-lesson to prevent sleep onset, despite the school being informed narcolepsy was a medical condition. Misunderstanding occurred in peer groups, where sleepiness and weight gain symptoms were often associated with laziness. CwN did not want to be seen as different from their peers, often impacting management strategies like napping as "*there's no way in the world [they're] going to be that loser that needs to go and have a sleep at school"* **[Mother1]**. As a result of this perceived misunderstanding, mothers described a breakdown of trust between their CWN and those closest to them, often resulting in social isolation and bullying. This misunderstanding continued into the workforce in later years, with one parent recounting senior staff at her child's employer lacked *"understanding of [accommodations]"* **[Mother 18].**

Application for social supports (e.g. the National Disability Insurance Scheme) and school or workplace accommodations under the Disability Discrimination Act (i.e. modifications to the school or work environment, their processes, or working condition) were widely considered a *"nightmare"* **[Mother 2]** for parents to navigate. Decision-makers were perceived to lack specific knowledge of narcolepsy and its impact on daily function, trivializing narcolepsy as just feeling sleepy.

Subtheme 2: Moving the goalposts – Aspirations and limitations of families living with narcolepsy

Both parents and CwN struggled with the functional impairment associated with narcolepsy. Impairment often resulted from daily fatigue, fluctuating energy levels and medication side effects impacting all domains (e.g. education, sport, recreation). There was broad concern for the mental health of CwN, specifically when faced with the possibility that they may not reach milestones along with their peers (e.g. acquiring a driver's license) or have the life they envisaged (e.g. independence). Struggles with mental health were amplified through social media use, encouraging the CwN to compare themselves with others. For some (n=4), this got to the point where they were concerned their child may harm themselves. CwN who experienced severe cataplexy were described to have lost confidence in their ability to perform everyday tasks (e.g. swimming, going for a walk, socializing). The child was perceived to withdraw and isolate themselves from friends and family to avoid triggering an attack, impacting these personal relationships. Mothers also spoke of their aspirations for their children and needing to adjust to the reality of functional impairment associated with narcolepsy (e.g. in competitive sport, starting a family). Mothers described having to *"let go"* **[Mother17]** of who their child was pre-narcolepsy and grieve, similar to the death of a loved one. Others could not reconcile their aspirations for their child with the lived experience of others living with narcolepsy. These mothers avoided narcolepsy-related social media and online support groups as they felt overwhelmed hearing first-hand accounts of how impairing narcolepsy could be, with one mother emphasizing, *"I'm not ready to accept that that is going to be [CwN]'s future"* **[Mother2].**

Subtheme 3: Cohesion – The impact on the family unit

Behavioural issues were often described as the most challenging part of caring for a CwN, negatively impacting family cohesion. One mother described it as sometimes *"feel[ing] like you're in an abusive relationship"* **[Mother1]**. The unpredictability of symptoms posed further challenges for families as the child transitioned into adulthood. Family members were expected to *"stop what they were doing"* **[Mother17]** to respond to the CwN's needs, especially around transportation in rural areas. Mothers raised concerns that their CwN felt excluded from the family, particularly when *"having a nap or [not] alert or awake"* **[Mother10],** as they missed out on bonding moments and quality time spent with family. Participants noted how cataplexy strained the interaction and relationship between siblings of the CwN. For example, some siblings avoided making the CwN laugh for fear of triggering a cataplexy attack, with some feeling responsible and guilty for triggering attacks that sometimes led to injury (e.g. hitting their head on a table).

Table 1: Summary and exemplar quotes from theme 1 – 'Changing Identities – Families Learning to Live with Narcolepsy'

Sub-theme	Summary of Synthesis	Exemplar quotation
"[he told me] it would be easier if I had cancer because they'd understand that" – Misperceptions and misunderstanding of narcolepsy	• Narcolepsy and its impact are misunderstood by three groups of people in CwN's life: social network (e.g. peers, family), healthcare professionals (GPs and specialists) and welfare, education and vocation (e.g. teachers, government departments, public servants) • Narcolepsy is seen as just sleepiness • Not seen as functionally limiting; an 'invisible disease' • Schools/workplaces lacked information about narcolepsy; implications for accessing adjustments to standard education/employment arrangements	• *"But so even now, after nine months, we got an email after camp because he fell over and cracked his head open. And we got an email to say, 'OK, we've now changed [CwN]s profile to say that he has a medical problem, not a learning enhancement condition."* **[Mother1]** • *"It was a show on television or something online. But it was this woman that had a saying and she would say, 'oh, I'm a lazy cow' in a Scottish accent. There was this funny thing, and all the kids used to say it to [name of CwN] all the time. So but I think it was quite harmful. She would laugh it off. But it was really funny saying to all the kids, 'I'm a lazy cow; I can't even do this project'."* **[Mother5]** • *"I guess it would be probably her mental state that she, she feels that she's different from everyone else. She can't do what everyone else does"* **[Mother16]** • *"[their sibling] doesn't understand that there are things that are rare diseases and internal things that you can't see. But it doesn't mean they're not causing a major problem."* **[Mother4].**
Moving the goalposts – Aspirations and limitations of families living with narcolepsy	• Parents and CwN struggled to adjust to the functional limitations of narcolepsy • CwN experiencing 'fear of missing out' on milestone events • Psychological support is needed for parents; the grieving process when a child is chronically ill	• *"So it's like the son that I raised, the one where he's 13 [pauses], it's like he died because the one that I've got now was very different to who he was back then. And it's not that you love this one any less. It's just it's not what it was, and that… and that's a really hard thing."* **[Mother13]**. • *"And as a mum, that's really hard to say to your child, 'Well, slow down, or maybe we have to choose, do we do this or do that?' So, it's just the frustration that she can't do… reach her potential or do what she wants to do because of this thing. This narcolepsy…"* **[Mother3]**
Cohesion – the impact of narcolepsy on the family unit	• Psychosocial sequelae (e.g. behavioural issues) of narcolepsy affected the relationship between CwN and other family members • Parents took on the role of 'support worker' due to the lack of services available • Cataplexy may cause siblings to feel guilty if they trigger a cataplexy attack	• *"So I think there was a lot around that, like my boys even now say, Oh, [name of CwN] can be, [name of CwN] can be such a bitch'. I said, 'Yeah, imagine how tired you are'. I said, 'You are never…when you guys are really tired, or you've been out partying a weekend, and you're not very nice to be around'. And I said, 'Imagine feeling like that, like all the time'. I said, 'Yeah, you would be a bitch. And I'd be a bitch too."* **[Mother17]** • *"what's normal for everybody else becomes a real chore for people living with narcolepsy, and as a consequence, their support people are the ones that sort of cop it [laughing]."* **[Mother4]**

Theme 2: Seeking, reaching, utilizing – The Help-Seeking Journey of Narcolepsy

Subtheme 1: "Ignored, ignored, ignored" – barriers faced when seeking help

Mothers often expressed concerns about the pathway to diagnosis and delays experienced. Falling asleep at school, in the car to and from school and at home after school were among the first signs their child was experiencing difficulties. The General Practitioner (GP - the primary health care provider in Australia) was the first point of contact on the parents' help-seeking journey. An existing, person-centric relationship between parent and GP was described as crucial in facilitating a timely referral to a specialist. Without such established relationships between GPs and parents, substantial diagnosis delays occurred, where concerns were not taken seriously, or symptoms trivialized as *"depression"* **[Mother16]**, *"low iron levels"* **[Mother14]** or simply *"because he was growing"* **[Mother19]**. Parental persistence was necessary to obtain a specialist referral by seeking alternate opinions or repeated help-seeking attempts. Most parents did not blame GPs for the delay in diagnosis, stating they were overworked, time-poor, and not expected to be knowledgeable about all conditions.

Parents also spoke of their experience with paediatricians and sleep and respiratory specialists (a combined speciality in Australia). Most mothers (n=15) described negative experiences, with a perceived lack of specific knowledge of narcolepsy and an overfocus on pharmacotherapy targeting daytime sleepiness. This impacted the parent-physician relationship, with one mother saying they felt *"pretty well abandoned, left to our own devices"* **[Mother5]**. Many questioned why they had been referred to a *"sleep apnoea specialist"* **[Mother5]**, *"lung specialist"* **[Mother4]** or *"respiratory physician"* **[Mother7]** rather than someone with perceived experience or expertise treating narcolepsy. Conversely, positive experiences with sleep physicians and paediatricians were described where mothers felt listened to, where the broader impact of narcolepsy *"not only for [CwN] but for the whole family"* **[Mother1]** was understood (e.g. one mother described her child's physician writing to their school to educate and advocate on their behalf).

Perceived lack of knowledge around narcolepsy, even by specialists, corresponded with suboptimal management options. Caregivers often felt person-centric management of other domains affected by narcolepsy was overlooked, particularly psychological support for the CwN and caregiver. No formal psychological interventions were reportedly offered as part of narcolepsy management. As such, some mothers independently tried to access services once they recognized their CwN was struggling (e.g. experiencing behavioural issues, risk of harming themselves).

Subtheme 2: Variability in accessible healthcare

As few sleep specialists practised in rural areas, healthcare access was another key issue. Often, overnight trips to urban centres were necessary to access sleep studies. Specialist access varied between states, with one mother describing hardship faced when the sole sleep specialist working in one state retired. Their CwN was without care for some time, ultimately requiring interstate travel to find an appropriate specialist. This came with additional difficulties filling prescriptions, with some narcolepsy treatments considered controlled substances by law. Pharmacies in select states were reportedly unable to fill scripts written by medical practitioners living in another state due to differences in legislation. Telehealth was used to connect with specialists around Australia who were perceived as more knowledgeable about narcolepsy, but similar issues concerning filling scripts were described.

Medication access was also variable. Xyrem, a first-line treatment for narcolepsy not yet registered for use in Australia, was described as prohibitively expensive and, therefore, inaccessible for most. Few reported receiving compassionate funding for this medication through their local public

hospital. One mother recounted that their paediatrician applied for funding for treatment. Approval could only be granted while the child was in the paediatric system and continued as they transitioned into the adult system. They were told funding was unlikely if the initial application was made after their child transitioned into the adult hospital system. Others had similar experiences, with medication access perceived as dependent on the treating specialist's connections or their standing in the public hospital system.

Subtheme 3: Empowering parents – The need for accessible information

Parents reported limited information and educational resources available to families and CwN. Information about the tangible day-to-day impact of narcolepsy, management strategies that have worked with other families, upcoming treatments, and potential prospects for their child were sought but primarily unavailable. Mothers desired the information to be easily accessible and shareable, as many wanted to use it as part of advocacy or awareness campaigns. Parents often wanted information on accessing accommodations through the healthcare, welfare, or education systems. While specialists were expected to provide this information, its creation was seen as the healthcare system's responsibility rather than the responsibility of healthcare professionals or NGOs. In the absence of readily available information, mothers used resources available on the internet and online support groups. This allowed mothers to share experiences, ask questions, find strategies that have worked for others, and gather recommendations about which specialist physicians were perceived as knowledgeable about narcolepsy.

Table 2: Summary and exemplar quotes of the theme 2 – 'Seeking, reaching, utilizing – The Help-Seeking Journey of Narcolepsy'

Theme	Description	Exemplar quotation
'Ignored, ignored, ignored' – barriers faced when seeking help	• GPs trivialized symptoms; a more patient-centric relationship led to fast diagnosis • Physicians perceived to lack knowledge specific to narcolepsy • Limited psychological services accessible for parents or their CwN; should be available as part of the treatment/management plan	• *"And I feel like I just remember saying to doctors. I've got two other sons; I know what a tired child is like, and this is different. This isn't the same as my two other sons when they get tired and cranky. This is different. This is constant; this is all the time. He is just constantly a wreck. He's constantly tired."* **[Mother2]** • *"I think if he had if he had brushed me off, I think that we would still be facing this long, long period of where people are saying that they have not been diagnosed for ten years or something"* **[Mother17]** • *"A lot of the time, I don't get listened to. I know this is really sexist, but unless my husband's with me, they don't want to listen because you're just a paranoid mum, you're too emotional about it, or they don't believe you that it happens."* **[Mother3]** • *"it's not respiratory; there's nothing in the slightest respiratory there. Like nothing, nothing. So you've got people that are well trained in something that is totally irrelevant to where we're at"* **[Mother13]**
Variability in accessible healthcare	• Access to physicians and diagnostic equipment varied between states and rural/urban settings • Variability in access to treatments and hospital funding	• *" The other thing, of course, is I don't know what it's like in other states, but here in (name_of_state), if she started on Xyrem as a child, there's an agreement with the public adult hospital to continue the subsidy of the Xyrem. But you if you started after 18, or you can't start it after 18. It's not something that you can access. So, I think it's one of those ethical things that you can't just continue something that's already been started but, but they have a bit of a line about not prescribing it for people or for adults."* **[Mother7]** • *This kind of flounders by yourself. There's no way that has the complete package. You kind of had to make it up as you go. Which I think would be quite hard if you don't have the resources or you don't have the time to do that"* **[Mother8]**
Empowering parents – The need for accessible information	• Parents unable to access quality information about narcolepsy across different domains (e.g., treatments, daily impact, what school accommodations are available)	• *"So I think I think one of the issues with narcolepsy is people get diagnosed, and then that is it in terms of diagnostics or following the disease or having a look at how that progresses over time because we don't do any more diagnostic studies. Once you got it, you got it. That's the end."* **[Mother4]**

Theme 3: 'Is she going to be at home forever?' – Hopes and fears for the future

Subtheme 1: An uncertain future – perceived future needs of CwN

Uncertainty around not knowing how narcolepsy would affect their child and family in the future was described as among the most challenging part of caring for a CwN. The inability to predict when symptoms would occur, fluctuations in energy levels and fatigue, and possible side effects of treatment compounded this uncertainty. Participants speculated on their child's future with narcolepsy. As parents took on the role of caregiver and support person, they expressed fear about what their child would do when they were no longer around and whether there were services for their child to be assisted or cared for. Fatigue and daytime sleepiness were perceived as significant hurdles to achieving independence. Others feared their child would be unable to hold a full-time job, fearing for their financial security and ability to afford housing as *"her profession, it's not compatible with narcolepsy… she'll be without employment whatsoever, have no income"* **[Mother20]**. This intersected with fears that CwN would be unable to live in shared housing, as limited energy and fatigue would restrict their child from contributing equally to household chores and maintenance.

Subtheme 2: Advocating for change – who takes charge?

Support groups were viewed as the primary avenue for improving healthcare for CwN. Mothers often felt it was their responsibility to advocate for their CwN. Mothers with a CwN under 18 years perceived their child to lack independence to advocate for themselves, with advocacy seen as an extension of their parental role. Those with adult CwN spoke of the need to advocate if they thought their child could not. This stemmed from the belief that their child had limited energy and needed to prioritize more important daily living tasks rather than expending energy on advocacy, particularly *"if it doesn't produce any change... well, what's the point?"* **[Mother9]**. Physicians, peak bodies, and healthcare systems were regarded as responsible for improving healthcare quality. However, the tone of the conversation often shifted towards resignation and apathy when discussing this, as described by one mother that *"no one is pushing for anything... no one is fighting in that corner"* **[Mother4].**

Subtheme 3: Staying Safe – Safety Concerns of Narcolepsy

Parents had concerns about narcolepsy and their child's safety in two main areas: napping and cataplexy. Mothers of female CwN described concern about napping safely, regardless of age. They often spoke of needing to "lock" doors and have their own secure space when napping (e.g. in a car). One mother feared her daughter *"would be seen as vulnerable"* [Mother 9] if found asleep on public transport and the target of theft or assault. In contrast, mothers of male CwN saw public transport as an opportunity to nap and were more concerned their child would miss their stop. Cataplexy was described as particularly hazardous to their child's safety. While attacks could occur at any time, those at school, during sports or around bodies of water (e.g. swimming, surfing) often resulted in significant physical injury. One parent reported that their CwN had *"chipped his tooth. He's broken his wrist. So, there can be the small ones, but he's gone down several flights of stairs."* **[Mother1]**.

Table 3: Summary and exemplar quotes of the theme 3 – ''Is she going to be at home forever?' – Hopes and fears for the future

Theme	Description	Exemplar quotation
An uncertain future – perceived future needs of CwN	• Fear their child will be unable to live independently without parental support and question what they would do when the parent was no longer around to support • CwN will not be able to share a house with other adults due to limited energy, making cohabitation difficult	• *"The uncertainty of what your day is going to be, so lots of times [CwN] will be ready to go out, or we'll be ready to go out, or he'll be ready to go to school or training, and then he can't because his cataplexy is too bad or he's just too tired, or it's or his mood's revolting"* **[Mother1]** • *"And then I guess from my point of view, it's like, you know, she doesn't… she just doesn't have the energy, like, to really look after herself. Does that make sense? So, like, things like cleaning her room, putting out washing, getting food, it's, it's just all too much for her*" **[Mother16]** • "*I think it is not being able to, um, share a house because she's an adult, sharing a house, but not being able to share a house, as you would with another adult, you can't rely on them to do regular routine processes because there's no time*" **[Mother5]**
Advocating for change – who takes charge?	• Parents wanted to contribute their lived experience to health policy but did not know of any pathways to contribute • Parents of adult CwN still advocated as they perceived their CwN lacked the energy to do so themselves	• *"I suppose I understand like I don't think [Name of CwN] would fight for it, I think because he will just look at it and say 'that's going to consume too much of my energy that I already don't have"* **[Mother13]** • *"I mean the politicians you can keep writing to, but it doesn't seem to, you know, I mean, I suppose it all comes down to dollars. And if there's not that many people with on or with narcolepsy that are diagnosed compared to other drugs, you know, we seem to be getting sort of not the same results as other illnesses would"* **[Mother6]**
Staying Safe – Safety concerns of Narcolepsy	• Fears for the safety of female CwN on public transport • Fear cataplexy has the potential to cause physical injury	• *It's just about being vulnerable as a sleeping woman on public transport after 10 o'clock, and you think, 'my God*" **[Mother 5]**

Discussion

To our knowledge, this is the first qualitative evaluation of mothers' experience of caring for a child with narcolepsy (CwN) that also explores the impact this role has on the parent. While any type of carer was eligible to be interviewed, strikingly, only mothers agreed to participate. We are unsure whether this is because mothers are still the primary caregivers in most families of CwN or self-selection bias, with fathers less inclined to participate in research.

A key finding of this study was that the psychological and behavioural aspects of narcolepsy were perceived to be one of the most challenging aspects of caring for a CwN. A high prevalence of psychological comorbidity in adolescent narcolepsy is well established [1,4,7,11,13,19,20] and has shown to have a substantial impact on health-related quality of life [20,21] [7]. However, it appears that healthcare professionals did not address psychological comorbidity, with many unsure where to turn for support. Caring for a CwN also had a substantial psychological impact on the whole family unit. This is consistent with existing evidence of family dysfunction in adolescents with narcolepsy[11]. These findings are important as they contextualize the psychological challenges CwN and their families face and suggest a need for tailored interventions, support, and services to address these issues. They also suggest that assessment of these psychosocial domains is required as part of determining what 'well-managed' narcolepsy looks like.

Most mothers described overwhelmingly negative experiences when navigating Australia's healthcare, welfare, and education systems. However, few avenues were known to mothers where they could voice their concerns or contribute to developing health policy and practice. It suggests the healthcare system may need to be far more proactive in including parents and carers, particularly if challenges faced in paediatric narcolepsy are to be addressed. While mothers were aware of issues facing their children, many reported they did not know any available supports, services or how to access them. Lack of information was repeatedly identified as a key concern, driving many maternal hopes and fears associated with their child's narcolepsy. Some US-based advocacy and charity organizations (e.g. Project Sleep) have created free, high-quality information resources. However, much of the requested information is related to Australian-specific services and thus unavailable. Requested information included education and vocation domains, education and workplace accommodations available under Disability Discrimination Legislation, and access to welfare and national disability support. Thus any information requested would need to be jurisdiction-specific and locally produced.

We also observed substantial misalignment in care priorities between healthcare professionals and mothers caring for a CwN. Specialists were perceived as overly focused on treating EDS rather than providing holistic care for narcolepsy. This could be related to the heterogeneity of narcolepsy, the rarity of the illness, or simply a lack of knowledge among healthcare professionals [3]. Some of the concerns raised by parents did appear to be compounded by organizational structures specific to the Australian healthcare system. The fields of sleep and respiratory medicine are closely linked in Australia. Regulatory bodies categorize sleep specialists as 'respiratory and sleep medicine' practitioners as there is no independent sleep speciality [22]. Health professionals and peak bodies have raised concerns about a lack of diversity amongst specialists trained in Australia, where most sleep specialists were also respiratory specialists [23]. For those looking to specialize in sleep, training focused primarily on respiratory sleep disorders [23]. The close link between sleep and respiratory medicine likely explains why mothers described their treating child's physician as a 'lung doctor' or 'sleep apnoea specialist' when speaking of their frustrations around quality of care. Overall, it raises questions about whether even specialist physicians have sufficient expertise to manage narcolepsy.

The lack of narcolepsy expertise is particularly problematic for those that live rurally or in a state with few sleep and respiratory specialists. Due to the low number of practising specialists, parents and CwN entering the Australian public health system lack a choice of specialists they are referred to. This presents a possibility that someone with limited expertise or experience in non-respiratory sleep disorders may treat someone with narcolepsy. Specialists in public hospitals also act as gatekeepers to hospital funding, treatments, and social support services, which can have far-reaching consequences for the quality of life and illness trajectory. Distinguishing the practice of sleep medicine from respiratory medicine may be an important step for improved management of non-respiratory sleep disorders beyond narcolepsy. Lastly, fostering a multidisciplinary approach towards sleep medicine like that found in Europe and the USA may help improve the management of narcolepsy and other sleep disorders. An ideal solution would result in diversifying physicians trained in sleep, including training psychiatrists, neurologists, general practitioners, and internal medicine physicians in sleep medicine [24].

Strengths and Limitations

The first author (AS) is a lived-experience researcher with narcolepsy type 1 and is considered a strength and a potential limitation of this study. Having lived experience provided a unique opportunity during interviews as participants could engage with a member of their community, offering insight that they otherwise may not have shared. Conversely, AS acknowledges his bias associated with the topic, given his own experience with narcolepsy. Using a reflexivity diary and having a large team with diverse experiences and backgrounds (e.g. healthcare professionals, psychologists, pharmacists, and other academics from outside of sleep research) helped to challenge preconceived ideas. All interviews were in English; therefore, this study lacked representation of non-English-speaking populations that may have different cultural perceptions of sleep [25].

Similarly, we were unable to recruit any fathers of a CwN. As such, our interviews may not represent the diversity in experience of all carers. We also acknowledge potential sampling bias, where some parents with negative experiences may have been more inclined to participate. Lastly, some themes and experiences were explored from the mother's perspective, not the CwN. Further research should be conducted to expand the sampling frame of individuals involved in the care of CwN and to explore the concerns of people with narcolepsy directly.

Conclusion

This study highlights the challenges faced by mothers caring for a child with narcolepsy (CwN). It also contextualizes the whole-person impact narcolepsy has on a CwN from the carers' perspective. The results highlight the need for more person-centred healthcare systems, including establishing pathways for carers to contribute to developing health policy and practice and creating jurisdiction-specific information to empower parents as informed decision-makers. These findings also provide a useful guide for future co-design of paediatric narcolepsy resources, designed to capture what matters most to parents/carers across research and clinical practice.

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Chapter 8: Making Sense of Narcolepsy: A Qualitative Exploration of How Persons with Narcolepsy Perceive Symptoms and Their Illness Experience

The following chapter has been submitted for publication in a peer-reviewed journal:

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Making Sense of Narcolepsy: A qualitative exploration of how persons with narcolepsy perceive symptoms, daily impact, and the illness experience

Abstract

Introduction: Understanding how persons with narcolepsy conceptualise symptoms, daily impact and illness experience is key to facilitating dialogue between patients and healthcare professionals. These concepts are usually explored from the perspective of healthcare professionals and researchers, with the perspectives of those living with narcolepsy rarely examined.

Methods: 127 self-reported persons with narcolepsy were recruited from an Australian patient support group. A short demographic survey was completed. All agreed to participate in a subsequent 1:1 semi-structured interview. Saturation was reached after 24 interviews (mean age of interview participants = 33 years (SD 11) with 44% reporting cataplexy). A multidisciplinary team of researchers/clinicians analysed interview transcripts using thematic analysis.

Results: Physical fatigue, sleepiness, and two separate experiences of 'falling asleep/sleep attacks' were perceived as distinct symptoms. These symptoms are often grouped as 'excessive daytime sleepiness'. Two experiences of cataplexy were identified, one triggered by acute emotion and another triggered by a stressor (e.g. high-stress situation). The severity of narcolepsy was often determined by the level of functional impairment rather than the frequency of symptoms. Almost all participants described experiencing anticipated stigma and internalised or 'self-' stigma, likely stemming from the societal devaluation of sleep and conflation of sleepiness with laziness.

Conclusion: Descriptions of common symptoms often differed between participants and the existing literature. Our results contextualise the lived experience of persons with narcolepsy and help clarify their healthcare needs and priorities. It also indicates that differences may exist between how 'well-managed' narcolepsy is perceived by persons with narcolepsy and healthcare professionals.

120-word statement of significance

Our findings suggest the symptom experience of narcolepsy is more heterogeneous than what is described in diagnostic manuals and the literature, with participants attributing their own meaning and experience to commonly used terminology (i.e sleep attack). The discrepancy in terminology could affect patient-physician communication, with both parties utilising the same terminology to communicate different concepts. It could also have implications for research that utilise PROMs to capture symptom severity/experience. We also observed persons with narcolepsy experience similar stigma as those with a concealable stigmatised identity. These identities can be hidden from others but are socially devalued and negatively stereotyped (e.g. mental health, sexual orientation). This finding is important as it likely contributes to the psychological comorbidity associated with narcolepsy.

Introduction

Identifying, diagnosing and assessing treatment efficacy in narcolepsy relies heavily upon the subjective experience of symptoms [1,2]. Often, the symptom experience is described from the clinical perspective of healthcare professionals rather than from the perspective of those living with narcolepsy. Narcolepsy is a rare sleep disorder characterised by several core symptoms, including excessive daytime sleepiness (EDS), cataplexy, hypnagogic hallucinations, sleep paralysis and disrupted nocturnal sleep [3]. Cataplexy is a key symptom of narcolepsy, described as a temporary loss of muscle tone, usually in response to positive emotion [3]. Identification and assessment of 'well-managed' cataplexy rely exclusively on subjective measures detailing the frequency of attacks, with objective testing rarely used [1]. The presence of cataplexy differentiates between the two types of narcolepsy: narcolepsy with cataplexy (narcolepsy type 1; NT1) and narcolepsy without cataplexy (narcolepsy type 2; NT2)[2].

EDS is another key symptom of narcolepsy. However, it is a non-specific term describing various phenomena related to sleepiness (e.g. sleep attacks, involuntary napping, difficulty sustaining attention). While these terms are used in clinical practice and across the literature, it is unclear whether persons with narcolepsy (PwN) use these terms in a similar way to healthcare professionals or even attribute the same meaning to these terms. Understanding how PwN conceptualises symptoms is essential for facilitating dialogue between patients and healthcare professionals, ensuring that the needs, concerns and impact associated with narcolepsy can be communicated and addressed [4].

There is substantial evidence showing narcolepsy has an adverse impact on health-related quality of life, long-term disability, and absenteeism and is associated with poor socioeconomic and psychosocial outcomes [5-9]. Much of this research comes from European or US narcolepsy populations, with little known of the impact of narcolepsy on other populations. In Australia, we know little of the impact narcolepsy has on daily life, nor whether the healthcare system is meeting the needs and concerns of PwN. Australia offers universal healthcare and welfare and disability support programs, yet many of the narcolepsy treatments considered first-line internationally are not registered for use or considered second-line, likely affecting illness trajectory. At a recent government-mediated stakeholder meeting, Australians with narcolepsy made written submissions detailing their concerns with healthcare and unmet needs. The final report and policy recommendations from this meeting addressed healthcare infrastructure and resources [10]. Conversely, a document analysis of the written submissions by PwN and their family/carers found they were primarily concerned with unmet psychological needs, access to government services and treatment, and knowledge of healthcare professionals [11]

This study explores these issues in further detail, including the needs, concerns and challenges faced by PwN when navigating the Australian healthcare system.

Specifically, we sought to gain an in-depth understanding of the following:

1. how persons with narcolepsy describe symptoms that impact their daily life, and,
2. the needs, concerns, barriers, and facilitators to care faced by those living with narcolepsy in Australia.

Methods

Ethics and design

The design of this study was a short cross-sectional survey and a 1:1 semi-structured interview that was analysed thematically [12]. Ethics approval was granted by The XXXXXXX Human Research Ethics Committee (reference 2021/110). The consolidated criteria for reporting qualitative research (COREQ) checklist was also used [13] (Supplementary A). A qualitative semi-structured interview schedule was developed by authors XX and XX (Supplementary B), informed by the findings of a previous thematic analysis of narcolepsy patient and family/carer submissions made to a public stakeholder meeting on the current state of sleep health in Australia [11].

Recruitment and consent

Flyers, emails, and social media posts were used to recruit potential participants. A patient advocacy group, 'Narcolepsy Support Australia', assisted with recruitment by distributing these materials via their social media account. To be included, potential participants needed to live in Australia and have self-reported receiving a diagnosis of narcolepsy by a registered sleep specialist. Participants had the opportunity to review the participant information and consent form and ask questions before giving informed consent. Interviews were conducted using a consecutive and iterative approach, with purposive sampling [14] used to recruit a diverse sample of NT1/NT2, male/female experiences.

Survey questions

Participants completed a short survey that collected demographic and other information about symptoms and delay in diagnosis. Specifically, participants indicated whether they experienced cataplexy brought on by emotion to assign them to NT1 and NT2 subtypes (with both subtypes included). Participants were also asked whether they were interested in participating in a subsequent one-hour semi-structured interview.

Interview Procedure

One interviewer (XX) conducted semi-structured interviews during COVID restrictions from 30/06/2021 – 14/10/2021 using Zoom, an online meeting platform. Both audio and video recordings were collected, with field notes written throughout all interviews. Data saturation was determined to have occurred when no new needs, concerns, or barriers to care were mentioned or different perspectives were given on existing topics across three consecutive interviews. Saturation was based on field notes and decided by three authors (XXXXXXX) during fortnightly meetings.

Data analysis

Survey data were analysed using statistical software package SPSS (version 25.0). Interview recordings were transcribed using the NVivo Transcription Service, then anonymised and checked for accuracy by an author (XX) and research assistant (XX). Data was interpreted thematically using the established six-step process of qualitative analysis [12], as it provides a flexible method of analysing and interpreting substantial amounts of qualitative data. Five authors from diverse backgrounds (e.g. qualitative research, medicine, pharmacy and lived experience) participated in the analysis (XXXXXXXX). The six steps include: (1) Become familiar with the data: Five randomly selected transcripts were allocated to each team member to familiarise themselves with the ideas and concepts discussed in the interviews. Insights, concepts and ideas identified by the analysing team were recorded; (2) Generate initial codes: the research team initially explored a sub-sample of data

by making comments in the participants' own words in a Microsoft Word document of the de-identified transcripts to develop a preliminary coding framework; (3) Search for themes: Open coding was conducted using NVivo 12 Software by one of the analysis team members; 4 & 5) Review and define themes: the themes in the coding framework continued to be collaboratively refined and named through an iterative process of reading, coding, reflection and discussion in fortnightly team meeting until all significant parts of the data had been considered. A codebook was collaboratively developed, which included sub-themes and overarching themes. All interviews were subsequently coded by author XX, with 20% double coded by author XX to check for reliability. The collaborative approach to analysis supported reflexivity as it encouraged comparisons and sharing of diverse perspectives the research group offered with their various backgrounds and lived experiences [15]; and 6) Write-up: the results were written up and reviewed by all authors.

Results

Description of participants

We recruited 127 participants who self-reported receiving a diagnosis of narcolepsy from a registered healthcare professional. All participants indicated they would like to take part in subsequent interviews. Saturation was reached after twenty-four semi-structured interviews (ranging from 34 min 43s to 68 min 13s in length, averaging 51 min 01s). Half of the participants reported experiencing cataplexy, while 70% reported experiencing a "sleep attack". Approximately 60% reported experiencing symptoms in adolescence, yet only 23% received a diagnosis before turning 18. Further, 22% reported a delay in diagnosis of > 10 years from symptom onset.

Thematic analysis

Our analysis identified four themes: 1) The symptom experience of narcolepsy – perspectives of excessive daytime sleepiness and cataplexy; 2) Making sense of the illness experience – perspectives of identity, daily impact, and the label of narcolepsy; 3) Making sense of long-term care: narcolepsy management following diagnosis; and 4) Making sense of the perception of narcolepsy – how do people with narcolepsy and others perceive the disorder.

Theme 1: Making sense of the symptom experience of narcolepsy – perspectives of excessive daytime sleepiness and cataplexy

Subtheme 1: Excessive Daytime Sleepiness – perceptions of a multidimensional construct

All participants reported experiencing symptoms that are usually grouped under the term Excessive Daytime Sleepiness (EDS) every day, with three broad components described: 1. Fatigue / physical lack of energy, 2. The feeling of being sleepy / sleepiness, and 3. the act of falling asleep (often called a "sleep attack"). Each component was perceived as a distinctly separate construct from other aspects of EDS (figure 1). Each component was also associated with varying degrees of functional impairment (ranging from minimal to substantial impact on daily life, e.g. an inability to work). Participants also used the term 'tiredness' interchangeably used to describe either fatigue or sleepiness.

Fatigue was described as exhaustion and a lack of physical energy that was explicitly separate from sleepiness and falling asleep. Participants described fatigue as synonymous with physically feeling "drained", with some describing it as the most functionally impairing component of EDS.

"I often also get very fatigued; drained and physically can't do much" [P24, NT2]

Sleepiness was described as a *"crushing need to sleep"* [P18, NT2] and often referred to as a physical pressure. This feeling was sudden and acute for some, while others described it as a dull, day-long physical pressure and a "*a need to be prone and close your eyes and lie down*" (P18, NT2). This symptom was perceived to contribute to poor concentration and cause 'brain fog'.

Two distinct accounts of the act of falling asleep were described. The first would only occur when the participant was seated and was not actively engaged, often described as situations where they were bored, unfocused/inattentive, or performing a menial task. These participants explicitly stated that they did not fall asleep while standing or actively engaged in a task, as they could 'overcome' or' push through' their sleepiness in these situations (Box 1).

The other account of the act of falling asleep was described by fewer people (n=4) as a sudden, acute onset of sleep that could occur despite being active, physically moving, standing, or mentally engaged in a task (e.g. socialising, walking, or when the participant was talking "*mid-conversation with my partner*" (P6, NT1)). This was preceded by a sudden, acute feeling of "sleepiness" or sleep pressure. One participant said that if they avoided their scheduled nap and tried to "*push through"* (P22, NT1), a sleep attack would eventually occur regardless of the activity being performed. Another described this occurring multiple times a day, with family and friends able to recognise external signs of when this episode would occur, where they would *"see my eyes glaze over and he can spot the signs a mile off"* (P6, NT1). The act of falling asleep when 'active or engaged' was only described by participants self-reporting cataplexy associated with acute positive emotion. Participants who described their cataplexy as "*not full-blown cataplexy*" (P2, NT1) or "*not dropping completely with, you know, high, like, emotions*" (P9, NT1) reported that they did not fall asleep while actively engaged.

Perhaps most important was the language used to describe these symptoms. Participants clearly distinguished between two distinct acts of falling asleep when describing their symptoms. However, terms like "sleep attack" and "falling asleep mid-task" were used interchangeably to describe their experiences, even by persons who experienced both types. While some participants only experienced one of the two described acts of falling asleep, they were also aware that others with narcolepsy had a different experience (box 1).

> *"They were type 1 and they just fell asleep throughout the day randomly, and I was like, oh, I don't just fall asleep randomly throughout the day. I'm like, I just get tired real quick when I'm not doing anything, it's not like I just drop off involuntarily. I'm like, it's a…it's something that just is, um, I just am prone to getting tired very quickly when not doing anything. It's like, it's definitely different."* [P3, NT2]

Box 1: A participant with narcolepsy type 2 describing the perceived differences between symptoms experienced by someone with narcolepsy type 1

Subtheme 2: Lived experience of cataplexy – differences in triggers

There was variability in the descriptions and experiences of participants who self-reported cataplexy (figure 2). Six of the ten participants self-reporting NT1 described their cataplexy as general muscle

weakness, "*slurring*" [P9, NT1], tongue protrusions and knee-buckling that was infrequent, intermittent, or not impactful on daily life. Three of these also recalled uncertainty around whether their experience met the clinical definition of cataplexy, despite identifying with this label:

"*I don't feel like I've had [classic cataplexy] episodes*" [P9, NT1].

Another person described a loss of consciousness when describing their experience. Four participants reporting cataplexy (40%) described it as being triggered by acute emotion, with laughter as a specific trigger. All four described experiencing both full and partial attacks (i.e. cataplexy resulting in full body paralysis vs momentary weakness in limbs/face) that had caused them physical injury or embarrassment in the past. Notably, despite pharmacological management, these participants described their cataplexy as a permanent and persistent symptom, one where they needed to be constantly mindful of their emotions and potential triggers, with the participant constantly vigilant of an attack. This contrasted with the experience of the six participants who did not experience cataplexy associated with acute emotion and who described their attacks as single, intermittent or one-off events driven by chronic triggers (i.e. stress), that the cataplexy had resolved itself or not occurred for extended periods (e.g. > five years).

Several participants also used the term "cataplexy" for symptoms not consistent with the clinical criteria for cataplexy. In some cases, participants used the term to describe what the literature refers to as a "sleep attack", with cataplexy perceived as a version of falling asleep:

"I could fall asleep at the shops. Um, for me, though, I can fight it. I feel some people, some people can't, and that's where the cataplexy comes in" [P14, NT2]

Theme 2: Making sense of the illness experience – perspectives of identity, daily impact, and the label of narcolepsy

Subtheme 1 – "You may as well have something that's completely different than what I do" – Differences in illness identity

Participants distinguished their illness identity from others diagnosed with narcolepsy based on their experience of the two symptoms above: cataplexy and 'the act of falling asleep'. Almost all participants without cataplexy described NT1 as more severe and functionally impactful and perceived this as a separate illness experience from their own. Some (n=8) described themselves as "*thankful*" [P4, NT2] and "*lucky*" [P14, NT2] they did not have cataplexy, viewing their illness experience of NT2 as more favourable. This view was shared by participants with cataplexy not triggered by emotion, who described their experience of cataplexy as not impairing or limiting, where they have "*the blessing of not having full-blown cataplexy*" (P2, NT1). The small number of NT1 participants self-reporting cataplexy triggered by positive emotion similarly perceived their illness experience as different from NT2 on the basis of increased functional impairment and their understanding of narcolepsy physiology:

"I think that plays out completely different than it does for a narcoleptic who just has the sleepy side of things. It's a completely different mechanism. And I think that not having [orexin], I don't know

that it's just about fighting the urge to sleep. There is so much more to it than that. It plays out in everything." [P6, NT1]

Participants also distinguished their illness experience depending upon whether they experienced 'the act of falling asleep' while active and engaged. The majority who did not experience this aspect of EDS described frustration that the public perceived narcolepsy as falling asleep at any time, which did not align with their own experience. Many felt this contributed to the misunderstanding and confusion around narcolepsy and its impacts:

"It's the trope that I'll fall asleep while standing up" [P2, NT1]

Only a few participants did not limit descriptions of their illness experience to cataplexy or sleep attacks. Instead, these participants defined their illness experience of narcolepsy as extending beyond the typical symptoms associated with narcolepsy, attributing a wider range of symptoms, functional impacts, and other comorbidities to their experience of narcolepsy label.

"There is a lot more to the surface [of narcolepsy] than just the four main symptoms, I guess, it's definitely a lot more than just that" [P1, NT2]

Subtheme 2: Diagnosis and the Spectrum of Acceptance

Two distinct groups of participants were identified based on their acceptance of their diagnostic label. The first described their diagnosis as validating and embraced the label of narcolepsy as it provided answers to long-standing questions about health, unexplained symptoms or why they perhaps were not as functional as others:

"More relief that we finally found out what it was and no more rushing around doctors." [P19, NT1]

Conversely, the second group attributed negative connotations to the diagnosis, with some outright rejecting it, not wanting to be perceived as disabled or less functional. Others considered their diagnosis a mistake, with two describing their diagnosis as forced upon them by healthcare professionals. This was experienced by a group that was primarily defined by symptoms that fluctuated in severity or frequency or were now resolved:

"I literally didn't believe it. I did not believe it. I was like, nah, it must be some kind of mistake." [P11, NT2]

All participants attributed past experiences, such as poor performance in school, university, work or other life events, to their narcolepsy rather than themselves.

Subtheme 3 – Assessing well-managed narcolepsy by the daily impact of symptoms

Participants determined if their narcolepsy was well-managed by their level of functional impairment rather than symptom severity (i.e. a desire to be functional/productive at work rather than difficulties staying awake/feeling sleepy at work).

Most reported being able to work full-time. Participants that only fell asleep when seated and disengaged described a constant "battle" against sleepiness that persisted throughout the day that affected concentration and focus. Most were able to work full time and reported being able to "*overcome*" or "*push through"* symptoms by, for instance, remaining standing in meetings, choosing a role that kept them active, or having a scheduled nap, with few (n=2) describing symptom management as a *"frame of mind"* [P23, NT1]. Participants also described their medication regimes, with several describing it as optional:

"I don't really take my medication too much, but if I really do need to wake up, or like to focus, then I'll take my medication" [P1, NT2]

Those that fell asleep when active and mid-task described a constant fear of having an episode in public or without an appropriate or safe place to do so, with these episodes occurring regardless of activity. All three participants described difficulty finding or maintaining employment. Both groups described inadequate accommodations, with some describing themselves as seeking out bathrooms at work to *"nap in the toilet"* [P9, NT1].

Participants also described how they manage their fatigue. Most prioritised work or career at the cost of leaving adequate energy for basic self-care activities or carer responsibilities. Participants described that they "*can't do all those things and that something has to give*" [P24, NT2], often resulting in conflict within relationships as family members or partners had to take on the additional burden. Energy levels were managed by keeping strict routines and structuring daily activities to account for their reduced capacity. Self-preservation behaviour was described, with participants often becoming upset, distressed, or defensive when their routine was interrupted by unexpected or external circumstances, as this would exacerbate the severity and frequency of symptoms.

The few with cataplexy triggered by positive emotion (n=4) suggested this symptom often exacerbated other symptoms of narcolepsy, including increased fatigue and episodes of falling asleep:

"It's been really involved and full on like emotionally speaking, my functionality, that'll wipe me for the rest of the day" [P6, NT1].

The impact of cataplexy went further than the episode itself, with all describing the psychological impact of not being able to experience or regulate emotion. This affected the participants' ability to engage with others, maintain personal relationships and socialise, with a constant need to maintain vigilance over experiencing triggering emotion described:

"it's so scary having to like be sure that you don't accidentally trigger the cataplexy" [P17, NT1].

One participant spoke of his school experience where friends would try to trigger a cataplexy attack, describing the psychological impact of choosing between his friendship group or his safety.

Theme 3: – Making sense of long-term care – narcolepsy management following diagnosis

Subtheme 1: Sourcing information and support about narcolepsy

Digital media was a primary source of information about narcolepsy and upcoming treatments. Websites, online support groups, social media, online forums (i.e. Narcolepsy/Idiopathic hypersomnia Reddit community) and digital peer-reviewed journal articles were all described. Few (n=4) mentioned their specialist as their primary source of information, with most describing themselves as more knowledgeable about narcolepsy.

Three specific areas were identified where information was considered lacking. Firstly, participants knew of few educational resources they could give to workplaces or schools/universities to explain the impact of narcolepsy or potential accommodations. The second related to the eligibility and the application process for government support services (i.e., National Disability Insurance Scheme (NDIS)), with several participants unsure whether narcolepsy was considered a disability or how to apply:

"I kind of feel like we're a bit of a, you know, other group, like you're not recognised" [P5, NT2]

Lastly, women with narcolepsy described limited information about the safety of medications for narcolepsy, with several reporting they knew medications like modafinil were not suitable for pregnant or breastfeeding women. Participants spoke of a top-down approach taken by their treating specialist where they were told they were not allowed to continue their prescribed medication. These same participants said the ideal situation would have been sitting down and discussing the risks and benefits of continuing treatment with their treating doctors. A unique set of psychological challenges resulted from this, where women feared choosing between maintaining their functional status and independence or having a child.

"I didn't find any resources anywhere, and I think I'm a pretty good [at googling] about what narcolepsy and pregnancy means. So, I had no idea if having children or being pregnant was going to screw with me" [P7, NT2]

Subtheme 2: The relationship with healthcare professionals

Participant satisfaction with their treating sleep specialists varied across interviews. A steady, long-term specialist was perceived as key to instilling trust between patient and specialist, with some participants seeing the same specialist for >5 years. For most others, a misalignment in the treatment priorities and a perceived lack of understanding by clinicians of the whole person impact of narcolepsy was described. This misalignment affected the patient-specialist relationship, where many perceived their doctor as a passive provider of medication rather than an active decision-maker involved in managing their narcolepsy:

"my ongoing relationship with him is the script, to the extent that I want the script, and he would check-in, like as a 'high-level' like, are you okay?" [P7, NT2].

While some were satisfied with this approach, others perceived this as their specialist lacking knowledge and training specific to narcolepsy. Several participants attributed this to sleep medicine and respiratory medicine being combined under one speciality in Australia, with sleep specialists perceived as lacking training specific to non-respiratory sleep disorders. This had a reported impact on the management of narcolepsy through public hospital sleep clinics, where participants were not

given a choice of physician they were referred to, with some describing referrals to physicians who specialised primarily in respiratory medicine rather than in sleep disorders:

"the specialist I see is a thoracic surgeon, an ear, nose and throat doctor because it's the [public hospital] sleep and respiratory unit" [P6, NT1]

Some participants brought their research and information to their specialists, with few specialists described as receptive to discussing the information. For others, their research was dismissed, which was particularly damaging to the patient-physician relationship.

Others described themselves as treatment-seeking rather than seeking out the expertise or knowledge of a specialist:

"shop around a fair bit to get medical professionals that are understanding or knowledgeable enough to, to sort of continue with my treatment" [P24, NT2]

Theme 4: Making sense of the perception of narcolepsy – how do people with narcolepsy and others perceive the disorder

Subtheme 1: What do others think of my narcolepsy? – others' perceptions of narcolepsy

In every interview, participants universally feared being caught asleep, shamed or *"being judged or misunderstood or um, I guess, being seen that I'm not capable"* [P5, NT2]. These negative sentiments were not directed towards narcolepsy itself (i.e. part of a stereotype of narcolepsy). Rather, these sentiments were directed towards attitudes to sleep, sleepiness, and napping, all conflated with laziness and being unproductive. Those closest to the participant, including family members and work colleagues, often held these negative sentiments. These individuals often trivialised or normalised the experience of the PwN by comparing it to their own experiences of fatigue and sleepiness or not considering these symptoms to be a medical condition:

"I'm not some tired piece of crap who can't stay awake. I'm genuinely fighting something" [P3, NT2]

The trivialisation resulted in a breakdown of trust and confidence for some, with participants describing an unwillingness to communicate their healthcare needs or the impact of narcolepsy with others:

" I was like 'making it up' type of thing or like 'it wasn't real' type of thing. It definitely added some strain to the relationship, and it's definitely made me more secretive about my health problems" [P1, NT2]

Participants also described encountering negative perceptions towards narcolepsy treatments. Several medications used to treat narcolepsy were known to be misused as study aids amongst university students and as performance enhancers in the workplace, and participants thought they might be viewed as using them for similar purposes. Some healthcare professionals also perceived as stigmatising narcolepsy treatments, with one participant describing they *"get that whole drug-o thing feeling [from my pharmacy]"* [P16, NT2] when collecting their monthly stimulant medication.

Several participants described specific instances where they felt discriminated against in the workplace, not based on the diagnostic label of narcolepsy but rather the symptoms or functional impairment (e.g. being late for work, falling asleep or mistakes made due to issues with concentration/brain fog). Participants also feared being discovered to have narcolepsy as they did not want to be perceived as less capable. Often, this fear intersected with the different experiences of sleep attacks, with participants concerned that employers might search the internet for information on narcolepsy and assume they would fall asleep mid-task and thus be perceived as a liability:

"Even though I'm all right, I'm fully medicated and it doesn't, you know, I can get through most of the day, they'll still go, yeah but when I googled you, you could fall asleep" [P22, NT1]

While most did not describe experiencing actual discrimination, almost all feared or assumed they would be discriminated against (i.e. anticipatory stigma). The fear of discrimination led some to engage in potentially unhealthy behaviours to try and stay awake, such as substantial consumption of caffeine and energy drinks in addition to stimulant medication, or one case, through pain:

"I keep a rubber band around my wrist, like just to flick, keep myself awake, drink cold water, wash my face, I'll even bite a lemon, that extreme" [P23, NT1]

Subtheme 2: How is narcolepsy perceived by those living with it

Almost all participants appeared to have internalised their stigma, either agreeing with negative stereotypes around sleepiness and unproductivity and subsequently trying to distance themselves from the label of narcolepsy or hide their symptoms. This extended to participants who were amongst the most functional, including those employed full-time or who did not describe the substantial daily impact. Some felt shame stemming from being diagnosed with narcolepsy while others were even sympathetic to the idea that employers would discriminate against someone with narcolepsy, often describing the rationale behind such discrimination as understandable:

"I was literally just [pauses] not reliable. If I was my own employee, I would have sacked me." [P11, NT2]

Perceptions of narcolepsy also varied with levels of daily function. PwN who were more functional described the limited functionality of others with narcolepsy as by choice or a consequence of their own decisions:

"people seem to make excuses for themselves rather than help themselves out" [P2, NT1].

Participants also had negative perceptions of others with narcolepsy based on their symptom experience. Some of those with NT2 who described themselves as less functionally impaired perceived those with NT1 or persons that fell asleep while standing and mid-task as lazy or unproductive, with one NT2 participant describing someone with NT1 as *"dopey and like just constantly asleep like a human sloth. Whereas [my narcolepsy] was never like that."* [P8, NT2].

Discussion

To our knowledge, this is the first qualitative exploration of the symptom experience of narcolepsy from the perspective of persons with narcolepsy (PwN). Qualitatively, we found that persons with NT1 and NT2 described different experiences of symptoms and illness, identities, and levels of functional impairment. Participants distinguished between the two subtypes of narcolepsy, with some stigmatising those less functional or with different symptom experiences than their own. Our results raise questions about whether NT1 and NT2 should be considered subtypes of a single disorder or two different disorders, as many PwN themselves appeared to consider these separate.

We found that PwN reported four distinct and distinguishable symptoms often grouped under the umbrella term 'EDS'. We also observed two distinct experiences of cataplexy. Each symptom carried varying degrees of functional impairment and impact on daily life and should be considered and measured as separate constructs to reflect the lived experience of narcolepsy (e.g. in PROMs). While umbrella terms like 'EDS' are standard in the sleep field, its use appears to lack the specificity to describe and convey the symptom experience. Further, ongoing use of shorthand could contribute to trivialising narcolepsy symptoms, as 20% of the general population is also purported to experience EDS [16]. There are also implications for narcolepsy clinical trials, as the choice of primary outcome measure for EDS is likely underpinned by a false assumption of content validity (e.g. outcome measure used to capture all aspects of EDS, as experienced by PwN [1,17]). It suggests a need to move away from selecting outcome measures for EDS in efficacy trials towards the assessment of each individual symptom. Not only would this allow healthcare professionals to create tailored treatment plans, but also the ability to better meet the needs and priorities of PwN.

There was also a lack of common language and terms that PwN could use to convey their symptom experience. Participants used "sleep attack" and "falling asleep mid-task" interchangeably to describe their symptom experience, where each person attributed their meaning to these terms (e.g. describing a sleep attack but calling this experience 'cataplexy'). The meaning prescribed to these terms often differed between subtypes of narcolepsy and from definitions given throughout the literature. Overall, there appears to be a discrepancy between the language used by the medical establishment and PwN when describing symptoms experienced, with much lost in translation [3,18]. For effective communication between patients and healthcare professionals, there needs to be a shared understanding and language to convey the subjective experience of symptoms, ensuring all relevant domains are defined [19]. It suggests the need for an agreed-upon, clearly defined language developed by PwN, healthcare professionals and researchers before we can effectively communicate the illness experience. Defining these symptoms is a necessary first step towards creating a valid patient-reported outcome measure and ensuring the validity of existing data collection systems that use these terms and explore these experiences.

We also found discrepancies between how 'well-managed narcolepsy' is perceived and measured. Most participants assessed the severity of their narcolepsy by their level of functional impairment rather than the frequency or severity of symptoms, which are the core of how clinicians and researchers measure treatment efficacy in trials. This implies that narcolepsy is not just a disorder to be treated but a functional disability to be managed. Previous studies support such an approach, with self-reported sleepiness and global improvement strongly correlated with measures of function and health-related quality-of-life rather than objective measures of sleepiness [20]. However, clinical guidelines for the management of narcolepsy appear to reflect the opposite, with symptom frequency prioritised over the whole person's functional impact of the disorder [21,22]. To bridge this gap and assess whole-person function, simple analogies that help PwN describe their perceived

energy levels and ability to perform daily tasks can be valuable tools for healthcare professionals (e.g., spoon theory or battery analogy – see SUPPLEMENT C [23]). In the interim, healthcare professionals can use these to help understand how patients convey the functional impact of their disease. While useful, our results suggest a need for patient-reported outcome measures that assess narcolepsy using endpoints considered more meaningful to patients.

Another key finding was the characterisation of the stigma participants described experiencing. Participants reported this as directed towards symptoms rather than the diagnostic label of 'narcolepsy', where sleepiness, falling asleep and napping were all conflated with laziness and being unproductive. In the context of this study, anticipated stigma refers to the extent a person with narcolepsy believes other people would devalue/distance themselves if others found out they were overly sleepy, fell asleep more often or required regular naps [24]. Considering that those with narcolepsy have a biological propensity to fall asleep, the chronic stress of trying to hide their symptoms or being 'outed' likely contributes to psychological comorbidity observed in narcolepsy [25-27]. This anticipated stigma likely reflects the devaluation of sleep in Western culture [28] and also appears to be held by those closest to the PwN (e.g. family and colleagues). Living in a society that denigrates sleepiness, falling asleep and napping may also explain the internalised stigma observed in almost all participants [24]. Both anticipated and internalised stigma has been shown to strongly predict psychological distress in populations with a concealable societal devalued identity, similar to narcolepsy (e.g. persons with HIV-AIDS or mental illness) [24]. This likely contributes to the high prevalence of depression, anxiety, suicidal ideation, and other psychological comorbidities observed in narcolepsy [26,27,29]. With much of this stigma described as experienced in a workplace setting, it also highlights a broader socio-legal implication related to occupational health and safety. If employees with narcolepsy anticipate stigma and hide their symptoms, they may decide not to disclose this to their employer, despite having a condition that might increase the probability of an accident during work hours due to a sleep attack or cataplexy. One possible solution would be the creation of jusristiction-specific educational programs or information packs for employers that include details about narcolepsy symptoms and appropriate accommodations (e.g. including work-from-home practices, allowed to stand during meetings)[30].

Strengths and Limitations

The first author (XX) is a lived-experience researcher diagnosed with narcolepsy type 1, which may be a strength, as it allowed participants to engage with a fellow community member, sharing insight and experiences that they otherwise may not have shared with someone without narcolepsy. Conversely, XX acknowledges that this may have biased the direction of the interviews and inferences, given his experience with narcolepsy and the contention raised between distinguishing between subtypes. Using a reflexivity diary and having a large research team with diverse experiences and backgrounds (e.g., healthcare professionals, psychologists, pharmacists, and other academics from outside of sleep research) helped challenge preconceived ideas and encouraged XX to remain aware of potential biases. Another strength was the substantial response of potential participants to the screening survey. This enabled us to purposively sample based on narcolepsy subtype and sex, increasing the possibility that the experiences described were indicative of the narcolepsy community at large. Limitations of this study include that all interviews were conducted in English and therefore lacked representation of non-English-speaking PwN who may have different cultural perceptions of sleep and experiences of an English language-dominated health care system, which is essential considering the multicultural population of Australia. Our study was also limited to those self-reporting a diagnosis of narcolepsy. No objective measures or clinical data were collected or a way to confirm the diagnosis, perhaps contributing to the heterogeneity observed in our cohort.

Conclusion

Our findings highlight the importance of including the perspective of persons living with narcolepsy when developing healthcare policy and practice related to narcolepsy. Further work is needed to bridge the gap between persons with narcolepsy and healthcare professionals, including the development of a clearly defined taxonomy of symptoms to facilitate communication. Only then can we be sure of the validity of PROMs currently being used. Having characterised the stigma experienced by PwN as both anticipated stigma and internalised stigma, it presents opportunities for future research exploring the impact and possible development of tailored interventions to reduce the psychological burden often associated with narcolepsy.

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Data Availability Statement

The data underlying this article cannot be shared publicly due to privacy and ethical concerns of individuals that participated in the study.

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Figure caption list:

Figure 1: How persons with narcolepsy perceive the symptom Excessive Daytime Sleepiness (EDS). The yellow boxes represent individual symptoms that were explicitly differentiated between by participants. These symptoms are often considered related to one another or unidimensional by the medical establishment. The green boxes represent two distinct symptom experiences that are often referred to as a 'sleep attack'.

Figure 2: How persons with narcolepsy perceive the symptom cataplexy (complete and partial episodes). The yellow boxes represent the two distinct experiences of cataplexy, as described by participants.

Table

Table 1: Demographics of interviewed participants

Demographic	Interviewed participants (n = 24)
Age – mean (range, SD)	33.4 (22 – 58, 10.8)
Sex – Female (n, %)	15 (63%)
Resides in capital city – n (%)	16 (67%)
Symptoms	
Cataplexy – n (%)	10 (42%)
Sleepiness *	
Sleep attack – n (%)	16 (70%)
Fatigue – n (%)	22 (96%)
Never rested – n (%)	16 (70%)
Symptom onset *	
> 18 years of age	14 (61%)
≤ 18 years of age	9 (39%)
Age of diagnosis *	
> 18 years of age	5 (23%)
≤ 18 years of age	18 (77%)
Delay in diagnosis from onset of symptoms *	
< 3 years	7 (30%)
Between 3 - 10 years	11 (48%)
> 10 years	5 (22%)

* n = 23

[redacted]

Perceived dimensions of EDS

Fatigue / Physical lack of energy

Feeling of being sleepy / Sleepiness

Falls asleep when active OR engaged (e.g middle of stimulating conversation)

Falls asleep when seated AND disengaged (e.g inattentive during a work meeting

[redacted]

[redacted]

Perceived dimensions of cataplexy

- Triggered by an acute emotion (e.g laughter, surprise)
- Recurring, always vigilant of emotional threshold triggering attack

- Triggered by stressors (e.g. high stress situation)
- Infrequent, intermittent or delay between trigger and episode

[redacted]

Supplementary A

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Developed from:
Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

No. Item	Guide questions/description	Reported:
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	Methods – interview proceedure
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Title Page
3. Occupation	What was their occupation at the time of the study?	Title Page
4. Gender	Was the researcher male or female?	Title Page
5. Experience and training	What experience or training did the researcher have?	Title Page
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	Strengths and limitations
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Methods, Strengths and limitations
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Strengths and limitations

Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Methods – Data analysis
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Methods – Recruitment and Consent
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Methods – Recruitment and Consent
12. Sample size	How many participants were in the study?	Results
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Results
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Methods – Interview Procedure
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Methods – Ethics and Design (inferred from 1:1 interviews)
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Results – Participant Characteristics
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Methods, Appendix B
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	N/A – inferred from methods
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	Methods – Interview Procedure

20. Field notes	Were field notes made during and/or after the inter view or focus group?	Methods – Interview Procedure
21. Duration	What was the duration of the interviews or focus group?	Results – Participant Characteristics
22. Data saturation	Was data saturation discussed?	Methods – Interview Procedure
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	N/A – inferred from methods
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	Methods – Data Analysis
25. Description of the coding tree	Did authors provide a description of the coding tree?	Methods – Data Analysis
26. Derivation of themes	Were themes identified in advance or derived from the data?	Methods – Data Analysis
27. Software	What software, if applicable, was used to manage the data?	Methods – Data Analysis
28. Participant checking	Did participants provide feedback on the findings?	N/A – inferred from methods
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	Results – in text and tables 1-3
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Yes, Results
31. Clarity of major themes	Were major themes clearly presented in the findings?	Results
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Results

SUPPLEMENTARY B: Participants perspective living with narcolepsy interview guide

Thank you for agreeing to take part in our study. I would like to remind you that participation in this research project is completely voluntary, and you may withdraw from the study at any time, and are free to choose not to answer any of the questions that you are asked. We are recording this interview so that your thoughts can be accurately captured for analysis. If you prefer, you can switch off your camera. At any point during the interview, if you feel uncomfortable, please let me know and I can stop the recording. Is it okay if we go ahead and start the interview and record the session?

Question	Prompt	Rationale
Impact of narcolepsy		

1. What do you find most challenging about living with narcolepsy?	• Has narcolepsy affected your ability to work or study?
	  ○ Have you disclosed your narcolepsy to your workplace/university?
	  ▪ **{YES} –** Were you granted any accommodations or support?
	  ○ Are there any strategies you use to help manage narcolepsy at work?
	• Has narcolepsy affected your ability to socialise?
	  ○ Has your relationship with your friends changed after you developed narcolepsy?
	• Has narcolepsy affected your relationship with your family?
	  ○ What effect has narcolepsy had on your relationship with your spouse/partner?
	  ○ [If participant has children]
	  ▪ Has narcolepsy affected the way you care for your children?
	• What prompted you to see someone when you first noticed symptoms of narcolepsy?
	  ○ (If delay to diagnosis is longer than 1 year from information gathered from the sign-up form)
	  ○ Why do you think it took so long to get a diagnosis?
		Explore the priorities and perceived lived experience of those with narcolepsy

SUPPLEMENT B: Participants perspective living with narcolepsy interview guide

Symptoms		

2. What aspect of narcolepsy do you find most difficult to manage?	• How would you describe excessive daytime sleepiness?
	  ○ How does it affect your day-to-day life?
	  ○ Do you get sleep attacks? (where you fall asleep suddenly or without noticing?)
	• **{Cataplexy specific/muscle weakness brought on by emotions like laughter}** How do you deal with cataplexy?
	  ○ Are there any strategies you employ to manage it?
	• How would you describe your night-time sleep?
	• Does narcolepsy cause you 'brain-fog'? Can you describe how it affects you?
		Exploring symptoms from the perspective of patients

Welfare/Support services/Disability recognition		

3. What has your experience been with social services such as Centrelink or NDIS?	***(Has experience with services)***
	• How did you first engage (referred) with the service? Did your specialist or healthcare professional refer you?
	• How easy was the application process?
	  ○ Where did you turn to for help?
	• Did you come across any hurdles when accessing these services?
	  ○ What did you like about the service/not like about the service?
	(No experience with this)
	• What do you think the reason is that you haven't had to deal with these services?
	  ○ What barriers do you think those with narcolepsy face when trying to access this service?
		End-user experience with non-healthcare related services

Patient-Clinician relationship		

SUPPLEMENT B: Participants perspective living with narcolepsy interview guide

4. Who is the main healthcare professional that manages your narcolepsy?	• Who co-ordinates the medications and treatments you are on?
	  ○ How often do you see them?
	• What has your experience been with your GP?
	  ○ Has this experience been similar with your sleep physician?
	  ○ If you could give advice to health professionals on how to improve the management of narcolepsy, what would it be?
		Exploring patient-centric care from the perspective of patients

Treatment		

5. Tell me about the treatments that you have used to manage your narcolepsy?	• How well have your medications been working for you to treat your symptoms?
	  ○ How do you tell that your narcolepsy is well managed?
	• **{Cataplexy specific}** Have any of your treatments for cataplexy affected your emotions?
	• Have you experienced any side-effects with any of your medications or have you noticed your medications becoming less effective over time?
	  ○ How did you manage these side effects?
	  ○ Have you brought it up with your treating physician?
	  ▪ Did you feel comfortable doing so/why didn't you?
	• Have you had any experience or interaction with Xyrem (sodium oxybate)?
	  ○ What do you think some of the challenges getting access to this?
	• Who should be playing a greater role in getting new medications and treatments in Australia? (e.g. sodium oxybate or other medication)?
	• Are there approaches other than medication that you've used/heard of to manage your narcolepsy?
	  ○ What about things like napping or diet?
		Experience with treatments and lack of access to new medications
		
		Alternatives to pharmacological treatments that patients may use

SUPPLEMENT B: Participants perspective living with narcolepsy interview guide

Information Seeking/ Support Groups		
6. Where do you get your information about narcolepsy from?	• **{Physicians}** Do you seek a second opinion? Do you do anything to double check advice? • **{Support groups or google}** Why do you rely on these sources rather than your treating doctors? • Has being part of a support group helped you when dealing with Narcolepsy?	Information seeking pathways that are used by those with rare diseases
Driving/Transportation		

7. Do you drive or catch public transport?	• Has narcolepsy affected your ability to drive?
	  ○ Do you have any strategies in place to manage your symptoms while driving?
	• Does narcolepsy affect your ability to catch public transport?
	• Have you ever had a conversation with your sleep physicians about driving or anything to do with your licence approval?
	  ○ **{YES} –** Has your physician assessed your ability to stay awake while driving?
		Transportation/mobility barriers faced by those living with narcolepsy

SUPPLEMENT B: Participants perspective living with narcolepsy interview guide

8. What would your life look like if you didn't have narcolepsy?	• Have you ever compared what you could do pre-narcolepsy to what you can do now that you have narcolepsy?
	  ○ Do you have goals and aspirations that you haven't been able to reach now that you have narcolepsy?
	• Tell me about how you came to terms with the disease when you were first diagnosed?
	  ○ Were there any services or resources offered to you to help cope with the diagnosis?
	  ▪ **{NO}** - Do you think that these services would have helped you cope with the diagnosis?
	• There are medications available overseas that aren't available here. What impact does not being able to access new medications have on your outlook of your narcolepsy?
	• Have you seen a psychologist or mental health professional to discuss your narcolepsy? Why/why not?
	• Support groups can sometimes show others with narcolepsy to be more functional than others (for example, working full time or more hours). Have you experienced this?
	• Did it affect your view of yourself or of narcolepsy?
		Exploring the mental health sequela and psychosocial issues associated with narcolepsy

9. Is there anything else about narcolepsy or your own personal experience living with it that you would like to share?		Final question

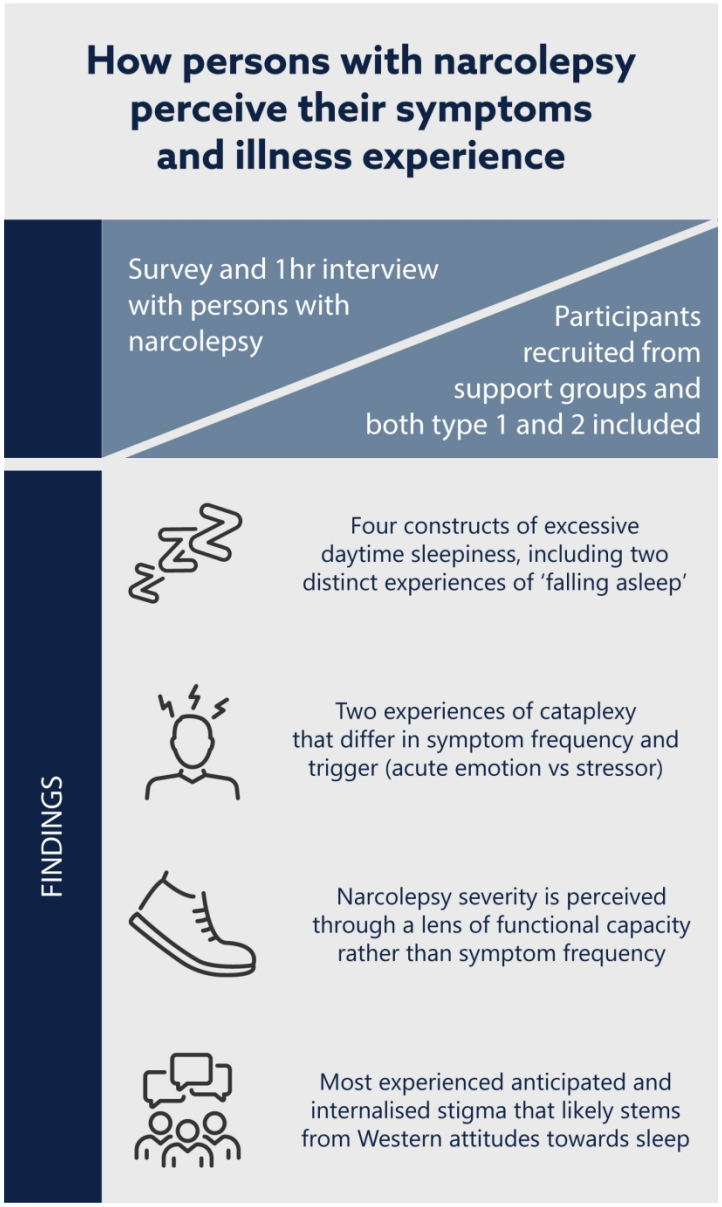
Supplementary 1: Spoon Theory

Some participants used the 'Spoon Theory' to convey their experiences with fatigue and functional limitation. Christine Miserandino came up with the allegory that uses simple, everyday objects (i.e. spoons) in response to being asked to explain what it is like living with a chronic illness. In the case of Miserandino, she had Lupus and wanted to explain the effect it had on her "energy levels" every day. It also appears to be a helpful analogy for describing narcolepsy.

"Most people start the day with unlimited amount of possibilities, and energy to do whatever they desire, especially young people. For the most part, they do not need to worry about the effects of their actions. So for my explanation, I used spoons to convey this point. I wanted something for her to actually hold, for me to then take away, since most people who get sick feel a "loss" of a life they once knew. If I was in control of taking away the spoons, then she would know what it feels like to have someone or something else, in this case Lupus, being in control. (Miserandino 2003)."

You can find more about this at: www.butyoudontlooksick.com/the_spoon_theory

Miserandino, C. (2003). The spoon theory. But you don't look sick, 9781315453217-19.



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Chapter 9: Discussion

9.1 Main findings

This thesis explored the needs, concerns, and barriers to care experienced by persons and their families/carers living with narcolepsy in Australia. It also explored how person-centric the healthcare system is in practice and what persons with narcolepsy and their families/carers perceive 'well-managed' narcolepsy to be. I identified several key findings across this body of work: **i)** There appears to be substantial misalignment between the quality of care that persons with narcolepsy expect to receive and the quality of care currently provided through clinical practice (chapters 3 – 6), **ii)** There are no clear or easily-accessible pathways for persons with narcolepsy and their family and carers to voice concerns they may have with their care, have these concerns addressed or contribute to healthcare policy **iii)** A lack of information and support services for persons with narcolepsy and their families and carers **iv)** Current patient-reported outcome measures used to assess treatment response and what constitutes 'well-managed' narcolepsy, do not appear to have been developed in best practice ways, be fit-for-purpose or capture many of the domains that persons with narcolepsy and their family/carers perceive as important (Chapters 3 and 6).

In Chapter 3, I conducted a document analysis of the submissions written by persons with narcolepsy and their families and carers to the federal Parliamentary Inquiry on Sleep Health Awareness in Australia 2018. Almost 80% of all submissions written by a patient, family or carer were about narcolepsy. The over-representation of narcolepsy could be due to several reasons described in that chapter, including persons with narcolepsy may not have other avenues to voice concerns and contribute to healthcare policy and practice. Many submissions also expressed dissatisfaction with the healthcare system, with healthcare professionals perceived to lack knowledge about narcolepsy. When comparing our findings to the recommendations made by the inquiry, it appeared policymakers were primarily concerned about healthcare engagement, infrastructure, and funding issues rather than addressing concerns prioritised by persons with

narcolepsy and their family and carers (e.g. sequela of narcolepsy, access to welfare and accommodations). The results of this study informed the hypothesis that there was a misalignment between persons affected by narcolepsy and other stakeholders around the perceived illness experience, impact and healthcare priorities of narcolepsy.

Clinical guidelines informing the management of narcolepsy are almost entirely pharmacological. As such, I wanted to explore how 'well-managed' narcolepsy is determined and measured in the context of clinical trials. To address this, I explored the outcome measures to assess treatment efficacy in narcolepsy randomised controlled trials (chapter 5). The ESS and MSLT were the two most common outcome measures used for EDS, while non-specific self-report diaries were used to assess cataplexy. Most patient-reported outcome measures used to evaluate treatment efficacy in narcolepsy RCTs were not adequately validated in a narcolepsy population. My findings indicated that treatment efficacy and what is considered 'well-managed narcolepsy' tend to be assessed by symptom control rather than any of the domains persons identified in submissions made to the parliamentary inquiry (chapter 3).

The misalignment in care priorities led me to explore the illness experience directly from persons with narcolepsy and family and carers, including how they perceived well-managed narcolepsy. I set out to explore the illness experience of narcolepsy from three perspectives using semi-structured interviews: i) persons living with narcolepsy, ii) parents/ carers who care for a child with narcolepsy, and iii) practising sleep specialists. While the response to recruitment for our qualitative interviews was substantial from persons with narcolepsy and their families and carers, I was unable to recruit enough sleep specialists to reach saturation (see 9.4 – strengths and limitations).

For parents who care for a child with narcolepsy, interactions with the healthcare system and healthcare professionals appeared all too often negative (chapter 7). A lack of quality information about the illness trajectory, available support and limited knowledge of narcolepsy among sleep specialists also made many parents feel abandoned by the healthcare system. Further, many felt

that their needs and concerns were not being addressed. These concerns contributed to the psychological burden that other members of the family unit experienced, particularly the hopes and fears parents had for their child's future living with narcolepsy. Importantly, we found that this also impacted the mental health of the parents and the family unit.

The study involving the lived experience of persons with narcolepsy provided insight into how symptoms are perceived, what constitutes 'well-managed' narcolepsy, and the stigma that persons with narcolepsy often encounter. I found that persons with narcolepsy likely perceived their symptom experience differently than described throughout the literature and as measured in trials (chapter 5). The Epworth Sleepiness Scale was the most common outcome measure in narcolepsy RCTs. However, the Epworth Sleepiness Scale purports to measure the propensity to sleep, only one of the four components of excessive daytime sleepiness perceived as important by persons with narcolepsy. These findings could have broader implications for registering medications with regulatory bodies, raising questions about the validity of RCTs that use the Epworth Sleepiness Scale as the only primary endpoint measure for excessive daytime sleepiness.

Persons with narcolepsy also often perceived healthcare professionals to be overly focused on addressing symptoms of narcolepsy rather than the functional impairment and broader impact on daily life. It suggests a misalignment between stakeholders and their perception of 'well-managed' narcolepsy and indicates that further work is needed to close this gap. It may also indicate that persons with narcolepsy want functional disability management from their healthcare professional, not just symptom treatment. Another important finding was that, strikingly, almost all persons with narcolepsy were observed to have experienced stigma in their daily lives. For the first time, we characterised this stigma as anticipated stigma and internalised, or "self-" stigma. The type of stigma experienced likely stems from Western societies' devaluation of sleepiness and the conflation of sleepiness, napping and laziness. This finding was significant considering the substantial psychological burden often associated with narcolepsy.

9.2 Discussion of Main Findings

Table 4: Summary of the main findings of this thesis

Finding 1: Misalignment between persons living with narcolepsy and the healthcare system around the quality of care provided
Misalignment at a **healthcare system** level stemming from: • Narcolepsy often being considered a single disorder of daytime sleepiness rather than distinct subtypes with varying priorities and needs • Inadequate diagnostic criteria • Differences between health policy and clinical diagnostic criteria around how narcolepsy is classified/defined • Power asymmetries in the field of sleep health and medicine
Misalignment between **healthcare professionals** and their patients stemming from: • A focus on treating specific symptoms rather than functional impairment • Sleep medicine is not a multi-disciplinary field in Australia, with few psychiatrists, psychologists and GPs who are also trained in sleep health and medicine • Some public hospitals lack staff with experience and training in managing sleep disorders
Finding 2: Limited options to voice concerns, improve quality of care or contribute to healthcare policy
• The Australian healthcare system does not appear to be person-centric, with concerns around narcolepsy persisting for 20+ years • Limited avenues known to persons with narcolepsy and their family/carers other than the parliamentary inquiry • Lack of funding support for patient support groups and NGOs
Finding 3: Lack of information and support services for persons with narcolepsy and their family/carers
• There is a need for high-quality information and education around narcolepsy if true shared decision-making is to be realised. • The absence of high-quality information may result in the spread of misinformation and could adversely affect the patient-physician relationship.
Finding 4: Assessment of narcolepsy is insufficient and does not reflect what end-users consider 'well-managed' narcolepsy
• Symptoms associated with narcolepsy are heterogenous and often poorly characterised • Outcome measures used in narcolepsy have poor psychometric properties and do not appear fit for purpose (e.g. failing to capture what matters to persons with narcolepsy) • Lack of recognition of functional impairment and access to support/services • Assessment of driving may not be fit for purpose • Lack of knowledge, research or interventions exploring stigma associated with productivity

9.2.1 – Misalignment between persons living with narcolepsy and the healthcare system around the quality of care provided

This body of work indicates that persons with narcolepsy and their families and carers are not satisfied with the current standard of care. Mothers responsible for caring for a child with narcolepsy mainly reported negative encounters when dealing with healthcare, education, and welfare systems, negatively impacting their personal health and ability to provide care. While the experiences of persons with narcolepsy were not as explicitly negative, a significant majority expressed a lack of confidence in their healthcare professionals' understanding of narcolepsy and how it affects daily life. These findings highlight a significant disconnect between the needs and priorities of narcolepsy patients, the healthcare professionals treating them, and the overall healthcare system.

9.2.1.1 – Misalignment at a healthcare system level

A likely contributing factor to the misalignment between end users and the healthcare system is a result of policy and practice guidelines that consider narcolepsy a homogenous disorder [39,93,118,120].

9.2.1.1.1 – Different subtypes, different needs

Narcolepsy type 1 and type 2 have been observed across the literature to have different pathophysiology, symptom priorities, and healthcare needs [22,48]. Across this thesis, we also observed differences between subtypes. Persons with narcolepsy type 1 and narcolepsy type 2 described different illness identities, functional impairment, and symptoms. Notably, persons with type 1 and type 2 narcolepsy often described each subtype as separate illnesses, with some stigmatising others based on subtype (chapter 7). Overall, it suggests that narcolepsy type 1 and narcolepsy type 2 should be considered different disorders for healthcare policy and planning. Separation of the subtypes should extend to developing clinical guidelines, decision tools and support structures designed similarly to other illnesses like diabetes type 1 and 2. This is important as narcolepsy type 1 appears to be a relatively homogenous condition with a definable pathophysiology that meets the criteria of a rare disease [36]. Whereas narcolepsy type 2 is far more heterogeneous with an unknown

prevalence. If these two subtypes are not separated, the different needs of persons with narcolepsy type 1 risk being lost amongst a far larger, heterogeneous population[6].

9.2.1.1.2 – Inadequate diagnostic criteria

Misalignment at a healthcare level likely stems from the current diagnostic criteria used to diagnose narcolepsy, the ICSD-3[3]. There is substantial evidence showing the MSLT, the current gold-standard diagnostic tool, lacks reliability as a diagnostic tool for narcolepsy or idiopathic hypersomnia when used with the current test protocol (a single MSLT study) and ICSD-3 criteria [6,37]. The MSLT is a sensitive and specific diagnostic tool for narcolepsy type 1 (specific for persons with confirmed reduction of hypocretin in CSF. Test-retest reliability for a positive MSLT in a narcolepsy type 1 population ranges from 72% to 78%, depending on medication status [37]. However, for individuals with narcolepsy type 2, the MSLT is not reproducible. Test-retest reliability for a positive MSLT score in a narcolepsy type 2 population is approximately 17-18%. Further, there was no statistically significant difference between the type-2 group and the control group (6%) [37]. The evidence suggests that for a conclusive diagnosis of narcolepsy in suspected individuals, a minimum of two MSLTs would be required. Yet this approach would only reliably diagnose persons with narcolepsy type 1.

Overall, there is perhaps a need to rethink the use of the MSLT and PSG diagnostic studies used narcolepsy in Australia [6] (particularly when combined with the current ICSD-3 criteria). These tests are expensive and financially burdensome for both healthcare system and individuals navigating the private system [121]. They are also resource-intensive, requiring substantial infrastructure and expertise. From a healthcare utilisation perspective, their ongoing may not make little sense in their continued use (particularly when combined with the current ICSD-3 and current protocol). Further, the current approach risks misdiagnosing individuals with narcolepsy when their symptoms may stem from other health conditions (e.g. depression, insomnia, sleep deprivation, etc.).

9.2.1.1.3 – Differences between health policy and ICSD-3 diagnostic criteria for narcolepsy

The Pharmaceutical Benefits Scheme is a key component of the federal government's National Medicines Policy. The scheme aims to balance the need for medicine with outcomes and economic limits, where access to subsidised medications requires specific criteria to be met.

Access to subsidised wakefulness-promoting medication for narcolepsy (e.g. Modafinil) is based on the results of the MSLT. The PBS criteria for individuals with narcolepsy type 2 is an average sleep latency of less than 10 minutes on the Multiple Sleep Latency Test [122]. The criterion is more lenient than the current International Classification of Sleep Disorders-3 (ICSD-3) standard for narcolepsy type 2 – an average sleep latency of less than 8 minutes. Further, studies have shown up to 30% of heathy individuals have a mean sleep latency of < 8 minutes [123,124], shorter than the current PBS criteria of 10 minutes.

It is unclear what evidence the PBS criterion for narcolepsy is based upon, particularly because there is no requirement for sleep-onset rapid eye movement periods (SOREMPs) [120]. Current evidence suggests the requirement of ≥ 2 SOREMPs is much more specific for narcolepsy than a short sleep latency score [123]. SOREMPs are also the only criterion that distinguishes between narcolepsy type 2 and idiopathic hypersomnia[3].

These policy settings carry implications for narcolepsy care. First, individuals who do not meet the diagnostic criteria for narcolepsy but do meet the PBS access criteria may inadvertently believe they have narcolepsy. This includes persons who instead have idiopathic hypersomnia (both with normal and long sleep duration) or others who may not have a sleep disorder. The current setting likely leads to misdiagnosis, wastes healthcare resource, and raises questions around paternalism and autonomy if it's not adequately explained to the person. It may also contribute to the observed distrust between patient-physician (chapter 7 and 8) if the individual visits another specialist who has a differing opinion, and wasted healthcare resources if repeat diagnostic studies are needed. Long term, it may also have a negative psychological impact on the individual (e.g. if a person forms an identify around an illness or develops self-stigma (chapter 8)).

Second, it likely impacts future treatment access, registration of new medications and access to supports and services. The only nationally collected data for people with narcolepsy type 1 and 2 is the number of authority approvals for PBS-subsidised medications. If this data is inaccurate, it has the potential to misrepresent the prevalence of narcolepsy, impacting future economic and policy decisions (e.g. medication access and whether narcolepsy type 1 is rare enough to be considered an orphan disease).

The issue does not appear to be specific for accessing subsidised medications. Other government and federal legislation similarly do not differentiate between narcolepsy subtype or recognise idiopathic hypersomnia. The *Social Security (Tables for the Assessment of Work-related Impairment for Disability Support Pension) Determination 2023* is used to guide assessment of work-related impairment when accessing the disability support pension and lists narcolepsy as an altered state of consciousness [125]. Guidelines have been created to assist administrative and other decision-makers around how to use the impairment tables [126]. A case study is included that describes a person living with narcolepsy. However, the case study specifically describes someone with narcolepsy type 1. It does not differentiate between subtypes, recognise persons with narcolepsy type 2 do not experience cataplexy, and simplifies narcolepsy as a disorder characterised by overwhelming daytime sleepiness. Ironically, the case study above the narcolepsy entry describes someone living with diabetes type 2.

As a consequence, the onus is placed on persons with narcolepsy to explain and educate decision-makers on basic information they should already know. These issues mirror the misalignment observed between persons with narcolepsy and healthcare professionals (chapter 7 and 8). Considering persons with narcolepsy perceived social and welfare services to fall under the jurisdiction of healthcare (chapter 3), these issues also likely contribute to the perceived dissatisfaction with the healthcare system.

9.2.1.1.4 – Power asymmetries in the sleep field

Lastly, power asymmetries within the sleep field may contribute to some of this misalignment at the healthcare system level. Power imbalances among certain groups may skew funding among certain health conditions[127]. To use an example of other conditions considered less 'glamorous', the World Health Organisation found mental health services receive 2% of funding. However, mental illness accounts for 13% of the healthcare burden of disease globally [128]. Experts attribute the disparity in funding to persons with mental health disorders and advocacy groups having less power than other more outspoken entities, such as those in cancer or heart disease fields. The parliamentary inquiry found sleep apnoea received approximately $75 million (54%) of all NHMRC funding awarded to sleep disorder research over the last 20 years [118], with 11% awarded to insomnia and less than 1% to narcolepsy [118]. While Australia has made remarkable progress in the research and management of respiratory sleep disorders, it appears to be a primary focus of the field, dominating education pathways and CPD opportunities [118]. Our results suggest that this adversely affects the quality of care received by persons with non-respiratory sleep disorders. While the cause of the disparity in research funding is unclear, it may represent such power asymmetries, with industry bodies such as ResMed and Philips (large multinational companies) directly contributing / co-funding research in specific fields.

9.2.1.2 – Misalignment at a patient-physician level

Recent reports show that doctors are Australia's most trusted profession, while most (74%) Americans trust their doctors to do a good job, show concern for patients' interests, and provide fair and accurate information[129,130]. However, dissatisfaction with healthcare professionals and sometimes a lack of trust were repeated concerns across all studies (chapters 3, 7 and 8). It is important to state that this does not apply to all specialists or health care professionals, nor are these views representative of everyone with narcolepsy. Our findings do suggest that a large part of this dissatisfaction and mistrust stems from the substantial whole-person impact of narcolepsy and the perception that healthcare professionals lack knowledge about narcolepsy. Limited knowledge of narcolepsy among healthcare professionals is not unique to Australia [33]. However, the close link between respiratory and sleep medicine in Australia appears to have exacerbated this issue, resulting in insufficient education and training in non-respiratory sleep disorders[118,131]. This is perhaps evident in the labels some mothers of a child with narcolepsy used to describe their specialist and lack of knowledge (i.e. lung doctor, sleep apnoea doctor, breathing specialist) (Chapter 7).

In Australia, sleep medicine is not a cross-disciplinary field as it is in the US. Regulatory bodies like the Australian Health Practitioner Recognition Agency categorise sleep specialists as 'sleep and respiratory medicine' practitioners.

The decision to link these two fields of medicine appears to have impacted training and education pathways, specifically around sleep medicine. Some experts consider new trainees ill-equipped to engage in sleep medicine more broadly [118]. The submission made by the Westmead Institute of Medical Research to the Parliamentary Inquiry highlights this issue[118], which stated:

"Virtually all sleep medicine practitioners spend most of their time in respiratory, not sleep medicine, and never get three years training in sleep medicine. Even with sleep training, there was an overwhelming emphasis on respiratory sleep disorders. For example, in a one-year training program

in sleep medicine, a trainee is only expected to see 30 new patients with non-respiratory sleep disorders—a truly worryingly low number, considering they are meant to see 500 new and old cases" [118]

The close link between sleep and respiratory medicine could account for the misalignment in needs and priorities. While the primary cause may be a lack of knowledge and experience of narcolepsy amongst specialists, it could have resulted in a lack of diversity among clinicians trained to meet patients' needs and concerns. In particular, persons with narcolepsy appear to want their healthcare professionals to help manage the functional impairment associated with narcolepsy, not just the symptom treatment (chapter 8). It suggests a need for psychiatrists, neurologists, and general physicians, amongst others, to be trained in sleep, domains from which some of the main healthcare needs identified arose (Chapters 7 and 8). A lack of diversity among clinicians and the close link between sleep and respiratory medicine was already raised as a concern amongst persons with narcolepsy in 2001, and it would appear the issue persists more than 20 years later.

The lack of diversity, training, and knowledge of narcolepsy amongst specialists also has implications for healthcare delivery through the public system. There is no guarantee that a sleep specialist seen through the public health system is adequately trained and knowledgeable of non-respiratory sleep disorders. These physicians act as gatekeepers for treatment access, diagnosis studies and access to public funding and provision of medical expertise to other gatekeepers for welfare and workplace accommodations (figure 2). The decisions made in this space have far-reaching consequences for the quality of life and illness trajectory of narcolepsy and highlight the importance of having specialists with specific knowledge of the broader, whole-person impact narcolepsy can have. It also raises questions about whether the care provided meets the current Australian Charter of Healthcare Rights, specifically around the right to access healthcare services and treatment that meets the person's needs [132].

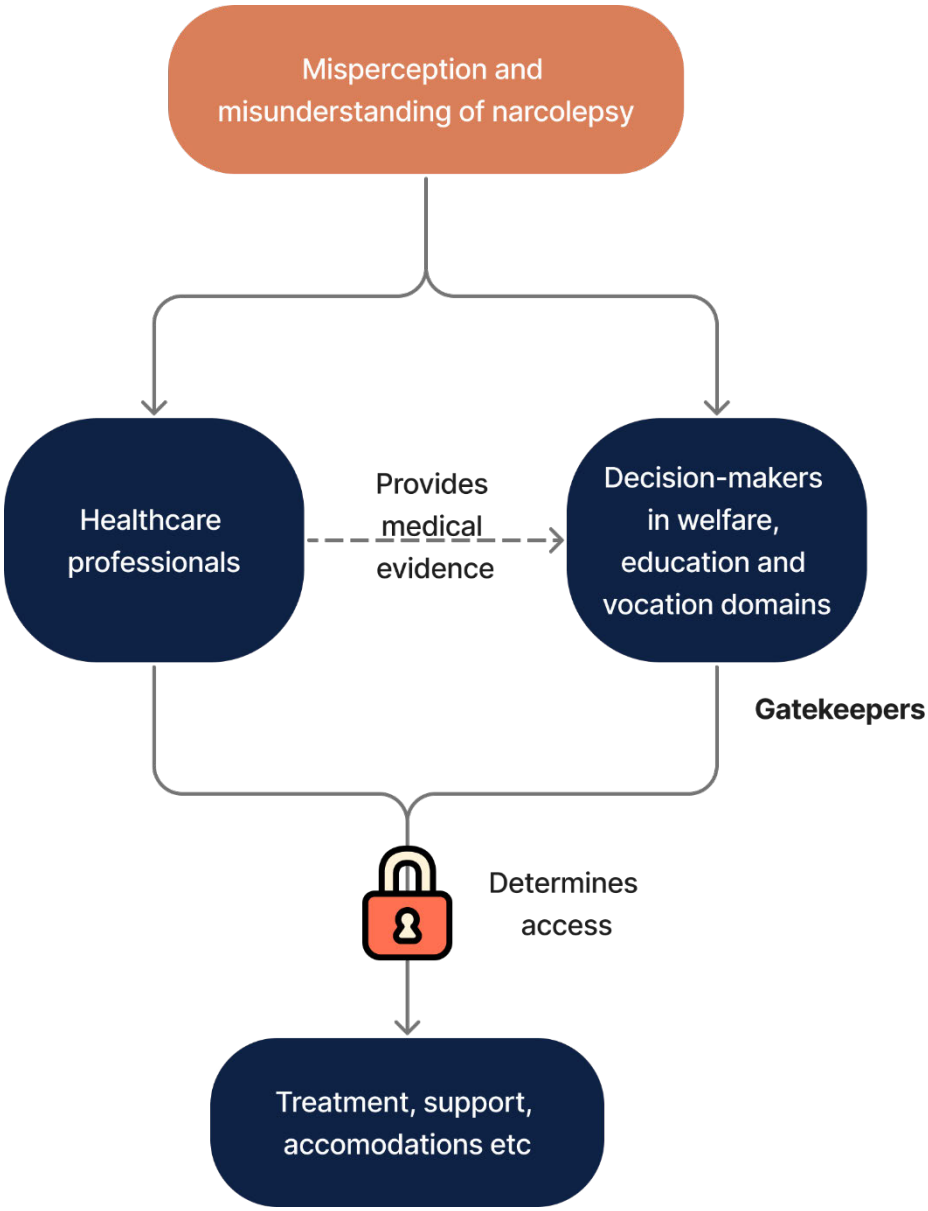

Figure 2: Conceptual diagram showing the relationship between healthcare professionals and social support decision-makers, both of whom act as gatekeepers when accesing treatment, supports and services.

9.2.2 – Limited options to voice concerns, improve quality of care or contribute to healthcare policy

Two decades ago, Bruck and colleagues (2001) found that the healthcare needs of persons with narcolepsy were unmet, with many dissatisfied with the quality of care received [92]. Persons with narcolepsy were dissatisfied mainly by the lack of available information about narcolepsy and accessible treatments. Bruck also wrote that because respiratory and sleep medicine is closely linked, it could prevent persons with narcolepsy from accessing specialists with knowledge of neurological sleep disorders [92]. Strikingly, many of these issues concerning persons with narcolepsy in 2001 appear similar to those experienced today, almost 20 years on. The Australian healthcare system purports to be person centric. However, this body of work suggests that there has been a lack of consultation, shared decision making and person-centric healthcare policy and planning around narcolepsy and perhaps sleep medicine in general.

Across this thesis, only one avenue or pathway was known to persons with narcolepsy and their family/carers to raise healthcare concerns – the Parliamentary Inquiry into Sleep Health Awareness in Australia 2018[118].

While the findings from the federal parliamentary inquiry have now been accepted by parliament (as of October 2023), the response to the inquiry has been lacking. All recommendations that addressed specific concerns related to narcolepsy were accepted in principle. However, no commitment or actionable solution was made by the government. The response is a missed opportunity for the government to have actively addressed the concerns of a relatively unknown yet impactful health disorder. It is also disappointing for persons living with narcolepsy, as (some of) their concerns are acknowledged in a federal government report, yet no concrete way forward has been proposed.

Considering the inquiry was run federally by a democratically elected parliament and recommendations based on diverse stakeholders' views, the lack of commitment to addressing

concerns raises questions about how committed the healthcare system is, at the highest levels, to person-centred care and shared decision-making.

No other mechanisms or pathways for contribution were known. It suggests limited avenues exist to represent the patient's voice in this domain. It is unclear whether this signifies a continuation of the older paternalistic style of medicine or a potential power imbalance between relevant stakeholders.

There are several patient advocacy bodies representing persons with narcolepsy in Australia. Many people with narcolepsy found support through these groups, including finding community, information, and a forum to discuss their challenges (chapters 3, 7, and 8). Support groups are ultimately perceived as a vehicle for empowerment by persons with narcolepsy and their families and carers (Chapters 7 and 8). However, these groups are reportedly underfunded and have difficulty attracting government assistance or donations, including industry support (chapters 3 and 7). An explanation for this could be a result of the observed stigma associated with narcolepsy (chapters 7 and 8) [133] or more likely that uncommon conditions and invisible disabilities lose out when fighting for space in a very crowded health NGO and advocacy arena. Symptoms associated with narcolepsy (i.e. sleepiness) form part of the typical human experience, possibly stymying regular fundraising pathways. Everyone experiences tiredness, fatigue, and sleepiness at times, including would-be funders and decision-makers, so it is easier to normalise the experiences of those with narcolepsy. Differences in PBS access criteria for narcolepsy in Australia, where some criteria for narcolepsy encompass 30% of the healthy population, may also contribute to this [134] (see 9.1.1).

Another challenge for fundraising and raising awareness is the observed anticipated and internalised stigma amongst persons with narcolepsy (chapter 8). For anyone with a stigmatised concealable identity (e.g. HIV status, mental health), it is perhaps unlikely that persons would 'out' themselves to make a statement, fundraise or enact change[135]. Our study participants also explained that they did not want to be the 'poster boy' for narcolepsy. It suggests that these more formal groups are likely limited in what they can achieve in policies they can influence.

9.2.3 – Lack of information and support services for persons with narcolepsy and their family/carers

A crucial aspect of person-centred care is shared decision-making by the person, family/carers, and healthcare professional [98]. Shared decision-making can only be realised if persons with narcolepsy and their families and carers are given access to high-quality, evidence-based information. The findings of this thesis suggest that there was a substantial concern among families and carers, where most had trouble knowing what services, supports, and treatments were available (chapter 7). The information sought covered various topics, including physiology, treatments, navigating healthcare systems, accessing medications through local hospitals, and information for workplaces and schools, including material explaining the impact and possible accommodations (chapters 7 and 8). A lack of information also drove many parents' hopes and fears for their children and appeared to add to the uncertainty associated with narcolepsy, adversely impacting their own mental health. Addressing these concerns will likely decrease the stress and additional challenges families and carers face when navigating healthcare, education, and welfare systems.

Without high-quality, accessible information, persons with narcolepsy and their family and carers may seek information from other sources, including webpages, support groups or online forums. Yet there is no guarantee this information is correct and may result in the spread of misinformation (chapter 8). While there is a clear role for healthcare professionals to address misinformation[136], the onus is better placed on the government and the healthcare system as a whole. Further, leaving it up to healthcare professionals to stem misinformation could prove problematic if the patient believes they are more knowledgeable about narcolepsy, thus negatively impacting the relationship between physician and patient.

9.2.4 – Assessment of narcolepsy is insufficient and does not reflect what end-users consider 'well-managed' narcolepsy

Across both research and clinical practice, it appears we are not measuring what persons with narcolepsy and their families and carers perceive as 'well-managed' narcolepsy. The medical establishment appears focused on pharmacotherapy of excessive daytime sleepiness. In contrast, those with narcolepsy and their family/carers appear to seek management of a functional disorder. Both the literature and our findings suggest different levels of functional impairment and differing needs and priorities between narcolepsy subtypes (chapters 7 and 8) [22]. These differences should be factored into the design of future assessments and strengthen calls for separate, tailored approaches across policy assessment to these disorders.

Below are several key issues associated with the interpretation of 'well-managed' narcolepsy and their implications for health policy and practice:

9.2.4.1 – Symptoms associated with narcolepsy are heterogenous and often poorly characterised

Symptoms described by one person with narcolepsy often differed from the experience of others with narcolepsy and the published literature (chapter 8). Terms used by the medical establishment to describe these symptoms (i.e. automatic behaviour, sleep attack) were often used non-specifically, with many prescribing their own meaning to these terms. For example, several persons said they experienced cataplexy. However, when asked to elaborate, their description resembled what others termed falling asleep or "sleep attacks".

Even across the literature, these terms appear to lack clear definitions. Complicating matters is the commonplace use of shorthand to group symptoms (e.g. excessive daytime sleepiness encompassing several constructs/experiences related to sleepiness). Further, symptoms like cataplexy are only measured subjectively through a diary asking if they have experienced it. With both patient and physician prescribing their own meaning to these terms, differences in perceived symptoms may

adversely impact symptom recognition, add to delays to diagnosis and result in miscommunication around healthcare needs and priorities.

9.2.4.2 – Outcome measures used in narcolepsy are likely not fit for purpose

Excessive daytime sleepiness was perceived as a multidimensional construct by persons with narcolepsy, with each construct carrying its own functional impairment and healthcare needs (chapter 8). These include physical fatigue, the feeling of sleepiness and two distinct constructs of the actual act of falling asleep: 1. mid-task or actively engaged; 2. seated and disengaged. In contrast, the most common outcome measure used for excessive daytime sleepiness in narcolepsy RCTs (i.e., the Epworth sleepiness scale) purports to measure an individual's propensity to fall asleep [134,137] (chapter 5). This outcome measure does not distinguish between the two different types of falling asleep we observed, nor does it capture the feeling of sleepiness or fatigue experienced. However, regulatory bodies have approved certain medications as efficacious in treating excessive daytime sleepiness rather than specifying a particular construct of EDS. Therefore, some treatments indicated for treating EDS may only be effective in relieving 'sleepiness', leaving the person with narcolepsy with fatigue and episodes of falling asleep that remain untreated. This finding could explain why almost 90% of PwN still experience symptoms of excessive daytime sleepiness despite being treated [22].

9.2.4.3 – Recognition of functional impairment and access to support/services

There appears to be a variable level of functional impairment amongst persons with narcolepsy, with those with type 1 generally describing more functional impairment than type 2 (chapter 8) [16]. That said, there is a need for better assessments and decision tools designed to measure functional impairment specific to narcolepsy. Few studies have explored functional impairment in narcolepsy in a formal setting.

Additionally, there are no narcolepsy-specific tools developed to evaluate the functional capacity of individuals with narcolepsy. These evaluations are often crucial for determining eligibility for disability support and services. Furthermore, decision-makers in public services likely lack understanding about narcolepsy, including its overall impact on a person's life and may trivialise these symptoms or equate sleepiness with laziness [133].

9.2.4.4 – Assessment of driving

An additional area of concern relates to the driving ability of persons with narcolepsy. In many of the interviews with persons with narcolepsy, the impact of symptoms on driving was often known. The Maintenance of Wakefulness test is often used to assess driving capability. However, protocol requires the person to be seated, showing they will not fall asleep over several time periods, i.e. typically 5 x 20 or 40-minute periods [138]. It is unclear whether this test can distinguish between the two perceived experiences of falling asleep, nor whether being seated impacts test results (chapter 8).

9.2.4.5 – Stigma associated with productivity

Almost all persons with narcolepsy were observed to have experienced both anticipated and internalised, or "self', stigma in their daily lives. These types of stigma experienced likely stems from Western societies' devaluation of sleepiness and the conflation of sleepiness, napping and laziness [133]. It may also reflect the political discourse observed in Australia over the last two decades, where economic output has often been linked with an individual's self-worth.

While our findings only explored the stigma experienced by persons living with narcolepsy, they are likely to have broader implications for the sleep field. Obstructive sleep apnea, insomnia and other sleep disorders similarly affect an individual's capacity to be productive[139], and it is possible this self-stigma would also be observed amongst these populations. However, considering persons with narcolepsy tend to feel sleepier and are more likely to fall asleep throughout the day than other

sleep disorder populations [123,140], both anticipated and self-stigma are likely to be more pronounced in persons living with narcolepsy.

9.3 Implications for healthcare policy and practice

The findings from this thesis have important implications for healthcare policy and practice. There appears to be a misalignment between individuals with narcolepsy, their families and caregivers, healthcare professionals, and the healthcare system around the healthcare needs and priorities of those affected by narcolepsy. Few pathways were available to persons with narcolepsy to voice concerns or contribute to healthcare policy and practice. Complicating matters further is that most persons with narcolepsy were found to have experienced anticipated and internalised stigma and describe experiences similar to someone with a concealable stigmatised identity (chapter 8). Therefore, it is unlikely that individuals with narcolepsy would 'out' themselves to enact change. It might also partially explain why parents of a child with narcolepsy appear more proactive when advocating for narcolepsy than the person themselves (chapter 7 and 8).

Other stakeholders that could influence healthcare policy change include family/carers, advocacy groups and healthcare professionals. However, families and carers lack high-quality information and educational materials to navigate healthcare, education, and other support services (Chapters 3 and 7). Advocacy groups specific to narcolepsy reportedly lack funding and thus are limited in their capacity (Chapters 3 and 7). As for sleep and respiratory specialists, our study found most are overly focused on daytime sleepiness, not addressing the whole person impact of narcolepsy (Chapters 3, 7 and 8) and perhaps lack of adequate training in non-respiratory sleep disorders [118].

Perhaps one of the biggest hurdles to addressing this misalignment appears to be the societal stigma around sleep/sleepiness that is common in Western society, including non-medical decision-makers (e.g. educators and administrators of welfare support)[133]. Many of the symptoms experienced in narcolepsy are part of the typical human experience and are easily trivialised. It could also be that narcolepsy and other sleep-related disorders are not considered impactful, meaningful, or seen as carrying minimal disease burden that requires a few nights of good sleep to fix.

These issues may explain some of the dissatisfaction and misalignment between relevant stakeholders around narcolepsy management and care. However, several pressing concerns of persons with narcolepsy identified in 2001 remain unaddressed more than 20 years later [92].

While the findings from the federal parliamentary inquiry have now been accepted by parliament (as of October 2023), the response to the inquiry has been lacking. All recommendations that addressed specific concerns related to narcolepsy were accepted in principle. However, no commitment or actionable solution was made by the government.

In light of these findings contained within this thesis, serious questions should be asked about how committed the healthcare system is to the principles of person-centred care.

Further, would the current healthcare approach towards narcolepsy be acceptable in other chronic illnesses?

Perhaps the proactive inclusion of persons with narcolepsy and their families and carers at all healthcare policy and planning levels is needed for change.

9.4 Recommendations for change

Table 5: Summary of proposed recommendations needed for change

Key finding	Recommendation for change
Misalignment between persons living with narcolepsy and the healthcare system around the quality of care provided	Review diagnostic tools and criteria used for narcolepsy type 1 and type 2: • Improved access to CSF testing • Incorporate a two-week actigraphy study ruling out sleep deprivation prior to MSLT/overnight PSG • Increased research into narcolepsy type-2 subtype • Ensure information, support and services are available for persons with narcolepsy type 2 if/when a substantial change to diagnostic criteria occurs
	Review healthcare policy approach to narcolepsy: • Clear delineation between narcolepsy type 1 and type 2 across healthcare policy and practice • Modify existing PBS criteria for narcolepsy that align with ICSD-3 criteria
	Creation of an Australian narcolepsy registry that systematically collects data that persons with narcolepsy consider important
	Creation of national guidelines specific to the diagnosis and management of narcolepsy
	Develop a strategy to make the field of sleep more multidisciplinary and diversify specialities trained in sleep
Limited options to voice concerns, improve quality of care or contribute to healthcare policy	Development of pathways for persons with narcolepsy and their family/carers to contribute to health policy and practice across both federal and state jurisdictions.
Lack of information and support services for persons with narcolepsy and their family/carers	Creation of information packs specific for persons with narcolepsy, family/carers, workplaces, and schools
	Clearer guidelines around functional impairment in narcolepsy and eligibility requirements for supports and services
Assessment of narcolepsy is insufficient and does not reflect what end-users consider 'well-managed' narcolepsy	Develop a framework that defines the symptoms of narcolepsy and the language used to describe these terms
	Creation of PROMs that capture domains considered important by persons living with narcolepsy

9.4.1 – Addressing misalignment in care

We identified a lack of differentiation between narcolepsy subtypes and the limitations of diagnostic tools used for narcolepsy as contributing to misalignment in care. Below are several recommendations for change that may address some of this misalignment.

- **Revisiting the diagnostic tools and criteria used for narcolepsy type 1 and 2**
    - There is a need for better diagnostic criteria, national guidance, and the development of decision tools to aid the diagnosis of narcolepsy. One approach that could be adopted is the European approach of increased use of actigraphy when diagnosing disorders of central hypersomnolence to rule out symptoms caused by chronic sleep deprivation or shiftwork [46].

        i. Narcolepsy type 1 can be objectively determined by measuring hypocretin levels in cerebral spinal fluid [7]. The burden of disease associated with this subtype is described across this body of work (chapters 3, 7 and 8) and well documented in the literature. It could warrant the increased use of this as a definitive test, reducing the substantial delay to diagnosis and misdiagnosis [32]. CSF testing is an invasive process. However, improving access to this test should be considered, perhaps on a circumstantial basis where typical cataplexy may not be present (e.g. triggered by emotion, always present – see Chapter 8). There is also increasing interest in the use of a multi-day (24-72 hour) ambulatory polysomnography test for the diagnosis of narcolepsy, as suggested by Emmanuel Mignot [6]. The diagnostic test draws on previous evidence that persons with narcolepsy do not sleep more than any regular person over a 24-hour period. Instead, sleep is fractured over that time[28]. It also aligns with our findings in chapter 8, where nocturnal awakenings and falling asleep mid-task were described by persons experiencing cataplexy

triggered by acute emotion. The main barrier to implementation appears to be polysomnography infrastructure, with the current set-up complex, bulky and impractical for use over several days. The development of wearable polysomnography technology is set to change this, and consideration should be given to incentivising implementation of these technologies in the future.

ii. There is a likely need to implement a two-week actigraphy study prior to a PSG or MSLT study to rule out EDS from sleep deprivation and shift work[38]. European healthcare professionals already utilise actigraphy when making a narcolepsy diagnosis and may provide a framework for a similar approach here in Australia (see 1.2.3.2).

iii. More research is needed into narcolepsy type 2 to understand better the disorder, pathophysiology, classification, and reliable diagnostic protocols for possible differentiation between type 2 and idiopathic hypersomnia.

iv. At the 7th International Symposium on Narcolepsy, clinician-scientists suggested separating narcolepsy type 1 and idiopathic hypersomnia with long sleep duration as identifiable subtypes[141]. In addition, narcolepsy type 2 and idiopathic hypersomnia without long sleep duration would combine into a spectrum disorder[141]. The approach is similar to the that of European sleep experts, who have suggested separating central disorders of hypersomnolence into three classifications: Narcolepsy, Idiopathic Hypersomnia and Idiopathic Excessive Sleepiness[38,46]. Adopting such an approach may help classify specific presentations of hypersomnolence better, allowing for targeted and tailored care. However, consideration

should be given to the potential impact associated with changing a long-term diagnosis. These individuals likely have built an illness identity and community around the diagnosis of narcolepsy type 2[142]. Such a change may contribute to the misalignment and distrust between these persons and the healthcare system in general.

- **Review of policy approach to narcolepsy subtypes**
    - Our results suggest that healthcare policy and practice need to better delineate between narcolepsy types 1 and 2. Each subtype was associated with differing levels of functional impairment, symptoms, healthcare needs, and priorities, and differentiation between the two subtypes is likely needed to meet the needs of persons with narcolepsy. A first step would be changing government and educational materials (Better Health Channel run by the government of Victoria, disability support pension guidebook, Sleep Health Foundation etc). Separation of subtypes should apply to the education and training of GPs and specialists, GP decision tools, information kits, and future public awareness campaigns.
    - A review of the current PBS criteria for accessing narcolepsy treatments is needed. Evidence suggests that 30% of the population would meet the current access criteria under narcolepsy type 2[134]. Any review should be evidenced-based and transparent, reflecting currently accepted diagnostic criteria for narcolepsy and including idiopathic hypersomnia as a category (considering the limitations of the MSLT [6,37]). Change would likely improve healthcare resource utilisation and clarify future healthcare policy decisions around current expenditure per subtype, new medication access and approval.

- **Creation of a systematic data collection system**
    - One of the main contributors to misalignment in narcolepsy care is likely related to the lack of systematic data collection systems. A narcolepsy registry would allow for collecting data related to narcolepsy, collecting information persons with narcolepsy and their families and carers perceive as important. Such systems should be longitudinal, providing multiple opportunities for persons with narcolepsy and their family and carers to interact and provide feedback over time (i.e. answering follow-up questions when medications change). Another essential feature of any registry in this space should seek to collect patient-reported experience measures (commonly referred to as PREMs). These PREMs capture the perceived quality of care and knowledge of healthcare professionals specific to narcolepsy, possibly addressing a frequently raised concern for both persons with narcolepsy and their families/carers. This could then be used to improve the education and training of healthcare professionals.

- **National guidelines for narcolepsy**
    - Another possible solution is the creation of national guidelines for the assessment and diagnosis of narcolepsy, similar in design to those that exist for autism spectrum disorder. A position statement on guidelines for sleep studies in adults has been published in 2017 by the Australasian Sleep Association [39]. However the publication only briefly mentions narcolepsy and does not acknowledge differences between subtypes and uses unspecific terms like 'typical cataplexy'.

      The purpose of a guideline is to make policy, practice, and diagnosis more consistent across Australia. Developing one that is specific to non-respiratory sleep disorders may be a useful step towards addressing the apparent inequity seen in narcolepsy care, along the lines of age and between states and hospital catchments. These

guidelines are usually created for more prevalent disorders. However, the substantial burden of disease associated with narcolepsy observed here and across the literature (chapters 3, 7 and 8), the lack of public awareness, limited medical knowledge, research and expertise and associated societal stigma all lend weight to the creation of such materials[33,48,49,51,59,61,62].

- **Making the field of sleep medicine multi-disciplinary and diversify specialities trained in sleep**
    - There is a specific need for sleep to be more multi-disciplinary. Persons with non-respiratory sleep disorders appear underserved by the close link between sleep and respiratory medicine. Management of sleep disorders often requires expertise across disciplines, thus there needs to be greater diversification in specialities that are trained in sleep. This including far more prevalent conditions like insomnia where the gold standard treatment is CBT-I [143].

      One possible solution is to implement the recommendation made in the recent parliamentary inquiry, which would see the separation of sleep and respiratory medicine into individual specialities under the Australian Health Practitioners Regulation Agency framework [118]. As per the parliament response to the inquiry, a first step would likely be to hold further discussions with the Medical Board of Australia and the Australian Medical Council, as these bodies assess applications for recognition of new medical specialties [144].

9.4.2 - Pathways for meaningful contribution to narcolepsy policy and planning

Co-design and shared decision-making are increasingly mandated across healthcare, yet often, these terms are not well defined and seldom evaluated [145]. Many of the concerns identified in this body of work appear to relate to a lack of person-centred care principles implemented at a macro policy and practice level [112,113]. It also extends to an apparent lack of consumer involvement and active influence over healthcare legislation and regulation of medical care [112].

A suggested proposal to improve inclusion could be the inclusion of government departments, policymakers and researcher institutions falling under the purview of existing accreditation bodies (i.e. ACSQHC) and standards (i.e. NSQHS). These bodies govern person-centred care in Australia and guide how best to partner with consumers, for example, how to include consumers at all levels and stages of research, governance, policy, and planning. The NSQHS has previously published frameworks and standards that provide clarity for governments, hospitals, healthcare organisations and consumer involvement in clinical trials. Perhaps something more formal like this is needed to drive change, considering persons with narcolepsy appear to have similar complaints about their care as they did 20 years ago.

9.4.3 – Information packs related to narcolepsy

The creation of information packs is an important part of addressing misalignment by empowering persons with narcolepsy and their family and carers to be informed decision-makers. These packs would ideally be shareable and written in layperson speak, different languages and cover a range of topics, including:

- Basic physiology of narcolepsy
- Impacts and how they can affect the daily life of someone with narcolepsy.
- Illness trajectory
- Symptom clarification

- Links to other health care professionals (specifically psychologists and psychiatrists knowledgeable or prior experience treating narcolepsy)
- Supports that are available for both persons with narcolepsy and their family and carers (i.e. support groups like Narcolepsy Australia)
- Workplace accommodations and rights under current legislation,

Information must be appropriate for people with narcolepsy and their family and carers and shareable with others within personal networks (e.g. family members, siblings). Any information pack should distinguish and inform between the subtypes of narcolepsy.

There is also a need for wider recognition of the functional impairment associated with narcolepsy, particularly narcolepsy type 1. Clearer support and welfare options should be made available under existing social/welfare services (i.e. NDIS, disability support pension), including information on eligibility and possible services that could improve participation in broader society.

Lastly, there is a need to create information packs that specifically cater to employers and education providers and include information about the best ways to support persons with narcolepsy.

9.4.4 – Measuring well-managed narcolepsy using validated patient-reported outcome measures (PROMs)

- **Framework defining symptoms and the language used to describe them**

  There is a need to develop a framework that defines and evaluates symptoms of narcolepsy from the perspective of those living with the disorder. An ideal framework should include clear definitions of symptoms and appropriate terminology for communicating changes. Development should be collaborative between persons with narcolepsy, their family, carers, and healthcare professionals. If completed, it would provide a common language to communicate with, which may assist healthcare professionals in meeting the expectations of their patients and addressing misalignment in care.

- **Development of patient-reported outcome measures**
    - There is a need for validated PROMs designed to capture the lived experience of narcolepsy. Ideally, this would involve PROMs that a) assess functional impairment and b) assess symptoms and severity. The development of a functional assessment tool for narcolepsy could be modelled on the one used to assess impairment in persons with autism. The findings from Chapter 8 provide a valuable guide for developing such a PROM by identifying and conceptualising important symptom domains.

    - There is also the possibility of creating a subjective diagnostic tool based on differences in symptoms experienced (figure 3). If developed and validated, it has the potential to reduce wasted healthcare resources on unreliable diagnostic tools previously mentioned (i.e. the MSLT – see 9.1.2)

    - There is also the ongoing unmet need for developing a PROM that caters to a narcolepsy type 2 cohort. Ideally, this would capture all aspects of symptoms experienced by this cohort [37]. However, this may be difficult due to the heterogeneity of this cohort and the overlap with idiopathic hypersomnia.

    - Lastly, there is a need to validate existing patient-reported outcome measures currently used for narcolepsy. As shown in Chapter 5, psychometric analysis of tools frequently used is minimal and further testing is required if we are to have confidence that we are assessing both disease severity and treatment efficacy in narcolepsy.

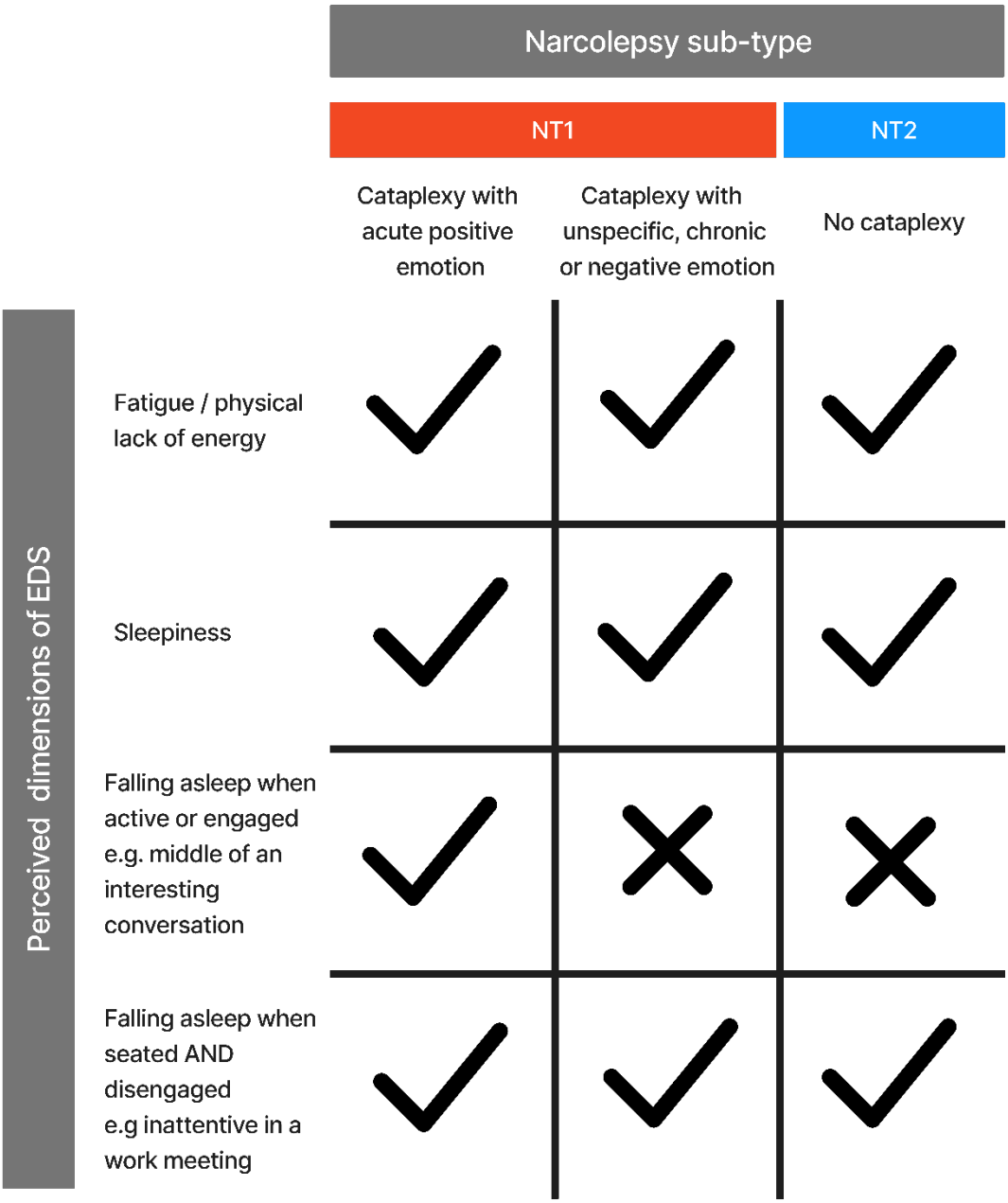

Figure 3: Experiences of dimensions of excessive daytime sleepiness (EDS) as described by our persons with narcolepsy study cohort, grouped by narcolepsy subtype.

A tick represents participants from sub-type experienced the dimension of EDS. A cross represents participants did not experience the dimension of EDS. NT1 – Narcolepsy type 1, NT2 – Narcolepsy type 2.

9.5 Reflection on being a lived experience researcher

As someone diagnosed with narcolepsy type 1, researching my disorder has been one of the most challenging things I have undertaken. Separating my feelings and experiences from my research is something I have had to be mindful of throughout this project, with varying degrees of success.

From the beginning, I was mindful of the potential for confirmation bias, personal bias, and emotional bias to impact my findings. The potential for bias is one of the reasons I have tried to include as many stakeholders as possible and researchers from diverse backgrounds on individual projects who felt comfortable challenging my preconceived ideas. It is also why I felt that having a much larger, diverse team of supervisors to guide and aid in reflexivity was essential. Perhaps the key to my success is my fantastic lead supervisor, who was not afraid to speak his mind, pulling me up more times than I could count to check my biases, challenge my arguments and preconceptions, and avoid overgeneralising issues that are likely common to all diseases and disorders.

From a researcher's perspective, I have been surprised by benefits associated with being a lived experience researcher. Any researcher can start a project with the best intention, and there are times when poor recruitment can derail a study. The relationships I have built as part of Narcolepsy Australia and with late narcolepsy advocate Mellissa Jose were instrumental to my success. The support from the community for my research was phenomenal, whether it be a willingness to participate in a specific study or tuning in to various presentations has been greatly appreciated and allowed me to gather a diversity of perspectives. I would say that I have taken comfort that a primary goal of this project was to improve the lives of persons living with narcolepsy and their family and carers because I have been there. I felt the same emotions and frustrations of not being heard, concerns not being taken seriously, and not being sure where to turn to for help, and I was left asking why the management of narcolepsy is so poor in Australia. Having the opportunity to explore these needs and the possible causes of an often-ignored population has been a privilege.

I also learned much about myself and my relationship with narcolepsy throughout this project. One of the biggest revelations was that most persons with narcolepsy experience anticipated and internalised stigma and that the experience of someone with narcolepsy is similar to a person with a concealable stigmatised identity. I had unknowingly found answers to questions I had been searching for, for some time. I still feel shame and inadequate that I feel so fatigued, sleepy and need to nap several times daily.

At times it has also been challenging to have healthcare professionals and others see me as more than just a patient or advocate and instead as a researcher in my own right. Complicating matters was that I completed my PhD in the same city I was raised, diagnosed and treated for narcolepsy. This meant I have often had to interact or meet specialists who have treated me in the past, a constant source of anxiety as I am often unsure of where I stand. If this happens to me, someone who is health literate and empowered, it likely happens to others who do not have these privileges. Overall, it has made me more aware of the power imbalance between patients and healthcare professionals and is something that I feel is often overlooked in stakeholder meetings, likely hampering meaningful engagement from the less empowered party.

9.6 Strengths and Limitations of this thesis

One of the strengths of this thesis was that the methodology used across this thesis represents a unique form of person-centred engagement and knowledge transfer. The Parliamentary Inquiry process provided a rare, 'boots on the ground' account of the lived experience of those living with narcolepsy, one that was unfiltered and unparsed by others (e.g. policy-makers, research teams, ethics boards, patient advocacy groups). Qualitative analysis of the submissions allowed for identifying broad areas of concern that warranted further investigation that informed the interview guide for semi-structured interviews (chapters 7-8), where concerns were explored in greater context and detail.

This body of work had several limitations, which have been addressed explicitly within each paper. Outside of these studies, this thesis's main limitation is that it does not explore the perspectives of other important, diverse stakeholders, including healthcare professionals or advocacy groups. I had originally planned to explore more diverse perspectives of the lived experience of narcolepsy, specifically that of sleep and respiratory specialists. I received ethics approval and had interviewed 11 physicians. However, unfortunately I was unable to sufficiently recruit enough physicians to reach saturation for qualitative analysis. A contributing factor to low participation rates was likely the 2019 pandemic. However, the years following the pandemic did not see a rebound in recruitment or interest in the project despite repeated attempts at recruitment.

Another limitation was that only self-identified persons with narcolepsy and their carers participated in our studies, only female carers registered to participate in our family/carer interviews, and few persons from culturally and linguistically diverse backgrounds. It means that it is likely that not all concerns around the management of narcolepsy were identified, likely warranting further investigation. I have previously written about other limitations specific to myself being a lived experience researcher and the potential for confirmational bias, personal bias, emotional bias, and selection bias, all of which I have tried to be mindful of throughout this project. To mitigate this, I

have tried to include a variety of diverse viewpoints and stakeholders in the analysis across all studies. Lastly, there are also limitations around the generalizability of the results found in an Australian population and how they apply to others.

9.7 Future research

Future research should consider exploring anticipated and internalised stigma's impact on persons living with narcolepsy and evaluating whether this translates into real discrimination in different domains. Considering the substantial psychological burden of narcolepsy, addressing it at a societal level and within an individual's network may help reduce the impact. Research exploring the intersection of stigma and productivity may also apply to other sleep disorders like insomnia and sleep apnea.

Future work should also consider exploring the needs, concerns, and barriers to care for specific subgroups identified in this work. These subgroups include pregnant women or women considering pregnancy and the impact of prescribed medication, persons from cultural and linguistic backgrounds and the perspectives of male parents caring for a child with narcolepsy. There is also a need to explore the long-term psychological impacts of cataplexy and repressing or avoiding emotional stimuli. Considering the culturally diverse population of Australia, it is also essential to explore the perspective of living with and caring for someone with narcolepsy amongst people from culturally diverse backgrounds that may not prescribe to Western society's disregard for sleep. This includes exploring the impact of narcolepsy on first nations people.

Several key life areas (e.g. driving) are insufficiently researched and warrant further investigation. Not much is known if tools like the maintenance of wakefulness test translate to a real-world scenario, especially as the protocol does not reflect daily routine and stimuli (i.e. playing music, having a nap before driving). Exploring narcolepsy and driving is essential for a large country like Australia, where transport infrastructure may be lacking in more rural areas. It should also explore the legal requirements around driving with a diagnosis of narcolepsy, whether mandatory reporting

to licencing bodies applies, and who is responsible for informing the person with narcolepsy of their legal responsibilities.

Further work is also around how the healthcare system will navigate a potential change to the diagnostic criteria of narcolepsy. The likelihood of this occurring appears to be gathering support, and both the healthcare system and other support services (i.e. PBS) should focus on mitigating the potential ramifications. Ramifications include PBS treatment access, diagnostic criteria, and, importantly, explaining these changes to those affected.

Future research should explore the prevalence of narcolepsy type 1 and type 2 in Australia, to better prosecute the case for the burden of disease, the scale of the impact, and whether appropriate healthcare resources are employed. Considering narcolepsy has a genetic component to the disorder, it would be interesting to explore the perspective of living with narcolepsy from someone who is Aboriginal and Torres Strait Islander, including the prevalence of the disease and management of cataplexy. With current diagnostic criteria requiring an overnight or daytime sleep study, it is doubtful that persons living in remote communities could access such infrastructure often found in larger cities.

9.7.1 – Creating a narcolepsy registry in Australia

It is clear from this body of work that those living with narcolepsy are not satisfied with the care they are receiving through the healthcare system. With no pathways to contribute to healthcare policy and planning, an alternative method for enacting change could be the systematic collection of data to inform decision-makers of the symptom experience, daily impact, and healthcare quality [114]. Ideally, a narcolepsy registry would be longitudinal and capture data that reflect changing circumstances (e.g. changing medications, fluctuating symptoms). This, along with the use of patient-reported experience measures and patient-reported experience measures, could be used to inform both research and clinical practice.

Creating a registry here in Australia would need to reflect several unique aspects of the Australian experience, including differences in medication access, the combined fields of sleep and respiratory medicine, access to social/welfare services (e.g. NDIS), and our unique multicultural and indigenous population (important considering NT1 is an autoimmune, genetic disorder [7]). Any registry must involve meaningful collaboration with relevant stakeholders, including clinicians, parents/carers, and patient advocacy groups like Narcolepsy Australia. This body of work lays the foundation for developing such a registry, systematically exploring the needs, concerns, and barriers to care of PwN and their family/carers living in Australia.

This includes capturing the following information:

- Experience of symptoms
- Functional impact (ability to complete activities of daily living, ability to self-care, employment status)
- Quality of care, including experience in HCP consultations, knowledge of narcolepsy
- Medication access including both PBS, non-PBS, and access through hospital compassionate access schemes
- Driving – licensing restrictions,
- Experience with stigma
- Workplace accommodations
- NDIS and welfare support/access
- Comorbidities: Listing of comorbidities
- Objective measures: MSLT scores, actigraphy data, CSF fluid analysis

9.8 Concluding remarks

This thesis explored the needs, concerns, and barriers to care for persons living with narcolepsy and their family and carers. It also explored how person-centric is the healthcare system, using narcolepsy as an example.

These findings suggest there is dissatisfaction with the quality of healthcare and management of narcolepsy in Australia. There is a clear need for the proactive inclusion of persons with narcolepsy and their families and carers in healthcare policy and practice at all levels.

The findings of this thesis also imply the healthcare system is not person-centric when navigated by persons with narcolepsy. Little progress has been made toward addressing the needs and concerns of persons with narcolepsy, with concerns identified in this thesis previously reported as early as 2001. It is doubtful these experiences are unique to persons with narcolepsy. If similar dissatisfaction and priority misalignment towards the healthcare system exists amongst persons with insomnia, idiopathic hypersomnia, or other sleep disorders, serious thought should be given towards structural/policy changes that can make the field of sleep in Australia person centric.

Moving forward, an excellent first step towards addressing these issues would be to have a 'round table discussion' with key stakeholders to discuss what can be practically done to address these concerns both immediately and into the future.

To summarise, the most significant findings and contributions of this thesis are:

- There is substantial dissatisfaction with the healthcare system likely due to misalignment in care priorities between persons with narcolepsy, healthcare professionals, and the healthcare system
- Effective treatment appears inaccessible for most persons living with narcolepsy
- Consumers have limited avenues to voice healthcare concerns or meaningfully contribute to healthcare policy development.
- There is a lack of easily accessible information about narcolepsy, including its impact and the accommodations and services, in a format accessible to the public, workplaces, and schools
- There is a lack of quality, validated outcome measures used in narcolepsy
- Persons with narcolepsy experience substantial anticipated and self-stigma that likely contributes to the high prevalence of depression and anxiety.

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